

Evidence-Based Imaging

Improving the Quality of Imaging in Patient Care

Series Editors: L. Santiago Medina · Kimberly E. Applegate · C. Craig Blackmore

Aine Kelly

Paul Cronin

Stefan Puig

Kimberly E. Applegate *Editors*

Evidence-Based Emergency Imaging

Optimizing Diagnostic Imaging of
Patients in the Emergency Care Setting

 Springer

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Series Editors

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Aims of the Series

Evidence-Based Imaging: Improving the Quality of Imaging in Patient Care series presents the radiologist and clinician with a user-friendly guide to the evidence-based science and the merit behind the diagnostic imaging performed in medicine. This ideal reference gathers contributions by internationally renowned specialists in the field. The series provides a systematic framework for understanding the best imaging choices for patient care. Chapters highlight key points that support the clinical applications, allowing fast access to pertinent information. Topics include patient selection, imaging, strategies, test performance, cost-effectiveness, and applicability.

By offering a clear understanding of the science behind the evidence, the book fills a void for radiologists, clinicians, physician assistants, nurse practitioners, residents, fellows, students and others with an interest in medical imaging and a desire to implement an evidence-based approach.

More information about this series at <http://www.springer.com/series/8865>

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To our patients, who are our best teachers

To our students, who are the healthcare providers of tomorrow

To the researchers, who made this book possible

To our families, friends, and mentors

AMK: To my loving family past, present, and future, Paddy, Anita, Paul, Alison, Anna, and Eva

PC: To my parents, Brendan and Claire. To my loving and supportive wife, Aine, who makes it all possible and our two children who are truly our pride and joy. To my sister, Alison

SP: To my wife, Rosi; my sons, Julian, Simon, and Sebastian; and my grandson, Liam

Foreword

The practice of emergency radiology encompasses the diagnostic imaging management of acutely ill and injured patients in the emergency setting. It is one of the newest subspecialties of diagnostic radiology and one of the fastest growing. Its growth parallels the escalation in emergency medical practice as emergency departments experience an ever-increasing patient volume each year. Many institutions have experienced an annual growth rate of emergency department volume greater than 5%. The sophistication of emergency imaging has also been increasing as trauma surgeons and emergency physicians expect and require the availability of all imaging modalities including radiography, ultrasound, computed tomography, and magnetic resonance imaging at all hours, every day of the week. Emergency physicians are also requesting rapid turnaround times with final image interpretations available days, evenings, and nights. Recent investigations have shown that the timely performance and interpretation of emergency imaging examinations cannot only increase emergency department throughput, decompressing busy centers, but also contribute to improved patient outcomes and decreased healthcare costs.

Emergency radiology as a radiology subspecialty has been experiencing increasing recognition for its advances in patient care. Both the Radiological Society of North America and the American Roentgen Ray Society include educational and scientific programs devoted to emergency imaging at their annual meetings. The American Society of Emergency Radiology (ASER) was established 28 years ago and currently has over 1000 members, a vibrant annual meeting with postgraduate course, and an official journal, *Emergency Radiology*, established in 1994. The journal has showcased original research relevant to emergency and trauma imaging. Emergency radiology fellowships have been established at many academic radiology departments, and an increasing number of radiology trainees are entering the practice of emergency radiology.

It would appear that the time is most appropriate for a compilation of scholarly communications on evidence-based emergency radiology available in textbook format to assist those in emergency practice. The editors have skillfully accomplished this goal. The text is organized into two main sections beginning with an introductory segment on the principles of evidence-based imaging, appraising the literature critically, emergency imaging information systems, and consequences of inappropriate imaging. The second segment is comprised of 36 chapters (in 5 subsections) covering common emergency conditions requiring high-quality, state-of-the-art imaging man-

agement. This unique text is not only intended to educate emergency physicians and emergency radiologists but all healthcare workers providing care in the emergency setting.

I have no doubt that this task will be successfully accomplished with *evidence-based emergency radiology*.

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Robert A. Novelline

Foreword

Emergency physicians often depend on sophisticated imaging for many of the patients evaluated in emergency departments (EDs). In fact, nearly 50% of the 130,000 million annual ED visits in the USA are accompanied by radiological imaging of some type, making the field of emergency radiology one that impacts a large percentage of the US population. While emergency imaging has become more sophisticated over the past decades, allowing clinicians access to immediate diagnostic tools, this has also come with costs, both financial and otherwise. As with all tests, sensitivity and specificity are not perfect, leading to under- and overdiagnosis. Although the risks to patients of underdiagnosis are more apparent to clinicians and patients alike, overdiagnosis has its own insidious and potentially harmful consequences. Incidental findings on radiological images can lead to unnecessary and potentially harmful testing and treatment, as well as undue patient anxiety. Concerns regarding radiation exposure from radiography, particularly computer tomography (CT), have also come to the forefront in the past decade, with many studies raising concerns over radiation-induced malignancies. Since 1980, the use of CT has increased approximately eightfold. This is of particular concern in children, given their greater sensitivity to radiation than adults, their longer life expectancies during which malignancies can be expressed, and the higher dose of radiation they frequently receive unless the CT scan radiation doses are appropriately adjusted to meet their body sizes.

Fortunately, CT use has decreased in recent years for a number of reasons, including the increasing use of ultrasound and other imaging modalities, quality improvement initiatives (which include monitoring and feedback of physician radiology use), and shared decision-making between clinicians and their patients regarding the tradeoffs of performing or avoiding specific imaging. Finally, the past decade has seen a sharp increase in the use of clinical decision rules and computer-based clinical decision support tools for the use of emergency imaging. This has led to more rational, evidence-based, and cost-effective use of diagnostic imaging. In addition, the Choosing Wisely Campaign of the ABIM (American Board of Internal Medicine) has been championing evidence-based and cost-effective use of diagnostic testing, including the use of imaging in the ED.

One specific example of research and efforts dedicated toward evidence-based imaging comes from the Pediatric Emergency Care Applied Research Network (PECARN), which has made emergency imaging decision rules one of its foci in the last decade given the previous lack of evidence around imag-

ing of injured children. Studies from several countries examining the implementation of the PECARN cranial CT decision rules for children with minor head trauma have demonstrated safe decreased use of CT in these children.

In 2015, the Society for Academic Emergency Medicine hosted the Academic Emergency Medicine consensus conference entitled “Diagnostic Imaging in the Emergency Department: A Research Agenda to Optimize Utilization.” Leaders in emergency medicine, radiology, and health services research and other experts came together to discuss and debate the issues described previously and to develop a consensus research agenda. After much preparation and discussion, six content areas emerged as those of greatest importance and in need of future study. These included the development and validation of clinical decision rules for emergency diagnostic imaging; the use of administrative data for emergency imaging research; patient-centered outcomes research; training, education, and competency; knowledge translation and barriers to imaging optimization; and comparative effectiveness research in alternatives to traditional CT use. Many of the issues considered at that conference are intertwined with the contents of this novel and timely textbook.

Evidence-Based Emergency Imaging will undoubtedly serve as an outstanding resource for all clinicians who care for acutely ill and injured adults and children. Within the pages of this text, the reader will find the principles of evidence-based imaging and the specific imaging needed for a variety of emergent conditions. This melding of the principles of radiology, clinical epidemiology, and health services research will help clinicians identify who to image in the emergency setting, what piece of technology to use, and what issues to consider and anticipate. I greatly welcome and applaud the arrival of this new textbook.

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Preface

Demand for emergency healthcare is rising consistently across the developed world, with the number of presentations to emergency departments (EDs) increasing by 3–6% per year over the last decade. The role of EDs within the US healthcare system is also changing with more than half of patients admitted to the hospital in the USA now starting their hospital stay in the ED. The ED is a location where subspecialty consultation and advanced diagnostic imaging technology are available at all hours. In the USA, EDs are unique sources for healthcare because services are provided to all persons regardless of insurance coverage or ability to pay. In addition, the proportion of elderly people in developed world populations is growing. This age shift has important implications for EDs, with a resultant increase in medical complexity of patients attending the emergency room.

Medical imaging has grown exponentially in the last three decades with the development of many promising and often noninvasive diagnostic studies. Several studies from the developed world have shown a steady increase in the use of imaging especially cross-sectional imaging such as computed tomography (CT) in the ED with the need for rapid and accurate diagnosis. These studies have also shown a trend toward less invasive diagnostic testing. Over the last decade, there have been profound changes in the diagnostic testing and work-up of patients presenting to their physician/healthcare provider with emergent symptoms or to the ED. The most profound change has been the increased availability, speed, and accuracy of imaging. This is in part due to technical improvements such as the development of multi-detector CT. This reflects a decade or more of increased utilization of imaging especially advanced imaging such as CT, magnetic resonance imaging (MRI), and positron emission tomography (PET) imaging. Although in the last few years high-end imaging use has plateaued in general, this is not the case in the ED. The dramatic increase in advanced imaging modalities such as MRI and PET, previously not commonly employed in the ED setting, continues. This increase in imaging is understandable since ED patients are more acutely ill, and there is constant pressure to make an accurate diagnosis as quickly as possible to facilitate prompt disposition or treatment and to ensure fast throughput and efficiency in ED services. There is also strong evidence for the beneficial use of imaging in the emergency setting which correlates with improved patient outcomes.

Therefore, the purpose of this book is to educate radiologists, physicians, and all healthcare providers who utilize diagnostic imaging in the ED or other

acute care settings regarding the best and most up-to-date evidence-based imaging. This book is also relevant to internal medicine (adult and pediatric) and family medicine physicians and healthcare providers who care for patients with emergent symptoms. The scope includes practicing radiologists, radiologists in training, clinicians in practice or in training, medical students, and allied personnel such as physician assistants and nurses who may practice in the acute care setting.

The book is organized into two sections, the first being an introductory section with chapters on the principles of evidence-based imaging, critical appraisal of the literature, information systems in emergency imaging, and consequences of inappropriate emergency imaging in adults and children. The second section, divided into five parts, includes chapters written by authors who practice in the fields of emergency care imaging and covers all aspects, including neuroimaging, head and neck imaging, musculoskeletal imaging, chest and cardiac imaging, abdominal and pelvic imaging, pediatric imaging, and women's imaging. Although other books in the evidence-based series cover the organ systems listed above, this book specifically deals with the emergent and acute presentations. The 40 chapters cover the most prevalent emergent conditions and diseases that affect those in developed countries. Additionally, this book contains the most accurate and up-to-date information with the latest evidence and protocols. Recommendations and society guidelines are also discussed. Emergency imaging in adults is covered with a special focus on emergent imaging in specific patient groups including women of childbearing age, pregnant women, and also adolescent and pediatric populations. Unique and defining features of this book include that it is the first book of its kind to focus on emergency imaging in adults, children, and special populations with chapters by a multidisciplinary team of experts, all contained in one volume. It also represents the most up-to-date evidence-based approach to acquiring the most appropriate and comparative effective imaging in patients who present to the emergency department or in the acute setting.

To make the book user-friendly and to enable fast access to pertinent information, we have organized all of the chapters in the same format. The chapters are framed around important emergent clinical questions relevant to the physician's daily practice. A short table of contents at the beginning of each chapter helps three different tiers of users: (1) the busy physician searching for quick guidance, (2) the physician seeking deeper understanding, and (3) the medical-imaging researcher requiring a comprehensive resource. The format for each chapter starts with the important clinical issues to be discussed. This is followed with a box of key points in bullet form with the strength of the supporting evidence in parenthesis. After this, there are sections covering definitions, etiology, pathophysiology and risk factors, relevant epidemiology, and costs to society in economic terms, followed by a section discussing the goals of imaging and a section detailing the methodology used to obtain the most up-to-date literature.

Next, the issue being discussed is framed with a summary of evidence including existing literature and guidelines if any. This is further elaborated by the supporting evidence with paragraphs discussing the diagnostic modali-

ties available, the imaging findings/criteria for diagnosis, the impact of imaging on treatment decision-making, and the treatment options if applicable. Given that all research and evidences are not created equal, we use a four-level classification detailing the strength of the evidence based on the Oxford Centre for Evidence-Based Medicine Criteria: Level I (strong evidence), Level II (moderate evidence), Level III (limited evidence), and Level IV (insufficient evidence). The strength of the evidence is presented in parenthesis throughout the chapters so the reader gets immediate feedback on the weight of the evidence behind each topic. If a cost-effectiveness analysis has been performed, these data are also presented. In addition, some chapters contain special cases (e.g., pregnant patients or children), and important issues which require a separate or additional discussion (such as radiation concerns) are also presented.

Each chapter text includes tables and figures, imaging case studies, and protocols. The tables summarize diagnostic test accuracy and summary statistics such as the sensitivity and specificity of different imaging studies. The figures show decision trees summarizing the evidence, e.g., risk factors, diagnostic performance, and algorithms/flowcharts with suggested protocols/guidelines. Imaging case studies are cases that highlight the diagnostic performance of the different imaging studies. Examples include important true-positive, false-positive, true-negative, and false-negative cases and imaging pitfalls if applicable. Suggested imaging protocols are a brief summary of imaging steps supported by the evidence. Future research discusses in bullet points the critical gaps in the evidence. All chapters are extensively referenced with the most up-to-date literature.

Finally, we had the privilege of working with a group of outstanding contributors from major medical centers and universities in North America and Europe. We believe that the authors' expertise, breadth of knowledge, and thoroughness in writing the chapters provide a valuable source of information and can guide decision-making for physicians and patients. In addition to guiding practice, the evidence summarized in the chapters may have policy-making and public health implications. We hope that this book highlights key points and generates discussion, promoting new ideas for future research. We value your suggestions and comments on how to improve this book. Please email them to us and the authors so that we can bring you the best of the evidence over the years.

Ann Arbor, MI, USA

Aine Marie Kelly
Paul Cronin

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Editors' Biographies and List of Contributors

Editors

Aine Kelly is a professor of cardiothoracic radiology at the Michigan Medicine, Ann Arbor, Michigan, USA.

She is board certified in internal medicine by the Royal College of Physicians in Ireland and in diagnostic radiology by the Royal College of Radiologists in the UK and the American Board of Radiology. Dr. Kelly graduated from the School of Medicine, Trinity College Dublin, Ireland. She completed an internship at St. James's Hospital, Dublin, and an internal medicine residency at the Dublin Federated Hospitals Scheme, followed by an endocrinology fellowship at the Meath Hospital, Dublin, Ireland. After this, Dr. Kelly pursued a radiology residency at the Leeds/Bradford/Huddersfield Radiology Training Scheme, before joining the University of Michigan. She completed two fellowships in thoracic imaging and body MRI imaging at the University of Michigan.

Dr. Kelly obtained a master's degree in clinical research design and statistical analysis from the University of Michigan School of Public Health. She also completed a master's degree in higher education from the School of Education at Michigan. Dr. Kelly has been principal investigator on multiple grants, including the General Electric-Association of University Radiologists Radiology Research Academic Fellowship (GERRAF), the Educational Scholar Award from the Radiological Society of North America (RSNA), and the American Roentgen Ray Society (ARRS) Leonard Berlin Scholarship in professionalism and ethics. She has been co-investigator on multiple other grants, including National Institutes of Health (NIH)-funded studies and the National Lung Screening Trial (NLST). Her research focused on evidence-based imaging, noninvasive cardiothoracic imaging, patient preferences, comparative effectiveness, efficiency, value-based insurance design, quality, and safety.

Dr. Kelly served on the executive board for the Association of University Radiologists (AUR) and is currently president elect of the Alliance of Medical Student Educators in Radiology (AMSER), past president of the Alliance of Clinician Educators in Radiology (ACER), past president of the Radiology Alliance for Health Services Research (RAHSR). She is past chairperson of the health services research committee of the RSNA and has served as grant

reviewer for the Radiological Society of North America (RSNA). She has been an international and national invited speaker and author on the topic of evidence-based imaging. Dr. Kelly currently serves as deputy editor for education at *Academic Radiology*. Dr. Kelly has authored or coauthored more than 70 peer-reviewed scientific manuscripts and 5 book chapters.

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Paul Cronin is an associate professor of radiology at the Michigan Medicine. He also serves as the cardiothoracic radiology fellowship director.

Dr. Cronin was born in Dublin, Ireland. After graduating from medical school at Trinity College Dublin, he completed an internal medicine residency and received his membership to the Royal College of Physicians of Ireland (MRCPI). He completed a radiology residency in Leeds, UK, and also received his fellowship to the Royal College of Radiologists (FRCR). Following that, he then went to the University of Michigan and completed two fellowships (in cardiothoracic and magnetic resonance imaging) and has stayed there as faculty. He received a master's degree in clinical research design and statistical analysis from the University of Michigan School of Public Health.

Dr. Cronin teaches medical students, residents, and fellows on a daily basis while maintaining a busy clinical practice. He has received an Excellence in Thoracic Radiology Award and multiple annual commendations for excellence in teaching at the University of Michigan. Dr. Cronin has received multiple honors and awards and has been invited to visiting professor programs in Australia, Europe, and North America. He has been on the "Best Doctors in America" list since 2011. He was awarded the GE-AUR Radiology Research Academic Fellowship (GERRAF). Dr. Cronin's research interests include evidence synthesis and outcomes research of multiple aspects of cardiothoracic radiology. He has been co-investigator on other grants, including the National Lung Screening Trial (NLST) and Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) III Trial. He has authored 142 scientific and educational papers, abstracts, posters, and book chapters; he has given over 190 local, national, and international lectures and is a member or chair of over 20 professional radiology society committees. He serves on the executive board for the Radiology Alliance for Health Services Research and is currently the immediate past president. He also serves on the research committee and as grant reviewer for the Radiological Society of North America (RSNA). Dr. Cronin is a reviewer for a dozen journals. He is the guest editor for the RAHSR edition of *Academic Radiology* and the deputy editor for health services research. He is an associate editor for the evidence-based practice subsection of *Radiology*. He has recently completed a 3-year term as the health services policy and research subcommittee chair of the scientific program committee at the RSNA. Dr. Cronin is also a fellow of the American College of Radiology.

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Stefan Puig is an associate professor of radiology and holds a master's degree in healthcare management.

Dr. Puig was born in Vienna, Austria. After graduating from medical school at the University of Vienna, he completed his internal medicine residency at the University Clinic of Radiology, Vienna, and continued working there as a senior radiologist. In 2003, he became associate professor of radiology, and in 2006 he received a master's degree in healthcare management from the Danube University Krems, Austria.

In 2008, he left the country to gain some working experience abroad and worked in the radiology departments of the American Hospital in Dubai, the University Clinic of Ulm in Germany, and the University Clinic of Bern in Switzerland. In 2015, he moved to Zurich, Switzerland, where he has been working as a radiology consultant at the Hirslanden Clinic while still teaching at the University Clinic of Bern, Switzerland.

In addition to gaining broad practical experience in the various fields of radiology in Austria and abroad, Dr. Puig authored and coauthored a long list of publications for scientific medical journals. His scientific expertise is focused on emergency imaging, pediatric radiology, interventional radiology, and evidence-based radiology. He has been a reviewer for a number of scientific journals and authored systematic reviews and decision support tools for the Austrian Ministry of Health and the General Association of Austrian Social Insurance Institutions.

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Kimberly E. Applegate is a tenured professor of radiology and pediatrics, division chief of pediatric radiology at the University of Kentucky in Lexington, and radiology liaison for quality at the Kentucky Children's Hospital. Dr. Applegate is a leader in radiology—she currently serves on the American College of Radiology Board of Chancellors, after completing a 2-year term as the first woman to be elected ACR Council Speaker. She is also the President of the Association for University Radiologists (AUR) Research and Education Foundation and a member of the National Quality Forum Patient Safety Committee and both the National and the International Councils for Radiation Protection.

Dr. Applegate's policy and research work has resulted in an improved understanding of the structure, process, and outcomes of how pediatric imaging is practiced, including the volume of ionizing imaging in children, the variation in radiation dose in pediatric CT, and the standardization of practice for both children and adults. She has worked tirelessly around the world with collaborators in the IAEA, WHO, and IRPA to improve access to best practices. In 2017, Dr. Applegate became a member of the ICRP Main Commission as the chair of the committee 3 (medicine).

Kimberly has received a number of awards that include an ABR Lifetime Achievement Award, Academy of Radiology Research Distinguished Investigator, ARRS Scholar, RSNA Editorial Fellowship, SPR Presidential Recognition, the Indiana ACR Chapter Gold Medal, and AUR Gold Medal. She enjoys mentoring talented colleagues and trainees—who have received over 20 mentee awards to date. At the 2015 RSNA meeting, Kimberly received the American Association for Women in Radiology's Marie Sklodowska Curie Award for her unique roles in leadership and outstanding contributions to the advancement of women in the radiology professions.

Dr. Applegate has published over 200 peer-reviewed papers and book chapters and presented scientific papers and lectures at medical and scientific assemblies around the world. She has an interest in health services research in radiology, coediting the evidence-based imaging textbook series. In 2006, she began work on the Steering Committee for the *Image Gently Campaign* to improve safe and effective imaging care of children worldwide. The campaign has received a number of awards for its advocacy, education, and collaboration to change imaging practice. She is also on the Executive Committees of the World Federation of Paediatric Imaging and *Image Wisely*. She and her husband, Dr. George Parker, have three sons, David, and twins Andrew and Eric.

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Part I

Introduction



Principles of Evidence-Based Imaging for Adults and Children

1

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What Is Evidence-Based Imaging?

The standard medical education in Western medicine has emphasized skills and knowledge learned from experts, particularly those encountered in the course of postgraduate medical education, and through national publications and meetings. This reliance on experts, referred to by Dr. Paul Gerber of Dartmouth Medical School as “eminence-based medicine” [1], is based on the construct that the individual practitioner, particularly a specialist devoting extensive time to a given discipline, can arrive at the best approach to a problem

through his or her experience. The practitioner builds up an experience base over years and digests information from national experts who have a greater base of experience due to their focus in a particular area. The evidence-based imaging (EBI) paradigm, in contradistinction, is based on the precept that a single practitioner cannot through experience alone arrive at the best course of action. Assessment of appropriate medical care should instead be derived through an evidence-based process. The role of the practitioner, then, is not simply to accept information from an expert but rather to assimilate and critically assess the research evidence that exists in the literature to guide a clinical decision [2–4].

Fundamental to the adoption of the principles of EBI is the understanding that medical care is not optimal. The life expectancy at birth in the United States for males and females in 2005 was 75 and 80 years, respectively (Table 1.1). This is slightly lower than the life expectancies in other industrialized nations such as the United Kingdom and Australia (Table 1.1). In fact, the World Health Organization ranks the United States 50th in life expectancy and 72nd in overall health. The United States spent at least 16.2% of the gross domestic product (GDP) in order to achieve this life expectancy. This was significantly more than the United Kingdom and Australia, which spent about half that (Table 1.1). In addition, the US per capita health expenditure

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Table 1.1 Life expectancy and health-care spending in three developed countries

	Life expectancy at birth (year)		Percentage of GDP in health care (year) (%)	Per capita health expenditure (year)
	Male	Female		
United States	76.3 (2011)	81.1 (2011)	16.2 (2012)	\$8745 (2012)
United Kingdom	79.1 (2012)	82.8 (2012)	8.9 (2012)	\$3289 (2012)
Australia	79.9 (2012)	84.3 (2012)	8.7 (2011)	\$3997 (2011)

Data from: Organization for Economic Cooperation and Development: <http://stats.oecd.org/Index.aspx?DataSetCode=HEALTH>
GDP gross domestic product

was \$8745, which was twice the expenditure in the United Kingdom or Australia. In short, the United States spends significantly more money and resources than other industrialized countries to achieve a similar or slightly worse outcome in life expectancy. This implies that a significant amount of resources is wasted in the US health-care system. In 2007, the United States spent \$2.3 trillion in health care or 16% of its GDP. By 2016, the US health percent of the GDP is expected to grow to 20% or \$4.2 trillion [5]. Recent estimates prepared by the Commonwealth Fund Commission (USA) on a High Performance Health System indicate that \$1.5 trillion could be saved over a 10-year period if a combination of options, including evidence-based medicine and universal health insurance, was adopted [6].

Simultaneous with the increase in health-care costs has been an explosion in available medical information. The National Library of Medicine PubMed search engine now lists over 18 million citations. Practitioners cannot maintain familiarity with even a minute subset of this literature without a method of filtering out publications that lack either relevance or appropriate methodological quality. EBI is a promising method of identifying appropriate information to guide practice and to improve the efficiency and effectiveness of imaging.

Evidence-based imaging is defined as medical decision-making based on clinical integration of the best medical imaging research evidence with the physician's expertise and with patient's expectations [2–4]. The best medical imaging research evidence often comes from the basic sciences of medicine. In EBI, however, the basic science knowledge has been translated into patient-centered clinical research, which deter-

mines the accuracy and role of diagnostic and therapeutic imaging in patient care [3]. New research may make current diagnostic tests obsolete and provide evidence that new tests are more accurate, less invasive, safer, and less costly [3]. The physician's expertise entails the ability to use the referring physician's clinical skills and past experience to rapidly identify individuals who will benefit from the diagnostic information of an imaging test [4]. Patient's expectations are important because each individual has values and preferences that should be integrated into the clinical decision-making [3]. When these three components of medicine come together, clinicians, imagers, and patients form a diagnostic team, which will optimize clinical outcomes and quality of life for our patients.

The Evidence-Based Imaging Process

The EBI process involves a series of steps: (a) formulation of the clinical question, (b) identification of the medical literature, (c) assessment of the literature, (d) types of economic analyses in medicine, (e) summary of the evidence, and (f) application of the evidence to derive an appropriate clinical action. This book is designed to bring the EBI process to the clinician and imager in a user-friendly way. This introductory chapter details each of the steps in the EBI process. Chapter 2, "Assessing the Imaging Literature: Understanding Error and Bias," discusses how to critically assess the literature. The rest of the book makes available to practitioners the EBI approach to important emergency imaging issues. Each chapter addresses common emergent disorders

encountered by the emergency care provider and radiologist evaluating the neurologic, cardiothoracic, abdominal, and pelvic and musculoskeletal systems in adults and children. Relevant clinical questions are delineated, and then each chapter discusses the results of the critical analysis of the identified literature. Finally, we provide simple recommendations for the various clinical questions, including the strength of the evidence that supports these recommendations.

Formulating the Clinical Question

The first step in the EBI process is formulation of the clinical question. The entire process of EBI arises from a question that is asked in the context of clinical practice. However, often formulating a question for the EBI approach can be more challenging than one would believe intuitively. To be approachable by the EBI format, a question must be specific to a clinical situation, a patient group, and an outcome or action. For example, it would not be appropriate to simply ask which imaging technique is better—computed tomography (CT) or radiography. The question must be refined to include the particular patient population and the action that the imaging will be used to direct. One can refine the question to include a particular population (which imaging technique is better in pediatric victims of high-energy blunt trauma) and to guide a particular action or decision (to exclude the presence of unstable cervical spine fracture). The full EBI question then becomes, in pediatric victims of high-energy blunt trauma, which imaging modality is preferred, CT or radiography, to exclude the presence of unstable cervical spine fracture? This book addresses questions that commonly arise when employing an EBI approach for conditions encountered by the emergency care provider and radiologist. These questions and issues are detailed at the start of each chapter. One popular method used to teach how to develop a good clinical question is called the “PICO” (*Patient, Intervention, Comparison, Outcome*) format. This method provides structure to formulate the necessary ele-

ments for a good clinical question that includes information about the patient, the problem to be solved, the intervention (such as a diagnostic test) and its comparison intervention (perhaps a newer diagnostic test), and the outcome of interest (e.g., what the patient wants or is concerned about).

Identifying the Medical Literature

The process of EBI requires timely access to the relevant medical literature to answer the question. Fortunately, massive online bibliographical references such as PubMed, Embase, Cochrane, and the Web of Science databases are available. In general, titles, indexing terms, abstracts, and often the complete text of much of the world’s medical literature are available through these online sources. Also, medical librarians are a potential resource to aid identification of the relevant imaging literature. A limitation of today’s literature data sources is that often too much information is available and too many potential resources are identified in a literature search. There are currently over 50 radiology journals, and imaging research is also frequently published in journals from other medical subspecialties. We are often confronted with more literature and information than we can process. The greater challenge is to sift through the literature that is identified to select that which is appropriate.

Assessing the Literature

To incorporate evidence into practice, the clinician must be able to understand the published literature and to critically evaluate the strength of the evidence. In this introductory chapter on the process of EBI, we focus on discussing types of research studies. Chapter 2, “Assessing the Imaging Literature: Understanding Error and Bias,” is a detailed discussion of the issues in determining the validity and reliability of the reported results.

What Are the Types of Clinical Studies?

An initial assessment of the literature begins with determination of the type of clinical study: descriptive, analytical, or experimental [7]. *Descriptive* studies are the most rudimentary, as they only summarize disease processes as seen by imaging or discuss how an imaging modality can be used to create images. Descriptive studies include case reports and case series. Although they may provide important information that leads to further investigation, descriptive studies are not usually the basis for EBI.

Analytic or *observational* studies include cohort, case–control, and cross-sectional studies (Table 1.2). Cohort studies are defined by risk factor status, and case–control studies consist of groups defined by disease status [8]. Both case–control and cohort studies may be used to define the association between an intervention, such as an imaging test, and patient outcome [9]. In a cross-sectional (prevalence) study, the researcher makes all of his measurements on a single occasion. The investigator draws a sample from the population (i.e., headache in 15–45-year-old females) and determines distribution of variables within that sample [7]. The structure of a cross-sectional study is similar to that of a cohort study except that all pertinent measurements (i.e., number of head CT and MRI examinations) are made at once, without a follow-up period. Cross-sectional studies can be used as a major source for health and habits of different populations and countries, providing estimates of such parameters as the prevalence of stroke, brain tumors, and congenital anomalies [7, 10].

In *experimental studies* or *clinical trials*, a specific intervention is performed and the effect

of the intervention is measured by using a control group (Table 1.2). The control group may be tested with a different diagnostic test and treated with a placebo or an alternative mode of therapy [7, 11]. Clinical trials are epidemiologic designs that can provide data of high quality that resemble the controlled experiments done by basic science investigators [8]. For example, clinical trials may be used to assess new diagnostic tests (e.g., CT perfusion imaging for stroke diagnosis and management) or new interventional procedures (e.g., catheter embolization for cerebral aneurysms).

Studies are also traditionally divided into retrospective and prospective (Table 1.2) [7, 11]. These terms refer more to the way the data are gathered than to the specific type of study design. In *retrospective studies*, the events of interest have occurred before study onset. Retrospective studies are usually done to assess rare disorders, for pilot studies, and when prospective investigations are not possible. If the disease process is considered rare, retrospective studies facilitate the collection of enough subjects to have meaningful data. For a pilot project, retrospective studies facilitate the collection of preliminary data that can be used to improve the study design in future prospective studies. The major drawback of a retrospective study is incomplete data acquisition and resultant bias [10]. Case–control studies are usually retrospective because the outcome or disease status needs to have occurred in order to form the comparison groups. For example, in a case–control study, subjects in the case group (patients with hemorrhagic stroke) are compared with subjects in a control group (nonhemorrhagic stroke) to determine factors associated with

Table 1.2 Study design

	Prospective follow-up	Randomization of subjects	Controls
Case report or series	No	No	No
Cross-sectional study	No	No	Yes
Case–control study	No	No	Yes
Cohort study	Yes/no	No	Yes
Randomized controlled trial	Yes	Yes	Yes

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hemorrhage (e.g., hypertension, duration of symptoms, presence of prior neurologic deficit) [10].

In *prospective studies*, the event of interest transpires after study onset. Prospective studies, therefore, are the preferred mode of study design, as they facilitate better control of the design (accounting for potential bias) and the quality of the data acquired [7]. Prospective studies, even large studies, can be performed efficiently and in a timely fashion if done on common diseases at major institutions, as multicenter trials with adequate study populations [12]. The major drawback of a prospective study is the need to make sure that the institution and personnel comply with strict rules concerning consents, protocols, and data acquisition [11]. Persistence and dogged determination are crucial to completing a prospective study. Cohort studies and clinical trials are usually prospective. For example, a cohort study could be performed in children with sickle-cell disease who are poorly compliant with their transfusion therapy in which the risk factor of positive transcranial Doppler studies is correlated with neurocognitive complications, as the patients are followed prospectively over time [10].

The strongest study design is the prospective randomized, blinded clinical trial (Table 1.2) [7]. The randomization process helps to distribute known and unknown confounding factors, and blinding helps to prevent observer bias from affecting the results [7, 8]. However, there are often circumstances in which it is not ethical or practical to randomize and follow patients prospectively. This is particularly true in rare conditions and in studies to determine causes or predictors of a particular condition [9]. Finally, randomized clinical trials are expensive and may require many years to conduct. Not surprisingly, randomized clinical trials are uncommon in radiology. The evidence that supports much of radiology practice is derived from cohort and other observational studies. More randomized clinical trials are necessary in radiology to provide sound data to use for EBI practice [3]. Also, more “outcomes-based studies” are needed in radiology to generate more relevant EBI data.

What Is the Diagnostic Performance of a Test: Sensitivity, Specificity, Positive and Negative Predictive Values, and Receiver Operating Characteristic Curve?

Defining the presence or absence of an outcome (i.e., disease and nondisease) is based on a standard of reference (Table 1.3). While a perfect standard of reference or so-called gold standard can never be obtained, careful attention should be paid to the selection of the standard that should be widely believed to offer the best approximation to the truth [13].

In evaluating diagnostic tests, we rely on the statistical calculations of sensitivity and specificity (see Appendix 1). Sensitivity and specificity of a diagnostic test are based on the two-way (2×2) table (Table 1.3). Sensitivity refers to the proportion of subjects with the disease who have a positive test and is referred to as the true positive rate (Fig. 1.1a and b). Sensitivity, therefore, indicates how well a test identifies the subjects with disease [7, 14].

Specificity is defined as the proportion of subjects without the disease who have a negative index test (Fig. 1.1a and b) and is referred to as the true negative rate. Specificity, therefore, indicates how well a test identifies the subjects with no disease [7, 11]. It is important to note that the sensitivity and specificity are characteristics of the test being evaluated and are therefore usually independent of the prevalence (proportion of individuals in a population who have disease at a specific instant) because the sensitivity only deals with the diseased subjects, whereas the specificity

Table 1.3 Two-way table of diagnostic testing

Test result	Disease (gold standard)	
	Present	Absent
Positive	<i>a</i> (TP)	<i>b</i> (FP)
Negative	<i>c</i> (FN)	<i>d</i> (TN)

Reprinted with the kind permission of Springer Science + Business Media from Medina LS, Blackmore CC. Principles of Evidence-Based Imaging. Evidence-based imaging: optimizing imaging in patient care. New York: Springer Science + Business Media; 2006. *FN* false negative, *FP* false positive, *TN* true negative, *TP* true positive

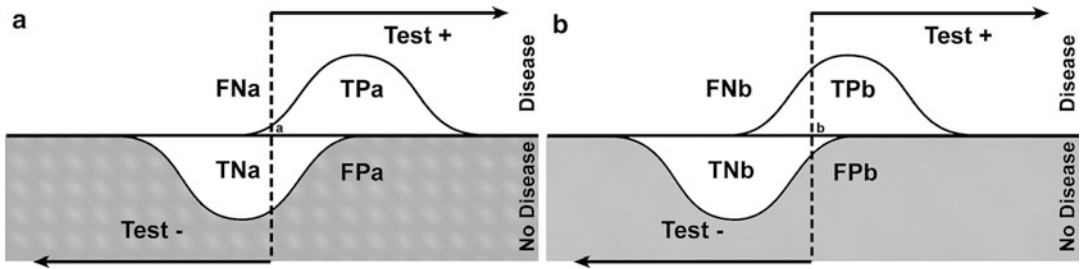


Fig. 1.1 Test with a low (a) and high (b) threshold. The sensitivity and specificity of a test change according to the threshold selected; hence, these diagnostic performance parameters are threshold dependent. Sensitivity with low threshold (TPa/diseased patients) is greater than sensitivity with a higher threshold (TPb/diseased patients). Specificity with a low threshold (TNa/nondiseased

patients) is less than specificity with a high threshold (TNb/nondiseased patients). *FN* false negative, *FP* false positive, *TN* true negative, *TP* true positive. (Reprinted with permission of the American Society of Neuroradiology from Medina L. AJNR Am J Neuroradiol 1999;20:1584–96)

only deals with the nondiseased subjects. However, sensitivity and specificity both depend on a threshold point for considering a test positive and hence may change according to which threshold is selected in the study [11, 14, 15] (Fig. 1.1a). Excellent diagnostic tests have high values (close to 1.0) for both sensitivity and specificity. Given exactly the same diagnostic test, and exactly the same subjects confirmed with the same reference test, the sensitivity with a low threshold is greater than the sensitivity with a high threshold. Conversely, the specificity with a low threshold is less than the specificity with a high threshold (Fig. 1.1b) [14, 15].

The positive predictive value is defined as the probability that a patient will have a disease given that the patient’s test is positive. In other words, when a group of patients test positive, we want to know how frequently they will have the disease. The formula for the positive predictive value (PPV) is provided in the table in Appendix 1. Similarly, the negative predictive value (NPV) refers to the probability that a group of patients that test negative for a disease or condition will actually not have the disease. It is important to understand that while sensitivity and specificity are relatively independent of disease prevalence, the PPV and NPV are not. Examples 1 and 2 (Appendix 2) provide a demonstration of what happens to the PPV and NPV with a change in disease prevalence. When there is concern about large prevalence effects, the likelihood ratio can

Example 1 Low prevalence of carotid artery disease

	Disease (carotid artery disease)	No disease (no carotid artery disease)	Total
Test positive (positive CTA)	20	10	30
Test negative (negative CTA)	4	120	124
Total	24	130	154

Example 2 High prevalence of carotid artery disease

	Disease (carotid artery disease)	No disease (no carotid artery disease)	Total
Test positive (positive CTA)	500	10	510
Test negative (negative CTA)	100	120	220
Total	600	130	730

Results: sensitivity = $500/600 = 0.83$; specificity = $120/130 = 0.92$; prevalence = $600/730 = 0.82$; positive predictive value = 0.98 ; negative predictive value = 0.55
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be used to estimate the posttest probability of disease. This issue is discussed in the next section.

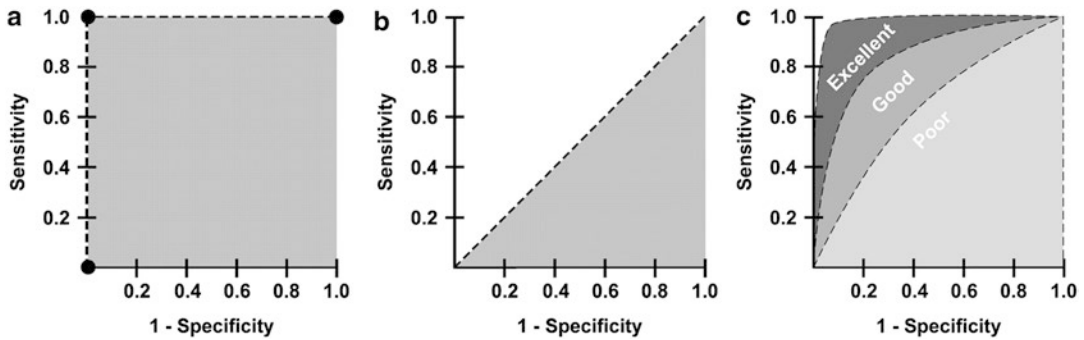


Fig. 1.2 The perfect test (a) has an area under the curve (AUC) of 1. The useless test (b) has an AUC of 0.5. The typical test (c) has an AUC between 0.5 and 1. The greater the AUC (i.e., excellent > good > poor), the better the

diagnostic performance. (Reprinted with permission of the American Society of Neuroradiology from Medina L. AJNR Am J Neuroradiol. 1999;20:1584–96)

The effect of threshold on the ability of a test to discriminate between disease and nondisease can be measured by a receiver operating characteristic (ROC) curve [11, 15]. The ROC curve is used to indicate the trade-offs between sensitivity and specificity for a particular diagnostic test and hence describes the discrimination capacity of that test. An ROC graph shows the relationship between sensitivity (y axis) and $1 - \text{specificity}$ (x axis) plotted for various cutoff points. If the threshold for sensitivity and specificity is varied, an ROC curve can be generated. The diagnostic performance of a test can be estimated by the area under the ROC curve. The steeper the ROC curve, the greater the area and the better the discrimination of the test (Fig. 1.2a–c). A test with perfect discrimination has an area of 1.0, whereas a test with only random discrimination has an area of 0.5 (Fig. 1.2a–c). The area under the ROC curve usually determines the overall diagnostic performance of the test independent of the threshold selected [11, 15]. The ROC curve is threshold independent because it is generated by using varied thresholds of sensitivity and specificity. Therefore, when evaluating a new imaging test, in addition to the sensitivity and specificity, an ROC curve analysis should be done so that the threshold-dependent and threshold-independent diagnostic performance can be fully determined [10].

What Are Cost-Effectiveness and Cost-Utility Studies?

Cost-effectiveness analysis (CEA) is a scientific technique used to assess alternative health-care strategies on both cost and effectiveness [16–18]. It can be used to develop clinical and imaging practice guidelines and to set health policy [19]. However, it is not designed to be the final answer to the decision-making process; rather, it provides a detailed analysis of the cost and outcome variables and how they are affected by competing medical and diagnostic choices.

Health dollars are limited regardless of the country's economic status. Hence, medical decision-makers must weigh the benefits of a diagnostic test (or any intervention) in relation to its cost. Health-care resources should be allocated, so the maximum health-care benefit for the entire population is achieved [10]. Cost-effectiveness analysis is an important tool to address health cost-outcome issues in a cost-conscious society. Countries such as Australia usually require robust CEA before drugs are approved for national use [10]. Health-care decisions are often made from a “societal perspective,” one that looks at a group benefit but which may not result in individual benefit.

Unfortunately, the term *cost-effectiveness* is often misused in the medical literature [20]. To say that a diagnostic test is truly cost-effective, a

comprehensive analysis of the entire short- and long-term outcomes and costs needs to be considered. Cost-effectiveness analysis is a technique used to determine which of the available tests or treatments are worth the additional costs [21].

There are established guidelines for conducting robust CEA. The US Public Health Service formed a panel of experts on cost-effectiveness in health and medicine to create detailed standards for cost-effectiveness analysis. The panel's recommendations were published as a book in 1996 [21].

Types of Economic Analyses in Medicine

There are four well-defined types of economic evaluations in medicine: cost-minimization studies, cost-benefit analyses, cost-effectiveness analyses, and cost-utility analyses. They are all commonly lumped under the term *cost-effectiveness analysis*. However, significant differences exist among these different studies.

Cost-minimization analysis is a comparison of the cost of different health-care strategies that are assumed to have identical or similar effectiveness [16]. In medical practice, few diagnostic tests or treatments have identical or similar effectiveness. Therefore, relatively few articles have been published in the literature with this type of study design [22]. For example, a recent study demonstrated that functional magnetic resonance imaging (MRI) and the Wada test have similar effectiveness for language lateralization, but the latter is 3.7 times more costly than the former [23].

Cost-benefit analysis (CBA) uses monetary units such as dollars or euros to compare the costs of a health intervention with its health benefits [16]. It converts all benefits to a cost equivalent and is commonly used in the financial world where the cost and benefits of multiple industries can be changed to only monetary values. One method of converting health outcomes into dollars is through a contingent valuation or willingness-to-pay approach. Using this tech-

nique, subjects are asked how much money they would be willing to spend to obtain, or avoid, a health outcome. For example, a study by Appel et al. [24] found that individuals would be willing to pay \$50 for low-osmolar contrast agents to decrease the probability of side effects from intravenous contrast. However, in general, health outcomes and benefits are difficult to transform to monetary units; hence, CBA has had limited acceptance and use in medicine and diagnostic imaging [16, 25].

Cost-effectiveness analysis (CEA) refers to analyses that study both the effectiveness and cost of competing diagnostic or treatment strategies, where effectiveness is an objective measure (e.g., intermediate outcome: number of strokes detected; or long-term outcome: life-years saved). Radiology CEAs often use intermediate outcomes, such as lesion identified, length of stay, and number of avoidable surgeries [16, 18]. However, ideally, long-term outcomes such as life-years saved (LYS) should be used [21]. By using LYS, different health-care fields or interventions can be compared. Given how few exist, there is a need for more "outcome-based studies" in radiology and the imaging sciences.

Cost-utility analysis is similar to CEA except that the effectiveness also accounts for quality of life. Quality of life is measured as utilities that are based on patient preferences [16]. The most commonly used utility measurement is the quality-adjusted life year (QALY). The rationale behind this concept is that the QALY of excellent health is more desirable than the same 1 year with substantial morbidity. The QALY model uses preferences with weight for each health state on a scale from 0 to 1, where 0 is death and 1 is perfect health. The utility score for each health state is multiplied by the length of time the patient spends in that specific health state [16, 26]. For example, assume that a patient with an untreated Chiari I malformation has a utility of 0.8 and he spends 1 year in this health state. The patient with the Chiari I malformation would have a 0.8 QALY in comparison with his neighbor who has a perfect health and hence a 1 QALY.

Cost-utility analysis incorporates the patient's subjective value of the risk, discomfort, and pain

into the effectiveness measurements of the different diagnostic or therapeutic alternatives. Ideally, all medical decisions should reflect the patient's values and priorities [26]. That is the explanation of why cost–utility analysis is the preferred method for evaluation of economic issues in health [19, 21]. For example, in low-risk newborns with intergluteal dimple suspected of having occult spinal dysraphism, ultrasound was the most effective strategy with an incremental cost-effectiveness ratio of \$55,100 per QALY. In intermediate-risk newborns with low anorectal malformation, however, MRI was more effective than ultrasound at an incremental cost-effectiveness of \$1000 per QALY [27].

Assessment of Outcomes: The major challenge to cost–utility analysis is the quantification of health or quality of life. One way to quantify health is descriptive analyses. By assessing what patients can and cannot do, how they feel, their mental state, their functional independence, their freedom from pain, and any number of other facets of health and well-being that are referred to as domains, one can summarize their overall health status. Instruments designed to measure these domains are called health status instruments. A large number of health status instruments exist, both general instruments, such as the SF-36 [28], and instruments that are specific to particular disease states, such as the Roland scale for back pain. These various scales enable the quantification of health benefit. For example, Jarvik et al. [29] found no significant difference in the Roland score between patients randomized to MRI versus radiography for low back pain, suggesting that MRI was not worth the additional cost.

Assessment of Cost: All forms of economic analysis require assessment of cost. However, assessment of cost in medical care can be confusing, as the term *cost* is used to refer to many different things. The use of charges for any sort of cost estimation, however, is inappropriate. Charges are arbitrary and have no meaningful use. Reimbursements, derived from Medicare and other fee schedules, are useful as an estimation of the amounts society pays for particular health-care interventions. For an analysis taken

from the societal perspective, such reimbursements may be most appropriate. For analyses from the institutional perspective or in situations where there are no meaningful Medicare reimbursements, assessment of actual direct and overhead costs may be appropriate [30].

Direct cost assessment centers on the determination of the resources that are consumed in the process of performing a given imaging study, including *fixed costs* such as equipment and *variable costs* such as labor and supplies. Cost analysis often utilizes activity-based costing and time motion studies to determine the resources consumed for a single intervention in the context of the complex health-care delivery system. Activity-based accounting is a type of accounting that assigns costs to each resource activity based on resource consumption, decreasing the amount of indirect costs with this method. Time and motion studies are time-intensive observational methods used to understand and improve work efficiency in a process. *Overhead*, or *indirect cost*, assessment includes the costs of buildings, overall administration, taxes, and maintenance that cannot be easily assigned to one particular imaging study. Institutional cost accounting systems may be used to determine both the direct costs of an imaging study and the amount of institutional overhead costs that should be apportioned to that particular test. For example, Medina et al. [23] studied the total direct costs of the Wada test ($\$1130.01 \pm \138.40) and of functional MR imaging ($\$301.82 \pm \10.65) that were significantly different ($P < 0.001$). The cost of the Wada test was 3.7 times higher than that of functional MR imaging.

Summarizing the Data

The results of the EBI process are a summary of the literature on the topic, both quantitative and qualitative. *Quantitative analysis* involves, at minimum, a descriptive summary of the data and may include formal *meta-analysis*, where there is sufficient reliably acquired data. *Qualitative analysis* requires an understanding of error, bias,

and the subtleties of experimental design that can affect the quality of study results. Qualitative assessment of the literature is covered in detail in Chap. 2, “Assessing the Imaging Literature: Understanding Error and Bias”; this section focuses on meta-analysis and the quantitative summary of data.

The goal of the EBI process is to produce a single summary of all of the data on a particular clinically relevant question. However, the underlying investigations on a particular topic may be too dissimilar in methods or study populations to allow for a simple summary. In such cases, the user of the EBI approach may have to rely on the single study that most closely resembles the clinical subjects upon whom the results are to be applied or may be able only to reliably estimate a range of possible values for the data.

Often, there is abundant information available to answer an EBI question. Multiple studies may be identified that provide methodologically sound data. Therefore, some method must be used to combine the results of these studies in a summary statement. *Meta-analysis* is the method of combining results of multiple studies in a statistically valid manner to determine a summary measure of accuracy or effectiveness [31, 32]. For diagnostic studies, the summary estimate is generally a summary sensitivity and specificity or a summary ROC curve.

The process of performing meta-analysis parallels that of performing primary research. However, instead of individual subjects, the meta-analysis is based on individual studies of a particular question. The process of selecting the studies for a meta-analysis is as important as unbiased selection of subjects for a primary investigation. Identification of studies for meta-analysis employs the same type of process as that for EBI described above, employing Medline and other literature search engines. Critical information from each of the selected studies is then abstracted usually by more than one investigator. For a meta-analysis of a diagnostic accuracy study, the numbers of true positives, false positives, true negatives, and false negatives would be determined for each of the eligible research publications. The results of a meta-analysis are

derived not just by simply pooling the results of the individual studies but instead by considering each individual study as a data point and determining a summary estimate for accuracy based on each of these individual investigations. There are sophisticated statistical methods of combining such results [33].

Like all research, the value of a meta-analysis is directly dependent on the validity of each of the data points. In other words, the quality of the meta-analysis can only be as good as the quality of the research studies that the meta-analysis summarizes. In general, a meta-analysis cannot compensate for selection and other biases in the primary data. If the studies included in a meta-analysis are different in some way, or are subject to some bias, then the results may be too heterogeneous to combine in a single summary measure. Exploration for such heterogeneity is an important component of a meta-analysis.

The ideal for EBI is that all practice be based on the information from one or more well-performed meta-analyses. However, there is often too little data or too much heterogeneity to support a formal meta-analysis. Understanding the hierarchy of next best available evidence, and how to find it, is then critical for readers of the literature.

Applying the Evidence

The final step in the EBI process is to apply the summary results of the medical literature to the EBI question. Sometimes the answer to an EBI question is a simple yes or no, as for this question: Does a normal clinical exam exclude unstable cervical spine fracture in patients with minor trauma? Commonly, the answers to EBI questions are expressed as some measure of accuracy. For example, how good is MRI for detecting acute ischemic infarction (<6 h)? The answer is that MRI has an approximate sensitivity of 91% and specificity of 95% [34]. However, to guide practice, EBI must be able to answer questions that go beyond simple accuracy; for example, should MRI then be used for the early detection of acute infarct? To answer this question, it is useful to divide the types of literature studies into a *hierarchical framework* [35]

(Table 1.4). At the foundation of this hierarchy is assessment of *technical efficacy*: studies that are designed to determine if a particular proposed imaging method or application has the underlying ability to produce an image that contains useful information. Information for technical efficacy would include signal-to-noise ratios, image resolution, and freedom from artifacts. The second step in this hierarchy is to determine if the image predicts the truth. This is the *accuracy* of an imaging study and is generally studied by comparing the test results to a reference standard and defining the sensitivity and the specificity of the imaging test. The third step is to incorporate the physician into the evaluation of the imaging intervention by evaluating the effect of the use of the particular imaging intervention on physician certainty of a given diagnosis (physician decision making) and on the actual management of the patient (*therapeutic efficacy*). Finally, to be of value to the patient, an imaging procedure must not only affect management but also improve outcome. *Patient*

outcome efficacy is the determination of the effect of a given imaging intervention on the length and quality of life of a patient. A final efficacy level is that of society, which examines the question of not simply the health of a single patient but that of the health of society as a whole, encompassing the effect of a given intervention on all patients and including the concepts of *cost* and *cost-effectiveness* [35].

Some additional research studies in imaging, such as clinical prediction rules, do not fit readily into this hierarchy. *Clinical prediction rules* are used to define a population in whom imaging is appropriate or can safely be avoided. Clinical prediction rules can also be used in combination with CEA as a way of deciding between competing imaging strategies [36].

Working Relative Value Unit

The relative value unit (RVU) was developed to assess productivity. It is the system currently used to determine Medicare/Medicaid reimbursement for procedures. The aim is to compare and quantify the effort needed in performing different specific tasks (e.g., interpreting a study). This works by assigning a different numerical value to the different imaging studies, such as a chest radiograph, an abdomen CT, or a brain MRI. The effort that a radiologist employs while interpreting each study is quantified with a numerical variable, which will ultimately correlate with the amount paid or reimbursed. This tool is not unique to radiology as it is currently used in different fields of medicine [37].

Each reimbursable procedure is represented by a Current Procedural Terminology (CPT) code which has an RVU assigned [38]. Therefore, it is important to describe the procedure being performed, the use of contrast, and the post-processing techniques applied in as much detail as possible. The total RVU assigned to a specific CPT code is also known as the global component. This is divided into a technical component (Part A in hospital-based billing) and a professional component (Part B in hospital-based billing). The professional component, from where the pay to the radiologist arises, represents on average 15–20% of the global component, with the rest

Table 1.4 Imaging effectiveness hierarchy

Technical efficacy: production of an image or information
<i>Measures: signal-to-noise ratio, resolution, absence of artifacts</i>
Accuracy efficacy: ability of test to differentiate between disease and nondisease
<i>Measures: sensitivity, specificity, receiver operator characteristic curves</i>
Diagnostic-thinking efficacy: impact of test on likelihood of diagnosis in a patient
<i>Measures: pre- and posttest probability, diagnostic certainty</i>
Treatment efficacy: potential of test to change therapy for a patient
<i>Measures: treatment plan, operative or medical treatment frequency</i>
Outcome efficacy: effect of use of test on patient health
<i>Measures: mortality, quality-adjusted life years, health status</i>
Societal efficacy: appropriateness of test from perspective of society
<i>Measures: cost-effectiveness analysis, cost–utility analysis</i>

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going to the technical component. The technical component goes to the owner of the facility and equipment where the study is being performed. The professional component of the RVU is further divided into the work fee, practice expenses, and malpractice insurance. The work fee is approximately 55–67% of the professional component and ultimately represents the amount paid to the interpreting radiologist [37].

Table 1.5 provides a few examples of how RVUs vary by imaging study. For example, a radiologist would need to read approximately 10 CXRs to get the same RVUs of a radiologist who reads one brain MRI, when comparing the professional component. Similarly, a radiologist would need to read approximately 6 CXRs to get the same RVUs of a radiologist who reads one abdomen CT, again when comparing the professional component. If we compare it with a non-contrast head CT for the professional component, a radiologist would have to read approximately 4 CXRs to get the same RVUs of a radiologist who reads one non-contrast head CT. A study by Hsiao and others concluded that the monetary-conversion factor yields an unreasonable low-level income for most specialties, while benefiting others [39]. In terms of medical imaging, one of the disadvantages of this system based on RVUs for reimbursement is that the complexity of the patient disease (e.g., a normal study versus the presence of a complex congenital malformation) is not taken into consideration. Therefore, the value given to a normal study is the same value given to a complex study, even though the time and effort for interpretation can be quite different.

Table 1.5 Relative value unit

Imaging study/CPT	Technical RVU	Professional RVU
CXR	0.66	0.3
Head CT NC	4.98	1.17
Abdomen CT	7.22	1.75
Brain MRI	26.3	3.24
Bone Scan	4.5	1.19
ICA	13.3	2.31

CPT Current procedural terminology, *CT* Computed tomography, *CXR* Chest radiograph, *ICA* unilateral internal carotid artery arteriogram, *MRI* Magnetic resonance imaging, *NC* Non-contrast, *RVU* Relative value uptake

Similarly, there are several imaging studies that are more time-consuming, such as fluoroscopy, yet are devalued in terms of the RVU assigned. Other disadvantages include that the system is not based in efficacy, cost-effectiveness, or quality [40]. For these and other reasons, some adjustments are made to the process to provide a fair end-result. One of these adjustments is the geographic practice cost indices (GPCI), which takes into consideration the local market (e.g., energy costs). Another potential alteration is the “adjusted RVU” which aims to equate the value of the procedures assigned higher RVUs (e.g., brain MRI) with the procedures assigned lower RVUs (e.g., upper gastrointestinal series). The “adjusted RVU” is an option adopted by some practices. On the other hand, the GPCI is established by the Center for Medicare & Medicaid Services (CMS) and applies to all practices [37].

Bayes’ Theorem, Predictive Values, and the Likelihood Ratio

Ideally, information would be available to address the effectiveness of a diagnostic test on all levels of the hierarchy. Commonly in imaging, however, the only reliable information that is available is that of diagnostic accuracy. It is incumbent upon the user of the imaging literature to determine if a test with a given sensitivity and specificity is appropriate for use in a given clinical situation. To address this issue, the concept of Bayes’ theorem is critical. Bayes’ theorem is based on the concept that the value of the diagnostic tests depends not only on the characteristics of the test (sensitivity and specificity) but also on the prevalence (pretest probability) of the disease in the test population. As the prevalence of a specific disease decreases, it becomes less likely that someone with a positive test will actually have the disease and more likely that the positive test result is a false positive. The relationship between the sensitivity and specificity of the test and the prevalence (pretest probability) can be expressed through the use of Bayes’ theorem (see Appendix 2) [11, 14] and the likelihood ratio. The positive likelihood ratio (PLR) estimates the likelihood that a positive test result will raise or lower the pretest probability, resulting in estimation of the posttest probability (where

PLR = sensitivity/(1 – specificity)). The negative likelihood ratio (NLR) estimates the likelihood that a negative test result will raise or lower the pretest probability, resulting in estimation of the posttest probability (where $NLR = (1 - sensitivity)/specificity$) [41]. The likelihood ratio (LR) is not a probability but a ratio of probabilities. The positive predictive value (PPV) refers to the probability that a person with a positive test result actually has the disease. The negative predictive value (NPV) is the probability that a person with a negative test result does not have the disease. Since the predictive value is determined once the test results are known (i.e., sensitivity and specificity), it actually represents a posttest probability; hence, the posttest probability is determined by both the prevalence (pretest probability) and the test information (i.e., sensitivity and specificity). Thus, the predictive values are affected by the prevalence of disease in the study population.

A practical understanding of this concept is shown in examples 1 and 2 in Appendix 2. The example shows an increase in the PPV from 0.67 to 0.98 when the prevalence of carotid artery disease is increased from 0.16 to 0.82. Note that the sensitivity and specificity of 0.83 and 0.92, respectively, remain unchanged. If the test information is kept constant (same sensitivity and specificity), the pretest probability (prevalence) affects the posttest probability (predictive value) results.

The concept of diagnostic performance discussed above can be summarized by incorporating the data from Appendix 2 into a nomogram for interpreting diagnostic test results (Fig. 1.3). For example, two patients present to the emergency department complaining of left-sided weakness. The treating physician wants to determine if they have a stroke from carotid artery disease. The first patient is an 8-year-old boy complaining of chronic left-sided weakness. Because of the patient’s young age and chronic history, he was determined clinically to be in a low-risk category for carotid artery disease-induced stroke and hence with a low pretest probability of 0.05 (5%). Conversely, the second patient is 65 years old and is complaining of acute onset of severe left-sided weakness. Because of the patient’s older age and acute history, he was determined clinically to be in a high-risk category

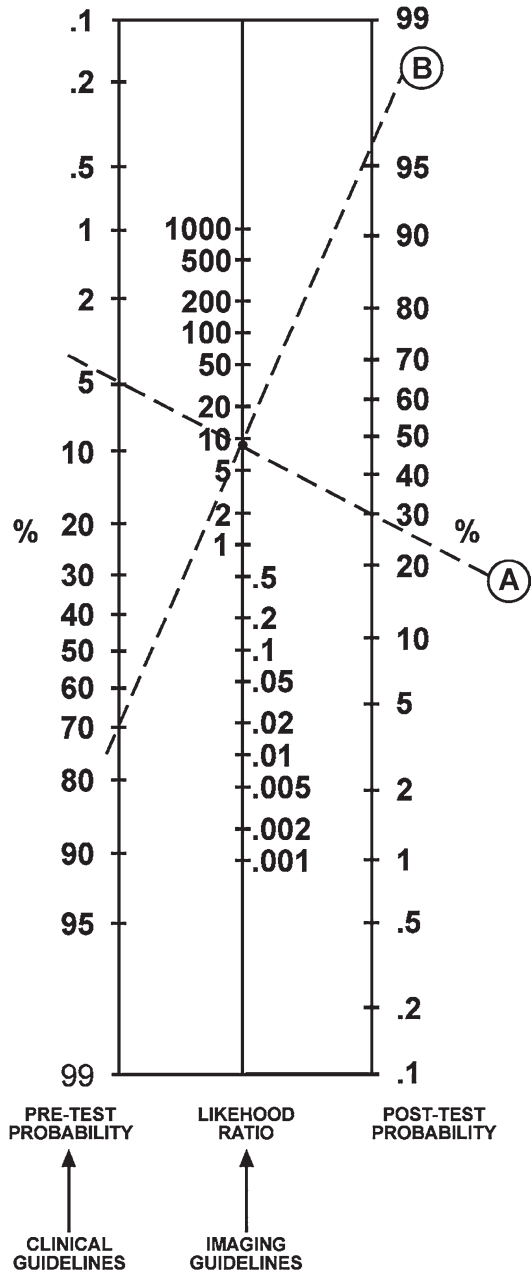


Fig. 1.3 Bayes’ theorem nomogram for determining posttest probability of disease using the pretest probability of disease and the likelihood ratio from the imaging test. Clinical and imaging guidelines are aimed at increasing the pretest probability and likelihood ratio, respectively. Worked example is explained in the text. (Reprinted with permission from Medina L, Aguirre E, Zurakowski D. Neuroimaging Clin N Am. 2003; 13:157–65)

for carotid artery disease-induced stroke and hence with a high pretest probability of 0.70 (70%). The available diagnostic imaging test was unenhanced

head CT followed by CT angiography. According to the radiologist's available literature, the sensitivity and specificity of these tests for carotid artery disease and stroke were each 0.90. The positive likelihood ratio (sensitivity/ $1 - \text{specificity}$) calculation derived by the radiologist was $0.90/(1-0.90) = 9$. The posttest probability for the 8-year-old patient is therefore 30% based on a pretest probability of 0.05 and a likelihood ratio of 9 (Fig. 1.3, dashed line a). Conversely, the posttest probability for the 65-year-old patient is greater than 95% based on a pretest probability of 0.70 and a positive likelihood ratio of 9 (Fig. 1.3, dashed line b). Clinicians and radiologists can use this scale to understand the probability of disease in different risk groups and for imaging studies with different diagnostic performance.

Jaeschke et al. [41] have proposed a rule of thumb regarding the interpretation of the LR. For PLR, tests with values greater than 10 have a large difference between pretest and posttest probability with conclusive diagnostic impact; values of 5–10 have a moderate difference in test probabilities and moderate diagnostic impact; values of 2–5 have a small difference in test probabilities and sometimes an important diagnostic impact; and values less than 2 have a small difference in test probabilities and seldom have important diagnostic impact. For NLR, tests with values less than 0.1 have a large difference between pretest and posttest probability with conclusive diagnostic impact; values of 0.1 and less than 0.2 have a moderate difference in test probabilities and moderate diagnostic impact; values of 0.2 and less than 0.5 have a small difference in test probabilities and sometimes an important diagnostic impact; and values of 0.5–1 have small difference in test probabilities and seldom have important diagnostic impact.

The role of the clinical guidelines is to increase the pretest probability by adequately distinguishing low-risk from high-risk groups. The role of imaging guidelines is to increase the likelihood ratio by recommending the diagnostic test with the highest sensitivity and specificity. Comprehensive

use of clinical and imaging guidelines will improve the posttest probability, hence increasing the diagnostic outcome [10].

How to Use This Book

As these examples illustrate, the EBI process can be lengthy [42]. The literature is overwhelming in scope and somewhat frustrating in methodological quality. The process of summarizing data can be challenging to the clinician not skilled in meta-analysis. The time demands on busy practitioners can limit their appropriate use of the EBI approach. This book can mitigate these challenges in the use of EBI and make the EBI accessible to all imagers and users of medical imaging.

This book is organized by major diseases and injuries. In the table of contents within each chapter, you will find a series of EBI issues provided as clinically relevant questions. Readers can quickly find the relevant clinical question and receive guidance as to the appropriate recommendation based on the literature. Where appropriate, these questions are further broken down by age, gender, or other clinically important circumstances. Following the chapter's table of contents is a summary of the key points determined from the critical literature review that forms the basis of EBI. Sections on pathophysiology, epidemiology, and cost are next, followed by the goals of imaging and the search methodology. The chapter is then broken down into the clinical issues. Discussion of each issue begins with a brief summary of the literature, including a quantification of the strength of the evidence, and then continues with detailed examination of the supporting evidence. At the end of the chapter, the reader will find the take-home tables and imaging case studies, which highlight key imaging recommendations and their supporting evidence. Finally, questions are included where further research is necessary to understand the role of imaging for each of the topics discussed.

Acknowledgment We appreciate the contribution of Ruth Carlos, MD, MS, to the discussion of likelihood ratios in this chapter.

Take-Home Appendix 1: Equations

Test result	Outcome	
	Present	Absent
Positive	a (TP)	b (FP)
Negative	c (FN)	d (TN)
(a) Sensitivity		$a/(a + c)$
(b) Specificity		$d/(b + d)$
(c) Prevalence		$(a + c)/(a + b + c + d)$
(d) Accuracy		$(a + d)/(a + b + c + d)$
(e) Positive predictive value ^a		$a/(a + b)$
(f) Negative predictive value ^a		$d/(c + d)$
(g) 95% confidence interval (CI)	$p \pm 1.96 \sqrt{\frac{1-p}{n}}$ <p><i>p</i> = proportion <i>n</i> = number of subjects</p>	
(h) Likelihood ratio	$\frac{\text{Sensitivity}}{1 - \text{Sensitivity}} = \frac{a(b + d)}{b(a + c)}$	

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^aOnly correct if the prevalence of the outcome is estimated from a random sample or based on an a priori estimate of prevalence in the general population; otherwise, Bayes’ theorem must be used to calculate positive predictive value (PPV) and negative predictive value (NPV). TP true positive, FP false positive, FN false negative, TN true negative

Take-Home Appendix 2: Summary of Bayes’ Theorem

1. Information before test × Information from test = Information after test
2. Pretest probability (prevalence) sensitivity/1 – specificity = posttest probability (predictive value)

3. Information from the test also known as the likelihood ratio, described by the equation: sensitivity/1 – specificity
4. Examples 1 and 2 predictive values: The predictive values (posttest probability) change according to the differences in prevalence (pretest probability), although the diagnostic performance of the test (i.e., sensitivity and specificity) is unchanged. The following examples illustrate how the prevalence (pretest probability) can affect the predictive values (posttest probability) having the same information in two different study groups.

Equations for calculating the results in the previous examples are listed in Appendix 1. As the prevalence of carotid artery disease increases from 0.16 (low) to 0.82 (high), the positive predictive value (PPV) of a positive contrast-enhanced CT increases from 0.67 to 0.98, respectively. The sensitivity and specificity remain unchanged at 0.83 and 0.92, respectively. These examples also illustrate that the diagnostic performance of the test (i.e., sensitivity and specificity) does not depend on the prevalence (pretest probability) of the disease. CTA, CT angiogram.

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Critically Assessing the Literature for Evidence-Based Imaging: Understanding Error and Bias

2

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Evidence-based imaging (EBI) requires the critical assessment and application of the best available evidence to patient imaging. Unfortunately, the published studies that comprise the available evidence are often limited by bias, small sample size, and methodological inadequacy. Further, the information provided in published reports may be insufficient to allow estimation of the quality of the research. Initiatives by journal editors to improve the reporting of research studies, including the CONSORT [1], STARD [2], SQUIRE [3], and others, provide useful guides but are incompletely implemented.

The objective of this chapter is to summarize the common sources of error and bias in the imaging literature to guide the critical assessment required for EBI.

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What Are Error and Bias?

Errors in the medical literature can be divided into two main types. The first is *random error* that occurs due to chance variation causing a sample to be different from the underlying population. Random error will tend to be more important when sample size is small. *Systematic error*, or *bias*, is an incorrect study result due to nonrandom distortion of the data. Systematic error is not affected by sample size but rather is a function of flaws in the study design, data collection, or analysis. A second way to think about random and systematic error is in terms of precision and accuracy [4]. Random error affects the precision of a result. Using the bull's eye analogy, precision is how close the measurements are to each other (Fig. 2.1). Higher precision indicates relatively less random error and more likelihood that two samples from truly different populations will be differentiated from each other. Systematic error on the other hand is a distortion in the accuracy of an estimate. Regardless of precision, the underlying estimate is flawed by some aspect of the

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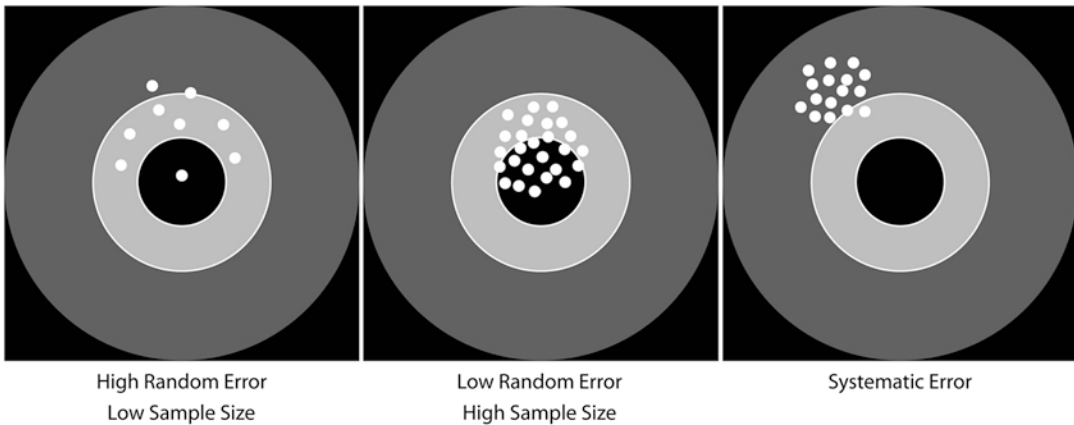


Fig. 2.1 Random and systemic error. Using the bull’s-eye analogy, the larger the sample size, the less the random error and the larger the chance of hitting the center of the target. In systemic error, regardless of the sample size, the bias would not allow the researcher to hit the center of the target. *Left:* High random error and low sample size leads to low precision. *Middle:* Low random error and high sample size leads to high precision. *Right:* High precision

can be accompanied by low accuracy if systematic error (bias) is present. (Reprinted with kind permission of Springer Science + Business Media from Blackmore CC, Medina LS, Ravenel JG, Silvestri GA. Critically Assessing the Literature: Understanding Error and Bias. In Medina LS, Blackmore DD (eds): *Evidence-Based Imaging: Optimizing Imaging in Patient Care*. New York: Springer Science + Business Media, 2006.)

research procedure. Using the bull’s eye analogy, in systematic error regardless of the sample size, the bias would not allow the researcher to hit the center of the target (Fig. 2.1).

What Is Random Error?

Random error is divided into two main types: Type I, or alpha error, is when the investigator concludes that an effect or difference is present when in fact there is no true difference, and Type II or beta error occurs when an investigator concludes that there is no effect or no difference when in the underlying population, a true difference exists [4].

Type I Error

Quantification of the likelihood of alpha error is provided by the familiar p -value. A p -value of less than 0.05 indicates that there is a less than 5% chance that the observed difference in a sample would be seen if there was in fact no true difference in the population. In fact, the difference

observed in a sample is due to chance variation rather than a true underlying difference in the population. It is important to remember that at a p -value of 0.05, we will still draw incorrect conclusions (make Type I errors) in 5 of 100 cases.

A second limitation of the ubiquitous p -value is that p -values are a function of both sample size and magnitude of effect. In other words, there could be a very large difference between two groups under study, but the p -value might not be significant if the sample sizes are small. Conversely, there could be a very small, clinically unimportant difference between two groups of subjects or between two imaging tests, but with a large enough sample size, even this clinically unimportant result would be statistically significant. Because of these limitations, many journals are underemphasizing use of p -values and encouraging research results to be reported by way of confidence intervals [5].

Confidence Intervals

Confidence intervals are preferred because they provide much more information than p -values. Confidence intervals provide information about

the precision of an estimate (how wide are the confidence intervals), the size of any effect (magnitude of the confidence intervals), and the statistical significance of an estimate (whether the intervals include the null) [6].

In general, you can be 95% certain that the confidence interval (CI) includes the true population mean. More precisely, if you generate many 95% CI from many data sets, you can expect that the CI will include the true population mean in 95% of the cases and not include the true mean value in the other 5% [5]. Therefore, if the 95% CI interval does not include the null, then the results will be statistically significant at the 0.05 level [7]. Whereas the p -value is only interpreted as being either statistically significant or not, the CI has the advantage of providing the range of probable values and allows the reader to understand not just the statistical significance but also the magnitude of any effect [7, 8]. CIs shift the interpretation from a qualitative judgment about the role of chance to a quantitative estimation of the biologic measure of effect [5, 7, 8].

Confidence intervals can be constructed for any desired level of confidence. There is nothing magical about the 95% that is traditionally used, except that it is consistent with the traditional $p < 0.05$ threshold. If greater confidence is needed, then the intervals can be wider (i.e., 99%) or narrower (i.e., 90%) if less confidence is sufficient. The trade-off is that wider CIs are associated with greater confidence but less precision [5].

As an example, two hypothetical transcranial circle of Willis vascular ultrasound studies in patients with sickle-cell disease describe mean peak systolic velocities of 200 cm/s associated with 70% of vascular diameter stenosis and higher risk of stroke. Both articles reported the same standard deviation (SD) of 50 cm/s. At first glance, both articles appear to provide similar information. However, the size of the confidence interval is a function of the sample size, with narrower confidence intervals for the larger study reflecting greater precision. In the smaller series, the 95% CI was 186–214 cm/s, while in the larger series, the 95% CI was narrower, at 196–204 cm/s [5].

Type II Error

The familiar p -value does not provide information as to the probability of a Type II or beta error. A p -value greater than 0.05 does not necessarily mean that there is no difference in the underlying population. The size of the sample studied may be too small to detect an important difference even if such a difference does exist. The ability of a study to detect an important difference, if that difference does in fact exist in the underlying population, is called the power of a study. Power analysis can be performed in advance of a research investigation to avoid Type II error.

Power Analysis

Power analysis plays an important role in determining what an adequate sample size is, so that meaningful results can be obtained [9]. Power analysis is the probability of observing an effect in a sample of patients if the specified effect size, or greater, is found in the population [4]. Mathematically, power is defined as 1 minus β (beta), where β is the probability of having a Type II error. Type II errors are commonly referred to as false negatives in a study population. The other type of error is Type I or α (alpha), also known as false positives in a study population [7]. For example, if β is set at 0.10, then the researchers acknowledge they are willing to accept a 10% chance of missing a correlation between abnormal CT angiographic finding and the diagnosis of carotid artery disease. This represents a power of 1 minus 0.10, or 0.90, which represents a 90% probability of finding a correlation of this magnitude.

Ideally, the power should be 100% by setting β at 0. In addition, ideally, α should also be 0. By accomplishing this, false-negative and false-positive results are eliminated, respectively. In practice, however, powers near 100% are rarely achievable, so, at best, a study should reduce the false negatives β and false positives α to a minimum [4, 10]. Achieving an acceptable reduction of false negatives and false positives requires a large subject sample size. Optimal

power, α and β , settings are based on a balance between scientific rigorousness, and the issues of feasibility and cost. For example, assuming an α error of 0.10, your sample size increases from 96 to 118 subjects per study arm (carotid and non-carotid artery disease arms) if you change your desired power from 85% to 90%, respectively [11]. Studies with more complete reporting and better study design will often report the power of the study, for example, by stating that the study has 90% power to detect a difference in sensitivity of 10% between CT angiography and Doppler ultrasound in carotid artery disease. Unfortunately, power calculations are often lacking, and it is left to the reader to determine if a study has sufficient power to interpret if a high p -value is actually an indication that a difference does not exist.

What Is Bias?

The risk of an error from bias decreases as the rigorousness of the study design and analysis increases. Randomized controlled trials are considered the best design for minimizing the risk of bias because patients are randomly allocated. This random allocation allows for unbiased distribution of both known and unknown confounding variables between the study groups. However, as described below, even randomized clinical trials are susceptible to some forms of bias. In non-randomized studies, appropriate study design and statistical analysis can only control for known or measurable bias.

Detection of and correction for bias or systematic error in research is a vexing challenge for both researchers and users of the medical literature alike. Maclure and Schneeweiss have identified 10 different levels at which biases can distort the relationship between published study results and truth [12]. Unfortunately, bias is common in published reports [13], and reports with identifiable biases often overestimate the accuracy of diagnostic tests [14]. It is not uncommon for the initial reports on an imaging test to be enthusiastic in the results, but biased in the methods. Subsequent, more rigorous investigation will often refute, or at least diminish the purported effectiveness of a procedure. Careful surveillance

for each type of bias is critical but may be a challenge. Well-reported studies will often include a section on limitations of the work, spelling out the potential sources of bias that the investigator acknowledges from a study as well as the likely direction of the bias and steps that may have been taken to overcome this. However, the final determination of whether a research study is sufficiently distorted by bias to be unusable is left to the discretion of the user of the imaging literature. The imaging practitioner must determine if results of a particular study are true, are relevant to a given clinical question, and are sufficient as a basis to change practice [15].

A common type of bias encountered in imaging research is that of *selection bias* [15]. Because a research study cannot include all individuals in the world who have a particular clinical situation, research is conducted on samples. Selection bias can arise if the sample is not a true representation of the relevant underlying clinical population (Fig. 2.2). Numerous subtypes of selection bias have been identified, and it is a challenge to the researcher to avoid all of these biases when performing a study. One particularly severe form of selection bias occurs if the diagnostic test is applied to subjects with a spectrum of disease that differs from the clinically relevant group. The extreme form of this spectrum bias occurs when the diagnostic test is evaluated on subjects with severe disease who are then compared to normal controls. In an evaluation of the effect of bias on study results, Lijmer found the greatest overestimation of test accuracy with this type of spectrum bias [14]. Selection bias is a particular challenge in nonrandomized studies.

A second frequently encountered bias in imaging literature is that of *observer bias* [16, 17], also called test-review bias and diagnostic-review bias [18]. Imaging tests are often subjective. The radiologist interpreting an imaging study forms an impression based on the appearance of the image, not based on an objective number or measurement. This subjective impression can be biased by numerous factors including the radiologist's experience; the context of the interpretation (clinical vs. research setting); the information about the patient's history that is known by the radiologist; the incentives

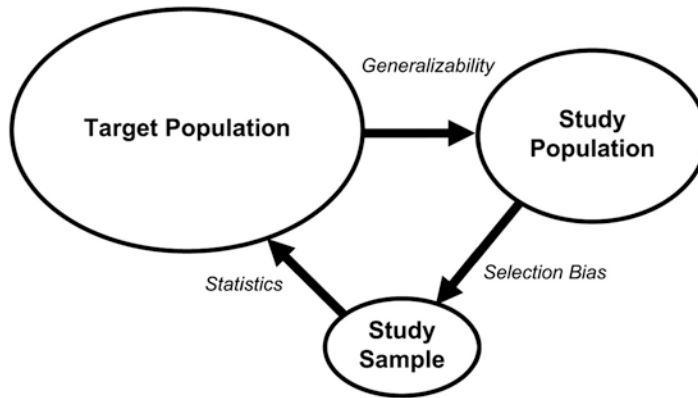


Fig. 2.2 Population and sample. The target population represents the universe of subjects who are at risk for a particular disease or condition. In this example, all subjects with abdominal pain are at risk for appendicitis. The sample population is the group of eligible subjects available to the investigators. These may be at a single center or group of centers. The sample is the group of subjects who are actually studied. Selection bias occurs when the sample is not truly representative of the study population. How closely the study population reflects the target popu-

lation determines the generalizability of the research. Finally, statistics are used to determine what inference about the target population can be drawn from the sample data. (Reprinted with kind permission of Springer Science + Business Media from Blackmore CC, Medina LS, Ravenel JG, Silvestri GA. *Critically Assessing the Literature: Understanding Error and Bias*. In Medina LS, Blackmore DD (eds): *Evidence-Based Imaging: Optimizing Imaging in Patient Care*. New York: Springer Science + Business Media, 2006.)

that the radiologist may have, both monetary and otherwise, to produce a particular report; and the memory of a recent experience. But because of all these factors, it is critical that the interpreting physician be blinded to the outcome or gold standard when a diagnostic test or intervention is being assessed. Important distortions in research results have been shown and observers are blinded vs. not blinded. For example, Schulz showed a 17% greater risk reduction in studies with unblinded assessment of outcomes versus those with blinded assessment [19]. In order to obtain objective scientific assessment of an imaging test, all readers should be blinded to other diagnostic tests and final diagnosis, and all patient-identifying marks on the test should be masked. Basically, the research setting should replicate clinical practice as closely as possible. Since the diagnosis is not known when an imaging test is interpreted in clinical practice, it should not be known in the research setting. Observer bias is important for both randomized and non-randomized studies.

Bias can also be introduced by the *reference standard* used to confirm the final diagnosis, called verification bias. First, the interpretation of

the reference standard must be made without knowledge of the test results. Reference standards, like the diagnostic tests themselves, may have a subjective component and therefore may be affected by knowledge of the results of the diagnostic test. In addition, it is critical that all subjects undergo the same reference standard. The use of different reference standards (called differential reference standard bias) for subjects with different diagnostic test results may falsely elevate both sensitivity and specificity [14, 17]. Of course, sometimes it is not possible or ethical to perform the same reference standard procedure on all subjects. For example, in a meta-analysis of imaging for appendicitis, Terasawa found that all of the identified studies used a different reference standard for subjects with positive imaging (appendectomy and pathological evaluation) than for those with negative imaging (clinical follow-up). It simply wouldn't be ethical to perform appendectomy on all subjects. Likely, the sensitivity and specificity of imaging for appendicitis was overestimated as a result [20]. Verification bias and differential reference standard bias are important in both randomized and nonrandomized studies.

What Are the Inherent Biases in Screening?

Investigations of screening tests are susceptible to an additional set of biases. Screening trials are vulnerable to *healthy volunteer bias*. For example, in the Prostate, Lung, Colorectal, and Ovarian Screening Trial, the individuals who volunteered to undergo screening were generally healthier and had lower mortality than the general population, even before the screening began. Hence, comparing only those who actually undergo screening to those randomized not to be invited to be screened will cause falsely elevated estimates of screening effectiveness. This bias can be avoided by including all of those invited to be screened, not just those who actually undergo screening [21]. Case-control studies are particularly problematic for screening, as screening is a choice in these studies, and people who present for elective screening

tend to have better health habits [22]. In assessing the exposure history of cases, including the test on which the diagnosis is made, regardless of whether it is truly screen or symptom detected, can lead to an odds ratio greater than 1 even in the absence of benefit [23]. Similarly, excluding the test on which the diagnosis is made may underestimate screening effectiveness. The magnitude of bias is further reflected in the disease preclinical phase; the longer the preclinical phase, the greater the magnitude of the bias.

Prospective nonrandomized screening trials perform an intervention on subjects, such as screening for lung cancer, and follow them for many years. These studies can give information of the stage distribution and survival from diagnosis of a screened population; however, these measures do not allow an accurate comparison to an unscreened group due to lead time, length time, and overdiagnosis bias [24] (Fig. 2.3). *Lead time bias* results

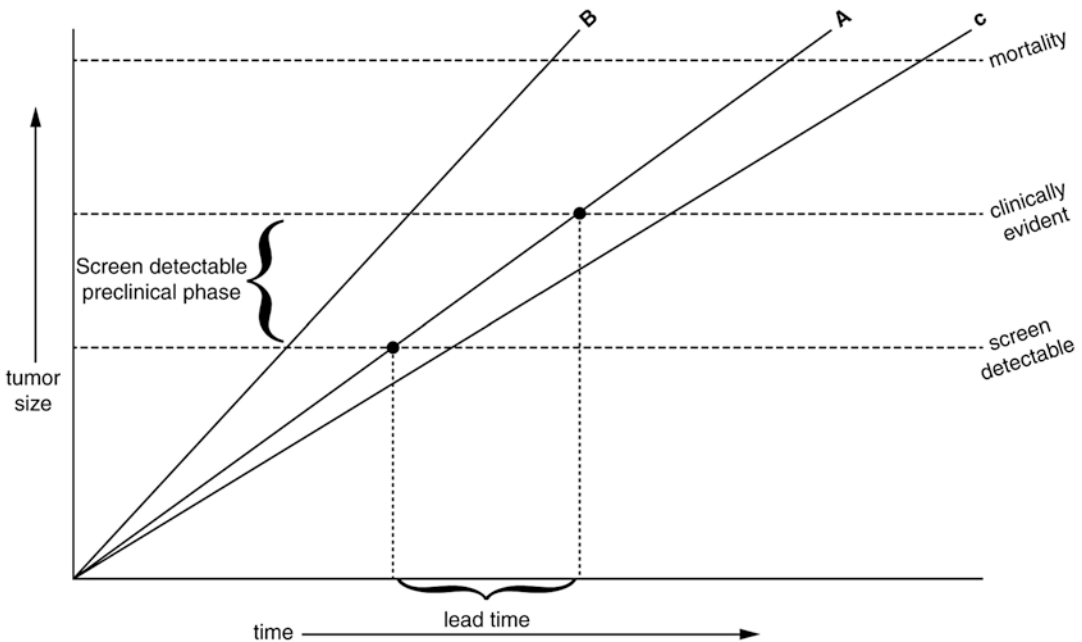


Fig. 2.3 Screening biases. For this figure, cancers are assumed to grow at a continuous rate until they reach a size at which death of the subject occurs. At a small size, the cancers may be evident on screening but not yet evident clinically. This is the preclinical screen detectable phase. Screening is potentially helpful if it detects cancer in this phase. After further growth, the cancer will be clinically evident. Even if the growth and outcome of the cancer is unaffected by screening, merely detecting the cancer earlier will increase apparent survival. This is the screening lead time. In addition, slower growing cancers (such

as C) will exist in the preclinical screen detectable phase for longer than faster growing cancers (such as B). Therefore, screening is more likely to detect more indolent cancers, a phenomenon known as length bias. (Reprinted with kind permission of Springer Science + Business Media from Blackmore CC, Medina LS, Ravenel JG, Silvestri GA. *Critically Assessing the Literature: Understanding Error and Bias*. In Medina LS, Blackmore DD (eds): *Evidence-Based Imaging: Optimizing Imaging in Patient Care*. New York: Springer Science + Business Media, 2006.)

from the earlier detection of the disease which leads to longer time from diagnosis and an apparent survival advantage but does not truly impact the date of death. In effect, individuals live longer with the disease as diagnosis is made earlier, but still die at the same age. *Length time bias* relates to the virulence of tumors. More indolent or slowly growing tumors will persist longer at a size that can be detected by screening but is not yet clinically evident (referred to as the preclinical screen detectable phase) longer than faster-growing tumors that are more likely to be detected by symptoms. Thus, screen-detected tumors will tend to be less aggressive even at the same size, when compared to clinically detected tumors. This disproportionately assigns more indolent disease to the intervention group in screening trials and results in the appearance of a benefit. *Overdiagnosis* is the most extreme form of length time bias in which a disease is detected and “cured” but is so indolent it would never have caused symptoms during life and therefore, in the absence of screening, would never have been diagnosed. Thus, survival from diagnosis alone is not an appropriate measure of the effectiveness of screening [25].

For this reason, a randomized control trial (RCT) with disease-specific mortality as an endpoint is the preferred methodology. Randomization should even out the selection process in both arms, eliminating the bias of case-control studies and allow direct comparison of groups who were invited to undergo the intervention and those who were not, to see if the intervention lowers deaths due to the target disease. The disadvantage of the RCT is that it takes many years and is expensive to perform. There are two additional biases that can occur in RCTs and are important to understand: *sticky diagnosis* and *slippery linkage* [26]. Because the target disease is more likely to be detected in a screened population, it is more likely to be listed as a cause of death, even if not the true cause. As such, the diagnosis “sticks” and tends to underestimate the true value of the test. On the other hand, screening may set into motion a series of events in order to diagnose and treat the illness. If these procedures remotely lead to mortality, say a myocardial infarction during surgery with death several months later, the linkage of the cause of death to the screening may no longer be obvious (slippery linkage). Because the death is not appro-

priately assigned to the target disease, the value of screening may be overestimated. For this reason, in addition to disease-specific mortality, all-cause mortality should also be evaluated in the context of screening trials [26].

Because of these biases in screening trials, it is important not to focus on irrelevant metrics, including survival, test sensitivity, disease prevalence, and detection of early stage disease. All of these are susceptible to bias that may make an ineffective screening test appear effective. Only disease-specific and all-cause mortality reduction (from invitation to screen or intention to treat analysis) are valid as measures of the effectiveness of screening trials [27].

Qualitative Literature Summary

The potential for error and bias makes the process of critically assessing a journal article complex and challenging, and no investigation is perfect. Producing an overall summation of the quality of a research report is difficult. However, there are grading schemes that provide a useful estimation of the value of a research report for guiding clinical practice. The method used in this textbook is derived from that of Kent [28] and is shown in Table 2.1. Use of such a grading scheme is by nature an oversimplification. However, such simple guidelines can provide a useful quick overview of the quality of a research report.

Table 2.1 Evidence classification for evaluation of a study

Level 1—Strong evidence:

Studies with broad generalizability to most patients suspected of having the disease of concern: a prospective, blinded comparison of a diagnostic test result with a well-defined final diagnosis in an unbiased sample when assessing diagnostic accuracy or blinded randomized control trials when assessing therapeutic impact or patient outcomes. Well-designed meta-analysis based on level 1 or 2 studies.

Level 2—Moderate evidence:

Prospective or retrospective studies with narrower spectrum of generalizability, with only a few flaws that are well described so their impact can be assessed but still requiring a blinded study of diagnostic accuracy on an unbiased sample. This includes well-designed cohort or case-control studies and randomized trials for therapeutic effects or patient outcomes.

(continued)

Table 2.1 (continued)*Level 3—Limited evidence:*

Diagnostic accuracy studies with several flaws in research methods, small sample sizes, or incomplete reporting OR nonrandomized comparisons for therapeutic impact or patient outcomes.

Level 4—Insufficient evidence:

Studies with multiple flaws in research methods, case series, descriptive studies, or expert opinions without substantiating data.

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Conclusion

In summary, critical analysis of a research publication can be a challenging task. The reader must consider the potential for Type I and Type II random error as well as systematic error introduced by biases including selection bias, observer bias, and reference standard bias. Screening includes an additional set of challenges related to the healthy volunteer effect, lead time, length bias, and overdiagnosis.

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Information Systems in Emergency Department Diagnostic Imaging

3

Jamlik-Omari Johnson and Nabile M. Safdar

Key Points

- Medical imaging greatly contributes to overall healthcare spending.
- Imaging in the emergency department (ED) setting is an area of continued growth.
- Health information technology (HIT) can help providers use imaging resources more appropriately and efficiently.
- HIT can help imagers provide services in an efficient, safe, and effective manner throughout the imaging value chain from inquiry to completion.
- HIT has the potential to bring value to multiple stakeholders in the emergency department setting.

the management of health information across computerized systems and provides a secure exchange between consumers, providers, payers, governmental, and quality entities. Within the context of this discussion, HIT includes but is not limited to:

- *Electronic health record (EHR) or electronic medical record (EMR)*: a computerized record of patient health information intended for clinical care. While these terms are sometimes used interchangeably, EHRs are considered by many to have a greater scope, potentially encompassing information from multiple EMRs.
- *Health information exchange (HIE)*: a communication network that mobilizes healthcare information between separate organizations within a region, community, or hospital system.
- *Picture archiving and communications systems (PACS)*: a HIT that provides storage and access to medical images from multiple sources. Implementations vary widely.
- *Computerized provider order entry (CPOE)*: the electronic entry of medical practitioner instruction for the treatment of patients. The instructions are communicated over a computer network to the parties (e.g., radiology, pharmacy, and nursing) responsible for fulfilling the request.
- *Clinical decision support (CDS)*: tools to enhance decision-making in clinical workflow.

Definitions, Trends, and Use

Health information technology (HIT) is an umbrella term applied to information technology in the healthcare sector. It broadly encompasses

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CDS provides clinicians, staff, and patients with appropriately filtered, individualized information and knowledge. The tools enhance appropriate decision-making and clinical workflow. CDS can be geared toward radiologists or their nonimaging colleagues.

- *Vendor neutral archives (VNAs)*: medical imaging technology in which documents, images, or other clinical data are stored with methods that enable flexible query, data consolidation, and multiple points of integration with other related systems.
- *Natural language processing (NLP)*: a field dealing with the automated processing and meaning of speech and text.

Over the span of this millennium, virtually every major industry has integrated computerization into its workflow to automate and streamline its processes. The purchase of virtually any product or service from the ease of a laptop or smartphone without leaving the comfort of home or the office is commonplace. If one decides to venture into a traditional brick and mortar store, computers can assist in price checks and self-checkout. Online education provides flexible distance learning opportunities. Despite the strong computerized presence in many sectors, the medical field largely lacks tightly integrated computerization. The American healthcare system is at the same time massive, fragmented, and potentially dangerous. New scientific evidence is not easily integrated into clinical practice [1]. Simple technologies commonplace in other industries are novel or largely absent in medicine. As Menachemi and Collum point out, “despite these advances in our society, the majority of patients are given handwritten medication prescriptions, very few patients are able to email their physician or even schedule an appointment to see a provider without speaking to a live receptionist” [2]. These stark differences in the adoption rates of computerization were not lost on healthcare advocates and lawmakers. In fact, healthcare payers, advocates, policymakers, and consumers identified robust health information systems as a critical component to modernizing the healthcare industry. As part of the 2009 American Recovery

and Reinvestment Act (ARRA), the Health Information Technology for Economic and Clinical Health (HITECH) Act provided incentives for providers to adopt meaningful electronic health record systems that could provide functionalities to reduce errors, contain costs, and improve efficiencies.

Healthcare information technology (HIT) has the potential to improve quality by increasing disease surveillance and adherence to guidelines, decreasing medical and medication errors, and improving efficiency. Much of HIT has focused on primary and secondary preventative care with the major benefit coming in the form of more appropriate utilization of care. However, additional benefits may come in the form of decreased time of care and improved safety (fewer adverse, sentinel, or preventable malpractice events) [3]. One in 50 hospitalized patients experiences a preventable adverse event, and an estimated 108,000 patients die annually from iatrogenic injury [4]. Zuccotti and colleagues quantified the impact of clinical decision support (CDS) systems and other forms of HIT. They estimated at least a 50% reduction of malpractice events and an indemnity savings of over \$40 million [3].

Overall Cost to Society

US healthcare expenditures grew 3.6% and exceeded 17% of gross domestic product in 2013. Spending topped \$2.9 trillion or \$9255 per person [5]. Imaging was a major contributor to overall healthcare costs representing approximately 14% of Medicare Part B expenditures. Imaging in the emergent setting represents not only a significant portion of overall imaging but also an area of continued growth [6].

During the first decade of this century, policymakers, advocates, and payers noted that imaging services were the most rapidly growing field of all physician services [7]. The escalating costs associated with increased imaging led to the adoption of various techniques to quell this unsustainable growth curve and to contain costs. Measures included reimbursement cuts, cost sharing with consumers (higher deductibles and

co-payments), pre-authorizations, code bundling, and HIT (most often in the form of computer decision support). While these aggressive measures succeeded in curbing the growth of advance imaging in outpatient and inpatient settings, imaging in the emergency department (ED) continued its rapid expansion undeterred by preventative measures [8]. Levin et al. reported that during a 10-year period (2002–2012), radiography (XR) utilization increased 29%, computed tomography (CT) increased 159%, ultrasound (US) increased 121%, and magnetic resonance imaging (MRI) increased 264%. In 2012, ED imaging represented 14% of all Medicare fee for service imaging; however, researchers concede this number is an underestimate as it does not account for patients who are imaged in the ER and subsequently admitted to the hospital inpatient service [9]. In 2008, upward of 95% of all ED imaging was interpreted by radiologists [10].

The volume and continued growth of imaging in the emergency setting suggest untapped opportunities for radiologists and ED providers to collaborate on imaging utilization. A variety of mechanisms have been proposed and include the development of, adoption of, and adherence to meaningful clinical decision support rules for imaging in the ED setting; increased awareness, education, and outreach to providers in the emergent care setting regarding appropriate imaging criteria and overutilized, low-yield imaging examinations (e.g., American College of Radiology (ACR) Appropriateness Criteria and Choosing Wisely) [11, 12]; and the integration of informatics, such as computerized CDS, into the routine ED clinical workflow. Despite its continued growth, imaging creates value for providers, patients, and payers when used appropriately.

When properly applied, medical imaging in the emergent setting facilitates accurate diagnosis and allows rapid patient triage. HIT can provide an efficient, effective, and robust healthcare delivery cornerstone. Within the imaging sphere and for the radiologist, HIT has the potential to not only help address issues related to imaging utilization but image planning, acquisition, interpretation, communication, and follow-up.

Goals of Information Systems in Emergency Imaging

In emergency settings, reaching the correct diagnosis in a timely fashion is critical to maximizing health outcomes. In its report, *Improving Diagnosis in Health Care*, the Institute of Medicine laid out its recommendations for improving the diagnostic process, including ensuring that “health information technologies support patients and healthcare professionals in the diagnostic process” [13]. The diagnostic imaging process involves value-added technologies at every step, including forming a diagnostic **inquiry**, performing a **diagnostic procedure**, accurately establishing a diagnostic **result**, and **completion** of that process, including communication, follow-up, and tracking of outcomes (Fig. 3.1). With this framework in mind, we will explore the potential use and state of the art of health information technologies most often utilized in emergency settings.

Methodology

A MEDLINE search was performed using PubMed research publications with the following keywords: imaging, utilization, emergency, radi-

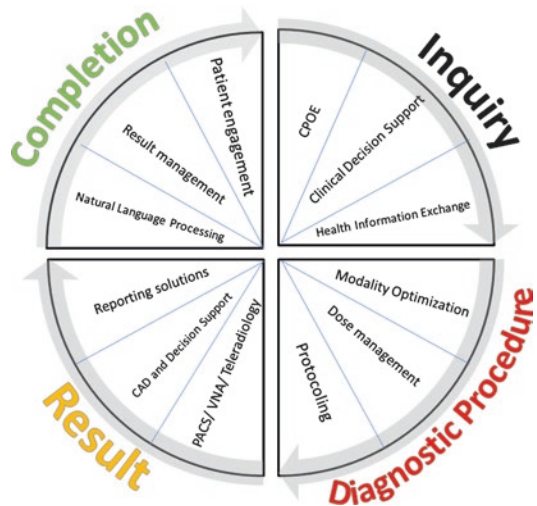


Fig. 3.1 The diagnostic imaging process. CPOE clinical provider order entry, PACS picture archiving and communications system, VNA vendor neutral archives

ology, medicine, department, informatics, health information, technology, systems, computer, and clinical decision support. The search covered a 10-year period from May 2005 to May 2015. Additional articles were identified by reviewing the reference lists of relevant publications.

Discussion of Issues

Forming a Diagnostic Inquiry: HIEs, CPOE, and CDS

Summary of Evidence Although impeded by questions of financial viability, HIEs have the potential to reduce redundant imaging in emergency settings. When implemented well, the combination of CPOE and CDS can improve adherence to guidelines for the utilization of advanced imaging [6].

Supporting Evidence Achieving improved health outcomes in emergency care requires effective collaboration between members of the clinical care team, including emergency providers and radiologists. However, emergency care providers face several challenges when accurately diagnosing their patients. Due to the nature of emergency and urgent care, patients in need of rapid diagnosis may not have an existing medical record readily available where they present. These patients may have received their care—and previous imaging—elsewhere. The lack of information about a patient's longitudinal health record can lead to redundant or unnecessary imaging that is requested only due to a paucity of available information. Well-implemented health information exchanges (HIEs) can remedy this conundrum by providing emergency care providers with a patient's previous medical notes, laboratory test results, and diagnostic imaging reports performed at other local or regional facilities. In some settings, HIEs have been shown to reduce redundant imaging or unindicated imaging in such settings as headache or back pain, reducing healthcare-related costs while maintaining or improving health outcomes [14–16]. Other investigations have questioned the utility or long-term

financial viability of HIEs, even with state or federal support [17, 18]. The success of HIEs in the United States has been variable, and its ongoing role in helping to manage emergency imaging remains uncertain. While it may not be particularly challenging for emergency providers to differentiate the strengths and weaknesses of basic imaging modalities, navigating the complexities of advanced imaging with a myriad of protocols in a time-sensitive setting may pose unique challenges. The increasing utilization of computerized physician order entry (CPOE) and clinical decision support (CDS) in emergency settings seems likely, despite some ongoing uncertainty regarding regulatory oversight of CDS software [19].

CPOE with CDS has long been available to optimize the safety and effectiveness of ordering medication. Depending on the implementation and setting, this strategy has had mixed results, in some cases improving medication safety and in others having deleterious effects [20–22]. Within the imaging strata, CPOE and CDS could follow similar patterns. Initial attempts to demonstrate the utility of imaging CDS in clinical settings were impeded when a significant fraction of imaging orders did not successfully map to an imaging appropriateness guideline, limiting utility and engendering dissatisfaction among users [23]. However, in other settings, the combination of CPOE and imaging CDS have been broadly accepted by users and improved adherence to guidelines for the use of advanced imaging [24]. With the proper attention to provider workflow and user interface and adequate integration of evidence-based guidelines, CDS for advanced imaging has the potential to reduce unnecessary imaging and ensure appropriate utilization.

CDS has the potential to improve efficiency and appropriateness by delivering knowledge at the point of care to inform clinical decision-making. Currently, wide practice variations among providers, practices, health systems, and geographic regions result in underuse, overuse, and misuse of imaging technology [25]. Practice variation increases the likelihood of inefficient and suboptimal care delivery. Variations in clinical practice may result from a number of sources

including knowledge gap about the clinical evidence, information gap about prior imaging, underestimated risks of recurrent radiation, the practice of defensive medicine, and a disconnect between provider accountability and the enterprise financial model [26].

Opportunities for clinical decision support in emergency departments are numerous. Focus areas include appropriate imaging, patient safety, and reporting quality. CDS must provide evidence-based clinical information about the appropriateness of the exam to the provider at the time of ordering. If an examination is inappropriate, recommendations for appropriate care (alternative imaging or no imaging) should be provided. When multiple options for imaging exist, a ranking of the most appropriate examination given the clinical scenario should be provided [26–29]. Expanding beyond the realm of exam appropriateness, CDS plays a role in patient safety. Well-integrated systems that interface with the patient’s EMR can provide clinicians with real-time alerts regarding patient renal function, allergies, or other pertinent clinical data. Radiation safety reminders and alerts can also be embedded in CDS. A CDS system may be viewed simply as tool to help ordering clinicians; however, well-designed and properly integrated systems may also benefit the radiologist at the time of reporting. Radiologists’ practice patterns also vary particularly when it comes to follow-up imaging recommendations for incidental findings [30–32]. CDS can help to appropriately standardize radiologist recommendations reducing variability and improving care.

Speed and functionality are categorically important features of an effective CDS [26]:

1. *Speed*: The relevant information must be delivered in real time and easily accessible to the end user.
2. *Functionality*: The system must be easy to use, navigate, and comprehend. Duplicate data entry is eliminated. CDS is embedded in the workflow and integrated with other information systems. The information must be actionable, evidence based, and up to date. The system allows for audits, feedback, and modification.

CDS can be a useful tool in appropriate imaging utilization and improved care delivery in the emergent setting.

The Diagnostic Procedure: Optimization, Protocoling, and Radiation Management

Summary of Evidence Once imaging is required for an emergent diagnosis, preparation is required to ensure modalities are optimized, imaging protocols efficiently answer clinical questions, and imaging-associated risk is minimized. Leadership in emergency imaging must ensure resources are dedicated to optimizing processes, including the deployment of appropriate HIT tools to communicate appropriate modality protocols and to minimize radiation exposure.

Supporting Evidence Emergency imaging is time sensitive. As the integration of imaging into pathways for acute stroke, pneumonia, and other conditions deepens, optimization of workflows to expedite imaging and to deliver results will involve technologists, nurses, administrators, radiologists, other physicians, and allied health-care providers. Efforts to maximize the value-added portions of this process and to eliminate waste will require a multifaceted approach, which may include workflow optimization, maintaining adequate human resources, and implementing tools such as digital whiteboards, instant messaging, or web forms [33].

When working together with physicists and technologists, emergency radiologists can optimize imaging protocols by indication and patient characteristics to balance speed and image quality while reducing risks from unnecessary radiation and contrast [34–36]. A number of techniques to reduce CT dose have been implemented while maintaining diagnostic accuracy [37–39]. Some patients may receive a significant portion of their care from various emergency departments; therefore, tracking and reporting radiation doses across encounters could alert provider teams to radiation risks that otherwise may not be detected [40–42].

The Diagnostic Result: PACS, VNAs, CAD, and CDS for Radiologists

Summary of Evidence PACS continue to evolve to better support a spectrum of uses, including advanced processing, remote viewing, and interpretation. While several computer-aided detection and diagnostic tools have shown promise, the lack of regulatory approval for diagnosis, vendor support, and reimbursement models remains obstacles for widespread adoption. Clinical decision support for radiologists at the point of interpretation is becoming more widespread.

Supporting Evidence Following the acquisition of imaging data, activities in the imaging value chain should maximize interpretive accuracy and efficiency through well-designed interpretive user interfaces, image processing systems, and clinical decision support designed for practicing emergency radiologists and other providers.

Picture archiving and communications systems (PACS) have long served as the primary systems used for imaging interpretation. Key functions typically found in a traditional PACS include worklist functionality, a diagnostic viewer, and storage for imaging-related data. Most PACS will provide integrated post-processing functionality. As other systems mature in their ability to provide such utility, we are seeing a shift from the current model. Increasingly, electronic medical records (EMRs) are integrating more imaging-centric modules such as worklist capability, integrated clinical context, diagnostic viewing, and voice recognition. The maturing imaging-related capabilities of EMRs in combination with the advent of tools such as diagnostic zero footprint viewers and vendor neutral archives (VNAs) enable more creative combinations of applied technology for emergency imagers who wish to add value from any location or setting, whether in the traditional reading room for a primary interpretation, at their home diagnostic workstation, or with a portable device for consultation when outside the hospital [43].

Traditionally, those desiring advanced image processing such as 3D surface-shaded displays

had to rely on dedicated advanced visualization workstations. Such functionality has been incorporated into PACS or other lightweight viewers, either through inherent capabilities of the viewer or a deep integration with an advanced visualization platform. While many basic reformats, such as orthogonal multiplanar reformats (MPRs), are processed by CT or MR technologists, ED radiologists should expect to be able to perform more advanced reformats of imaging data at the workstation on demand [44]. The most current diagnostic viewers offer integrated 3D reconstruction capabilities without the need to install locally any software, making them available to anyone with access to a secure connection and a browser [45]. We should anticipate the widespread availability of systems which allow remote viewing of any case with full post-processing capabilities through any device as these technologies obtain greater market penetration.

While the potential of ubiquitous computer-aided detection and diagnosis systems has generated much discussion, the applications which have achieved widespread adoption have focused on the detection and characterization of malignant processes such as breast, lung, and colon cancers. There is an increasing body of work describing techniques to detect urgent diagnoses likely to be discovered by an emergency radiologist. Such image processing algorithms have shown some promise in the ability to detect intracranial hemorrhage on CT scans of the head, detect coronary pathology, or detect ischemia in the brain or bowel [46–49]. While these techniques show some promise, adoption in clinical settings is still difficult because the market has not demanded support for these technologies by major vendors. The lack of regulatory approval for diagnosis, vendor support, and reimbursement models remains obstacles for widespread adoption.

A class of tools apart from computer-aided detection and diagnosis systems is being developed to provide decision support to radiologists at the time of interpretation. These tools focus on delivery of appropriate knowledge through textual resources, checklists, and guidelines to radiologists responsible for a wide range of clinical

expertise [50]. These resources emphasize a range of conditions that emergency radiologists may encounter, from non-emergent conditions such as the appropriate management of lung nodules to more acute clinical scenarios such as vertebral compression fractures [51]. Delivery of such decision support tools may be integrated with existing clinical systems or available on a mobile device [52–54]. To date, the number of such solutions catered to emergency imaging has been limited but is expected to increase as demand for “just-in-time” decision support for radiologists grows.

Completing the Diagnostic Process: Structured Reporting, NLP, and CTRM

Summary of Evidence Critical test result management systems have had variable success in helping emergency imagers manage critical and important incidental findings in diverse practice settings. The combination of structured reporting and natural language processing (NLP) shows some promise for automatically detecting the presence of critical findings, reporting discrepancies, or identifying outcomes. Increasing utilization of structured reporting and NLP may help emergency imagers participate in large-scale analytics using “big data” strategies.

Supporting Evidence Once a patient’s emergency imaging is displayed, processed, and interpreted, the next steps in the imaging value chain require a radiologist to effectively communicate results to the appropriate parties. While voice recognition software has largely displaced the role of transcriptionists, the adoption and maturity of associated technologies such as structured reporting, NLP, critical result management, and incidental result management systems vary greatly by location.

Structured reporting and NLP are methods for augmenting the semantic content of a radiology report. Advantages of structured reporting may include improved report completeness for clinical and charge capture purposes, improved standardization between different authors within the

same ED radiology group, and improved referring provider satisfaction [55]. While structured reporting is typically initiated by the reporting provider at the time of report initiation, NLP is utilized once a report has been authored. NLP techniques have been utilized to automatically classify CT reports in the emergency setting with some success [56]. NLP has been incorporated into reporting systems for radiologist decision support for detecting laterality or gender discrepancies within radiology reports or for identifying critical results such as pneumothorax, testicular torsion, or malpositioned lines and tubes within reports [57–60].

The automated reporting of critical results has long been sought after by radiologists. Commercial systems to help with the task of reporting and managing critical results have been marketed for several years. Some aim to facilitate the immediate communication of critical results according to the preferences of the referring provider [61]. However, if the patient has been admitted or discharged or if the original referring provider is off-shift, the radiologist and referring providers alike can quickly become frustrated with such systems. Other commercially available systems create lists to help facilitate the work of a dedicated employee tasked to deliver critical results in a timely fashion, with or without a computerized workflow management system [62, 63]. In some cases, rule-based NLP algorithms may be used to facilitate the creation and curation of these communication worklists. These systems rely on a human to deal with the “musical chairs” problem that occurs when numerous providers care for patients during different portions of their interactions with the medical system, regardless of the original requesting provider. In the emergency setting, delivery of important incidental findings, such as a worrisome pulmonary nodule, can be even more challenging. The referring ED provider may not be the best provider to manage and follow that result. The patient’s primary care physician is entirely removed from the emergency setting [64]. Mechanisms similar to those seen for managing critical results are now available commercially.

When combined, structured reporting and NLP techniques can enable the automated classification

of text reports that otherwise would require a human to decipher their meaning. The potential for automated processes to determine the meaning of radiology reports could enable better approaches to outcomes and correlation with other sources of data, such as genomics or pathology [65]. Furthermore, a failure to leverage structured reporting and NLP where appropriate may leave much radiologic report data undecipherable without human intervention, effectively limiting its full involvement in the impending “big data” revolution in healthcare [66].

Improving radiologists’ performance over time and demonstrating the value of imaging are dependent on the ability of imaging to be linked to outcomes. To date, there have been challenges in categorizing the nature of text-based radiology reports and linking results to outcomes. However, there has been progress in the development of systems which can alert radiologists to patient outcomes related to studies they have interpreted [67]. Such advances, along with the promise of big data in healthcare, suggest that demonstrating the value of imaging and the performance of individual radiologists in a more facile manner may be something we can look forward to in the future [68, 69].

Take-Home Figure

Figure 3.1 summarizes the various components of the imaging process.

Take-Home Points

- Information systems that support diagnostic imaging in emergency settings have the potential to improve efficiency, quality, and patient safety while moderating costs.
- The imaging value chain includes forming a diagnostic **inquiry**, performing a **diagnostic procedure**, establishing a diagnostic **result**, and **completing** communication and follow-up tasks. This cycle serves as a useful framework to assess existing information systems and emerging technologies.

- Information systems will enable health systems to track, assess, and analyze their impact, adoption, meaningful use, and barriers.

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The Consequences of Inappropriate Use of Emergency Imaging

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Key Points

- Utilization of medical imaging in the emergency department has increased in recent decades (moderate evidence).
- Medical radiation accounts for the largest percentage of artificial exposure to ionizing radiation (moderate evidence).
- A direct link between low-level radiation from diagnostic imaging and cancer development has not been proven. However, there is evidence suggesting increased risk of leukemia and brain cancer in children exposed to cumulative CT radiation doses of 50–60 mGy. Most estimates of long-term effects of low-level radiation exposure (100–150 mSv) come from the longitudinal survivor study of atomic bomb survivors (moderate evidence).
- Incidental findings are common and their workup is expensive and may cause undue anxiety, excess radiation

exposure, and risk of additional diagnostic procedures for mostly benign conditions (limited evidence).

- Application of the clinical decision support such as the American College of Radiology (ACR) appropriateness criteria could decrease overutilization in the emergency department setting (limited evidence).

Definitions and Pathophysiology

Overutilization of imaging is defined as application of imaging when it is unlikely to improve outcomes [1]. Over the last two decades, utilization of medical imaging in the emergency department setting has dramatically increased. While imaging undoubtedly saves lives, potential overutilization is concerning for patients, health care providers, and health care payers. For patients, medical imaging is now the largest contributor of radiation exposure to individuals in the USA, the majority attributed to CT. For health care providers, imaging can rapidly aid in diagnosis and identification of life-threatening conditions, but incidental findings may add challenge in patient management. For health care payers, increased imaging utilization has been a major contributor to rising health care costs in the USA.

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Epidemiology

According to the National Hospital Ambulatory Medical Care Survey, CT use during ED visits has increased 460% between 1995 and 2011, from 2.8% of encounters in 1995 to 15.8% in 2011 [2, 3]. In the same time, MRI utilization in the ED has increased 500% from 0.1% to 0.6%, and ultrasound has increased 210% from 1.2% to 3.8% of visits [2, 3]. Increased use of CT was seen in all 20 of the most common complaints presenting to the ED in this time period, with highest growth in abdominal pain, flank pain, chest pain, and shortness of breath [4]. In the pediatric population, CT use increased 23–435% depending on body part imaged between 2000 and 2006, far exceeding growth in patient volume and acuity and mimicking trends in the adult population [5]. In 2012, the last year for which complete data is available, 256.8 CT scans were performed per 1000 people, a rate 25% higher than for the next highest Organization for Economic Cooperation and Development (OECD) (developed) country. 104.8 MRIs were performed per 1000 people that same year, almost twice the average rate of OECD countries [6]. Several factors have likely contributed to the rise in imaging utilization in the USA, including advances in medical imaging, increased accessibility to imaging equipment, 24/7 interpretation by radiologists, fear of litigation, and shifting expectations of patients and emergency department clinicians [1, 7].

Overall Cost to Society

Inappropriate use of imaging in the emergency department results in excess radiation exposure, increased health care costs, and increased time of ED visits and imparts the additional anxiety, costs, and risks associated with incidental findings.

Goals of Imaging

The goal of imaging in the ED is to diagnose or exclude potentially life-threatening medical conditions in symptomatic patients. Screening of

non-symptomatic patients is also performed in the ED in certain scenarios, for example, in protocol-driven imaging of trauma patients and in cases of suspected child abuse.

Methodology

Information from this chapter was obtained primarily through a MEDLINE search using PubMed (US National Library of Medicine, Bethesda, Maryland; <http://www.ncbi.nlm.nih.gov/pubmed/>) from 1980 to March 2015. Keywords were “emergency department radiology overutilization,” “emergency department radiology utilization,” “incidental finding radiology,” and the resultant related fields from this original database. The search was limited to English-language articles. The authors performed a critical review of the title and abstracts of indexed articles followed by the full text of articles that were relevant. Additional relevant articles were selected from the references of reviewed articles and published guidelines.

Discussion of Issues

Overutilization of Diagnostic Imaging in the ED Setting

There has been dramatic growth in imaging utilization in the past two decades. While imaging can provide a key diagnostic step in diagnosis and contribute to swift and appropriate patient care, it is unclear that improvements in outcomes have been commensurate with increases in imaging utilization. For example, between 2001 and 2010, there has been a 2.5-fold increase in CT utilization among adult fall patient ED visits, while the proportion of fall visits with life-threatening conditions has only increased by 2.5% [8]. In patients presenting to the ED with flank or kidney pain, prevalence of CT use increased from 4.0% to 42.5% from 1996 to 2007, while the number of patients ultimately diagnosed with urolithiasis or other significant diagnoses or admitted to the hospital did not sub-

stantially change [9]. In patients presenting to the ED with injury-related conditions, the prevalence of CT and MR use increased from 6% in 1998 to 15% in 2007 without corresponding change in prevalence of visits for which patients were either admitted to the hospital or to an intensive care unit [10]. Growth of imaging utilization has been so dramatic that multiple national campaigns have been established to evaluate and combat overutilization, including Image Gently, Image Wisely, and As Low as Reasonably Achievable (ALARA), and initiatives by the National Council on Radiation Protection and Measurements, the Food and Drug Administration, and the American Board of Radiology Foundation [1, 11–16].

Studies have shown that ER physicians agree that overutilization of imaging is a problem, raising the question of why imaging is so frequently and at times inappropriately utilized. Fear of litigation has been cited as a factor driving imaging utilization in surveys of ED physicians, and imaging ordered for defensive purposes is thought to account for 5–25% of total imaging costs [1, 17, 18]. A survey of ED clinicians also found that concerns about patient satisfaction affect CT ordering decisions [18]. Lack of information about prior imaging studies may be a factor in overutilization, as studies have shown that ED physicians factor cumulative CT count into image ordering decisions only some of the time, but would take this information into account if information was more available [18]. Lack of education about risks of imaging is also a factor driving overutilization. A study of ED physicians found that the majority gave incorrect estimates of cancer risk from a 10 mSv exposure and incorrect estimates of effective radiation dose of a chest X-ray and CT abdomen-pelvis, two commonly ordered imaging exams [18]. Another study found that 75% of physicians underestimated cancer risk from CTs, and >90% of ED physicians and 50% of radiologists did not believe that CT scans increased cancer risk [19, 20]. Additionally, only 3% of surveyed patients believed that CTs increase lifetime cancer risk, and 7% of patients undergoing abdominal CT in the ED reported they had been told about the risks and benefits of their CT scan [20].

The current fee-for-service payment system for health services has been cited as a culprit for overutilization, though is probably less of an issue in the ED setting. Factors within the ED seem to affect utilization, as one study found that odds of low-cost imaging utilization are higher when the ED is slower and high-cost imaging higher when the ED is busier, possibly due to facilitated workup with increased cross-sectional imaging [21].

Risks of Radiation Exposure in Adults and Children

Radiation Terminology

Radiation is measured in standard international units (SI = Systeme Internationale). The intensity of X-ray radiation can be characterized by exposure in coulombs/kilogram or air kerma in Gray (Gy). The absorbed dose is the energy absorbed per unit of mass and is also measured in Gy. The equivalent dose describes the biologic impact to exposed tissue. The effective dose is the sum of products of dose equivalent multiplied by weighting factors depending on the radiosensitivity of exposed organs and is expressed in Sieverts (Sv). The effective dose is used to describe risks from medical imaging in which dose distribution is not homogenous and provides generic estimate of harm to the patient caused by radiation exposure. It should be noted that effective dose is only an estimate of true risk [22, 23]. CT accounts for a large proportion of diagnostic imaging-related radiation dose. CT dose index (CTDI) in mGy and dose length product (DLP), a measure that reflects the product of CTDI and the length of the scan in mGy-cm, describe radiation doses in CT. However, these reported doses represent dose to a phantom. Conversion factors for DLP into effective dose in the adult and pediatric patient have been published for a variety of examinations [24, 25].

Radiation Mechanisms of Effects

X-rays are a type of electromagnetic radiation that contains sufficient energy to overcome the binding energy of orbiting electrons, creating

ions. Ionization, mostly in the form of hydroxyl radicals, can result in DNA strand breaks and base damage. Most DNA damage is repaired, but some double-stranded breaks are not repaired or misrepaired, which can lead to point mutations, chromosomal translocations, and gene fusion. The resulting cell damage may be teratogenic or result in long-term carcinogenesis.

Types of Biological Effects

Radiation effects fall into two categories: deterministic or stochastic. Deterministic effects are only seen above a certain threshold. These effects include cataracts, skin burns, and epilation (Table 4.1) [26–28]. Diagnostic imaging does not typically result in radiation doses high enough to meet the threshold for deterministic effects. Stochastic effects do not have a radiation dose threshold. The risk of a particular effect increases with increasing radiation dose; however, the severity of the effect is independent of dose. Radiation-induced genetic damage and carcinogenesis are stochastic phenomena.

Radiation Exposure in Medical Imaging

Humans are exposed to background radiation from the ground (mostly from radon), building materials, cosmic rays, and food. Average annual background radiation is estimated at 2.4 mSv globally and 3.0 mSv in the USA, primarily due to higher naturally occurring radon levels in the USA [29–31]. An increasing proportion of total radiation exposure in the USA is due to radiation from medical imaging. The average annual dose

due to medical radiation exposure is 0.2 mSv globally and 3.0 mSv in the USA.

Approximately 50% of US annual radiation exposure is due to medical radiation, while in 1980 it contributed less than a quarter of annual radiation dose [1, 32]. Medical radiation is used for both diagnosis and therapy. Diagnostic imaging tests including radiography, fluoroscopy, nuclear imaging, and CT utilize ionizing radiation. Diagnostic imaging uses low-level radiation, defined by effective dose <100–150 mSv. CT accounts for the largest proportion of radiation dose in diagnostic imaging, with effective dose for a whole-body CT scan of approximately 12 mSv. A risk projection model based on Japanese atomic bomb survivor data estimates that 1.5–2.0% of cancers in the USA may be attributable to CT scans [22, 33]. Additional approximate radiation doses for common exams in adults and children are described in Tables 4.2 and 4.3 [29, 34, 35].

There is debate regarding potential carcinogenesis from radiation doses below 100 mSv. The linear no-threshold model for radiation effects is the most widely accepted model for quantifying radiation exposure and is endorsed by the National Research Council in their BEIR VII report. In this model, approximately 1 in 1000 persons will develop cancer from an exposure to 10 mSv over a 70-year lifetime, compared to approximately 420 in 1000 persons who develop cancer unrelated to radiation exposures [29, 36]. There is increased risk for carcinogenesis with radiosensitive tissues that are included in the field (e.g., breast, lung, and thyroid).

Table 4.1 Dose threshold estimates for tissue reactions from single exposure

Injury	Approximate threshold
Reduction of blood cell production in marrow	0.5 Gy
Detectable eye lens opacities	0.5–2 Gy
Skin erythema	2–5 Gy
Temporary epilation	2–5 Gy

Based on data from ICRP Publication 103 2007 [26], ICRP Statement on Tissue Reactions 2011 [27], and UNSCEAR Report to the General Assembly 2013 [28]

Table 4.2 Estimated effective radiation doses for adults

Source	Average effective dose (mSv)
Natural background radiation	3 mSv per year
Chest X-ray (single view)	0.02 mSv
Head CT	2 mSv
Chest CT	7 mSv
Abdominal CT	8 mSv

Based on US data from the National Research Council BEIR VII report [29] and Mettler FA, et al. Effective doses in radiology and diagnostic nuclear medicine: a catalog. *Radiology*. 2008;254–63 [34]

Table 4.3 Estimated effective radiation doses for children

Source	Estimated effective dose (mSv)
Natural background radiation	3 mSv per year
Chest X-ray (2 view)	0.02 mSv
Head CT	4 mSv
Chest CT	3 mSv
Abdominal CT	5 mSv

Based on US data and adapted from the National Research Council BEIR VII report [29] and Brody AS, et al. Radiation risk to children from computed tomography. *Pediatrics* 2007;120:677–82 [35]

Excess Radiation Due to Overutilization of Emergency Imaging

Concerns about radiation safety are particularly pertinent to imaging in the pediatric ED. Children are 2–5 times more sensitive to the effects of ionizing radiation than adults due to increased number of dividing cells and longer lead time to develop cancer [5, 22]. Although the exact effects of imaging-related radiation are not completely understood, studies have reported a positive association between CT radiation dose and subsequent development of leukemia and brain cancer in children and young adults. A recent retrospective study of patients in Great Britain estimated that cumulative CT doses of 50 mGy in patients less than 22 years of age nearly triples the risk of leukemia, and doses above 60 mGy may triple the risk of brain cancer [37]. A 2001 study estimated that with approximately 600,000 abdominal and head CTs performed per year in children <15 years old, 500 children will ultimately die from radiation-induced cancer [38]. Radiation sensitivity generally declines with age, reaching an adult plateau in the fourth decade of life and then slowly declining, with the exception of lung cancer (for which radiation-associated risk may increase into middle age) [38–40].

Many of the patients being imaged in the ED are men and women of childbearing age (or pregnant women). Studies which are occasionally repeated, such as CT for pulmonary embolism and

renal stone CT, place radiosensitive breast tissue or gonads in the radiation field. A study estimated that a single CT for pulmonary embolism may incur a 1.011 relative risk of breast cancer for 25-year-old females and 1.022 relative risk of lung cancer [41]. Non-contrast CT for renal stone detection, which is often performed in young adults, imparts a mean effective dose of 8.5 mSv and dose to the uterus of 23 mGy using multidetector scanners [42, 43]. These exams are often repeated, with one study reporting 4% of patients undergoing CT evaluation for renal colic receiving three or more scans in a 6-year study period [42].

Monetary Costs Associated with Overutilization of Emergency Imaging

The cost of health care in the USA has increased at a rate greater than twice the general rate of inflation and accounted for 16.9% of the GDP in 2014 [44]. Comparatively, the USA has the highest proportion of health care cost for GDP among OECD countries, which average 9.3% of GDP expenditure on health care costs, while life expectancy in the USA is 1.5 years less than the OECD average [44]. Imaging contributes to the high cost of health care in the USA, with a 2005 study estimating inpatient imaging to account for approximately 10% of total hospital cost [45]. Advanced imaging drives the cost of medical imaging. Insurance reimbursements for CT range from \$400 for a cervical spine CT to \$1400 for an abdomen and pelvis CT, with expenditures on CTs equipment estimated at over \$5 billion dollars between 2000 and 2005 [36]. Utilization of imaging in the ED accounts for a large part of imaging costs. For example, non-contrast head CTs in the ED in the USA cost an estimated \$6.1 billion per year [46]. Head CTs and MRIs ordered for dizziness in USA EDs cost \$470 million per year [47, 48]. Reduction in imaging overutilization will be necessary for any cost containment effort in US health care.

Does Imaging Increase Time in the ED?

Time Cost

The addition of medical imaging to diagnostic workup in the ED has been reported to increase patient visit time [49–51]. Imaging has been described as an independent variable in ED length of stay, with one study reporting increased length of stay of 1.0 h for X-ray, 4.7 h for ultrasound, and 0.7 h for CT [49]. Another study of ED visits for injury-related diagnoses found that visits during which CT or MRI was obtained lasted 126 min longer than those without CT or MRI [10]. Eliminating inappropriate imaging utilization may be a key step in reducing ED turnaround time and improving streamlined, effective patient care.

Impact of Incidental Findings in Emergency Imaging

Incidental findings, also known as incidentalomas, are findings identified on imaging that were not previously detected or clinically suspected. In the best scenario, these findings lead to expedited workup and treatment of previously unrecognized medical conditions that improves patient outcome. However, reporting of incidentalomas may also cause undue stress, radiation exposure, and potential morbidity of additional workup for mostly benign or indolent conditions. Additionally, a considerable amount of clinician time may be required to educate patients about implications of incidental findings and ensure appropriate follow-up. When coupled with the monetary cost of workup of incidental findings, this may challenge cost containment efforts for health care provision. Management of incidental findings is challenging due a paucity of data and clear guidelines on appropriate follow-up. Some incidental findings will almost certainly not yield a serious diagnosis and do not need further workup; however, the lack of definitive guidelines makes it difficult for many patients and physicians to accept any uncertainty in diagnosis and results in further testing that is most likely to

reveal a benign diagnosis and could lead to morbidity [52, 53].

Incidental findings are common in ED imaging. Rates of incidental findings in ED patients vary from 34% to 43% in abdominal trauma patients and up to 45% in renal colic patients [54–58]. Rates of incidental findings in all-comers to the ED with CT have been reported at up to 56% for abdomen-pelvis CTs, 46% for chest CTs, and 20% for head CTs. The most common incidental findings include sinus disease, hepatic lesions, pulmonary nodules, adnexal enlargement, and osseous change [54]. For example, one study of ED chest CT Angiograms (CTAs) evaluating for pulmonary embolism (PE) reported 24% of patients to have had incidental findings that required diagnostic follow-up, including new pulmonary nodule in 13% of patients and new lymph node enlargement in 9% of patients [19].

One challenge of detection of incidental findings is effectively communicating findings to patients and documenting this communication. Overall rate of disclosure of incidental findings documented in discharge paperwork varies from 10 to 27% [54, 58, 59]. A recent study found that documented reporting of incidental findings in the ED ranged from 8 to 11% by body area imaged and 0–33% by incidental finding, with highest rates of reporting to patients including aortic dilatations, meningiomas, pulmonary nodules, bone lesions, and enlarged adnexa [54]. While it may be understandable that common and almost certainly benign incidental findings, such as simple renal cysts, are not disclosed or acted upon, follow-up of even moderate and severe findings in the ED patients may be challenging. A study of incidental CT findings in renal colic patients rated findings based on clinical severity and determined that only 18% of patients with “moderate” or “severe” incidental findings had follow-up within 2 years; however, none of these patients had a serious diagnosis on further workup [58].

One common incidental finding on CT is a thyroid nodule. Studies have reported incidental thyroid nodules (ITN) on cross-sectional imaging including the thyroid in up to 16% of patients [60, 61]. These pose a management dilemma, as

their workup is expensive, often invasive, and often yields a benign diagnosis. ITNs are often followed with ultrasound and ultimately fine-needle aspiration (FNA) biopsy, an anxiety-provoking procedure costing up to \$3000 [62]. Of patients undergoing FNA for an ITN, 25–41% proceed to surgery and 36–75% of these surgically excised ITNs prove to have benign pathology [63–66]. Overall malignancy rates of ITNs detected on CT and MRI have been reported at 0% to 11%. However, many of these cancers are small papillary carcinomas, which many experts believe to be subclinical disease.

Hepatic lesions are another common incidental finding, with one study reporting incidental hepatic lesions in 17% of outpatients undergoing CT of the abdomen and pelvis [67]. Workup for incidental hepatic lesions exposes patients to further radiation and at times percutaneous biopsy, a procedure that has morbidity of 2.0–4.8% and mortality of 0.05% [53, 68–71]. Autopsy reports have found as many as 52% of the general population has benign hepatic lesions [72]. It is thus critical to question whether an incidental hepatic lesion places the patient at risk for adverse outcome and to clearly describe scenarios in which imaging characteristics can satisfactorily differentiate benign from malignant lesions.

Universally accepted guidelines for management of most incidental findings in ED patients have not been established. Comparison with prior exams to determine stability of a lesion is critical to radiologists' role in characterizing and managing incidentalomas. The American College of Radiology (ACR) has published a white paper outlining evidence-based recommendations for management of common incidentalomas detected on CT of the abdomen and pelvis based on size criteria, imaging characteristics, and patient comorbidities [53]. Adherence to these recommendations may reduce the variability, cost, and anxiety associated with workup of incidental findings. Further analysis is warranted to establish formal guidelines to establish the appropriate workup of common incidental findings.

Reducing Inappropriate Use of Imaging in the ED

Several methods have been proposed to reduce imaging overutilization in the emergency department. Radiologists may be tasked with an increased role in reviewing imaging orders for appropriateness before studies are performed. Educating clinicians about radiation dose, cost, and limitations of common imaging studies may substantially reduce overutilization [1]. This could be addressed in medical school and repeated throughout training and at meetings of referring physicians. Reducing duplicate imaging studies should be encouraged. Clinical decision support systems for clinicians requesting imaging is also being more widely implemented to reduce the inappropriate exam utilization.

Duplicate studies on ED patient transfer are common, with approximately 60% of patients transferred to a level 1 trauma center undergoing repeat CT exams, most of which do not alter outcomes [73–75]. Some institutions have adopted a standard CT protocol for all trauma patients transferred to the ED. A study at one such institution revealed that patients underwent an average of 4.5 additional CT exams due to fulfillment of the standard trauma imaging protocol. These studies demonstrated unexpected acute findings in 5.9% of transferred trauma patients; however, none of these findings changed clinical management [73]. Duplicate imaging can be reduced utilizing electronic image-sharing technology, which enables image sharing across institutions and should be encouraged to decrease the rate of unnecessary repeat scans. A study evaluating the impact of imaging CT import in ED transfer patients found a 17% reduction in mean rates of all subsequent diagnostic imaging and 29% reduction in post-transfer CT [76].

Clinical decision support is thought to be a key tool in reducing inappropriate radiologic exams. Clinical decision support (CDS) systems can be integrated into computerized order entry (CPOE), providing clinicians real-time evidence-based guidelines for consideration. CDS-CPOE integration has been mandated by the Department

of Health and Human Services and outlined in its Health Information Technology for Economic and Clinical Health Act [77, 78]. CDS has been shown to decrease utilization and increase documented adherence to evidence-based guidelines without delayed reporting of significant findings [79–81]. The optimal CDS-CPOE system is one that would provide real-time feedback with clear, evidence-based guidelines to ordering clinicians [78]. After implementation of a CDS-CPOE system derived from the New Orleans Criteria, Canadian CT Head Rule, and CT in Head Injury Patients Prediction Rule, rates of non-contrast head CT for ED patients with mild traumatic brain injury decreased by 13% with no change in rate of delayed diagnosis of radiologically significant findings [80]. Similarly, implementation of an integrated CDS-CPOE system decreased rates of CT pulmonary angiography in the ED and increased yield of performed studies [79]. The ACR guidelines recommended application of National Emergency X-ray Utilization Study (NEXUS) criteria, which identify patients with low probability of cervical spine injury who do not need imaging, has been estimated to decrease the number of screening cervical spine CTs by 20% in a level 1 trauma center [82, 83]. The ACR has published appropriateness criteria for the most commonly encountered clinical scenarios including radiation risk of commonly ordered exams [84]. These criteria are readily available on the ACR website and may be used as a starting point for imaging-related clinical decision-making [84].

Take-Home Tables

Tables 4.1, 4.2, and 4.3 serve to highlight key information and evidence regarding effective radiation doses for adults and children as well as tissue reactions to a single dose of radiation.

Future Research

Future research should provide:

- Cost-effective analysis of imaging studies based on patient presentation
- Comparative effectiveness research for the use of CT versus laboratory workup or non-ionizing imaging alternatives (US and MRI)
- Formal guidelines for workup of incidental findings
- Radiologist-driven educational interventions for medical students and ED clinicians and analysis of impact
- Analysis of impact of CDS mandate on imaging utilization in the ED

Summary

- There is growing concern that diagnostic imaging is overutilized in the ED setting.
- Inappropriate utilization of imaging can result in excess radiation exposure.
- Inappropriate medical imaging can increase ED turnaround time.
- Incidental findings are common and may result in undue anxiety, cost, and risks associated with additional workup.
- CDS is mandated by the Department of Health and Human Resources. Adherence to ACR appropriateness criteria may decrease overutilization of imaging in the ED setting.

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Part II

Neurological Imaging



Acute Traumatic Brain Injury in Adults: Evidence-Based Emergency Imaging

5

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Key Points

- Traumatic brain injury (TBI) is a heterogeneous group of disorders that encompasses markedly different severities, etiologies, patient ages, and clinical outcomes. Classifications of TBI (e.g., mild, moderate, and severe) are controversial and not universally applied, limiting cross study comparisons.
- No single imaging modality can be universally applied in the investigation of TBI. Each technique has advantages and disadvantages depending upon TBI severity and chronicity, among other factors.
- Non-contrast head CT remains the modality of choice in the acute setting, particularly for moderate to severe TBI, due to rapidity of acquisition, low cost, and widespread availability (strong evidence). These factors, in addition to its use for several decades, have helped contribute to a large body of evidence demonstrating the utility of CT in acute care

prognostication. Sensitivity of detection also increases with repeat scans in the acute period (strong evidence).

- Brain MRI is likely more sensitive and specific for the sequelae of TBI in comparison to CT, with the notable exception of fracture detection, despite the paucity of head-to-head comparison studies (limited to moderate evidence). In particular, MRI outperforms CT in the detection of traumatic axonal injury (TAI) (moderate evidence). Advanced MRI techniques such as diffusion tensor imaging (DTI) allow more exquisite characterization of structural dysfunction in TBI. However, the use of MRI is limited by the length of the exam; lack of availability, particularly in the emergency department setting; and technical difficulties in imaging unstable or uncooperative patients.
- Conflicting demands of patient triage and prognostication contribute to the lack of a universal imaging modality for TBI. In the acute setting, especially for moderate to severe TBI, CT may be the most useful for determination of which patients require immediate surgical or medical intervention (limited evidence). In contrast, MRI may provide better prognostication, particularly in the subacute to chronic time period and for patients with mild TBI.

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Definitions and Pathophysiology

Traumatic brain injury (TBI) encompasses a heterogeneous group of disorders in which intracranial injury is sustained. Historically, the modifying terms mild, moderate, and severe have been applied to TBI based upon the Glasgow Coma Scale (GCS) [1, 2]. Although GCS is widely used and is predictive of outcome in large case series, this scale is controversial due to the difficulty in evaluating patients in the setting of sedation and/or intubation, the effect of age upon GCS score and TBI severity, and the potential for significant patient impairment within the mild TBI group, despite the “mild” nomenclature [3, 4]. Acute TBI can be divided into two groups based on the GCS score: mild and moderate/severe [1]. In general, mild TBI is defined as GCS 13–15, moderate TBI as GCS 9–12, and severe TBI as GCS of 3–8. Moderate and severe TBI are grouped together when considering evidence-based imaging recommendations because they both have a much higher incidence of intracranial abnormality and have been studied more uniformly [5]. Studies of mild TBI have been more complex to review as this term is less well defined in the literature, with synonyms such as minor TBI or concussion in use [6]. Review of mild TBI studies has also been hindered by the use of different clinical inclusion and exclusion criteria. The term mild TBI was first introduced by Rime et al. and refined by Teasdale [7, 8]. In a review paper of acute imaging indications in mild TBI, the most common definition was a loss of consciousness or amnesia as well as GCS scores of 14–15 [9]. In addition, the Head Injury Severity Scale used GCS scores of 14–15 to define mild TBI. Concussion is generally defined as acute, transient disruption of neural function due to mechanical trauma; however, despite its long-term and frequent use both clinically and in research, there is no current consensus on its definition [10]. For the purposes of this chapter, we have avoided the use of the term “concussion” and have combined studies using this term with those investigating mild TBI.

Epidemiology

The Centers for Disease Control and Prevention estimates that at least 1.7 million individuals sustain TBI each year in the United States, with approximately 1.365 million patients treated and released from the emergency department, 275,000 patients hospitalized, and a mortality rate of approximately 52,000 [11]. However, the reported incidence is likely an underestimation as a number of patients with mild TBI never seek medical attention [12]. If these individuals are included in estimates, there may be up to 3.8 million cases of TBI each year in the United States alone, with mild TBI accounting for the majority of injuries [13]. TBI occurs in both civilian and military populations. It is estimated that at least 300,000 episodes of mild TBI occur each year in the United States due to sports or recreation activities. American football has the highest reported prevalence, with up to 15% of high school football players sustaining mild TBI per season [12]. In the United States Armed Forces, there have been an excess of 300,000 cases of TBI from 2000 to 2014, with more than 250,000 classified as mild TBI (mTBI) [13]. For all age groups, males are twice as likely to sustain TBI as females, and children aged 0–4 and 15–19 years old and adults aged 75 years or more are the most likely to experience TBI [14]. The leading causes of TBI in civilian populations in the order of frequency include falls, motor vehicle collisions, struck by/against, and assaults; however, motor vehicle collisions are the leading cause of mortality [14, 15].

Overall Cost to Society

The economic burden of TBI includes both the acute and long-term costs of treatment and lost productivity. A recent conservative estimate of the prevalence of the number of people in the United States living with disability due to TBI-related hospitalization is 3.2 million [16]. Similar to incidence rates, this is also likely an underestimation as this only accounts for individuals with

prior hospitalization and does not include short-term disability and lost productivity due to mild TBI. There are little or no data on costs of TBI related solely to imaging.

Goals of Imaging

The primary goal of acute imaging in TBI is to identify those patients that require urgent surgical and/or medical intervention. Secondary goals include detecting the presence of TBI to verify the diagnosis in cases in which a history of head trauma is not well established (e.g., patients who are “found down,” etc.) and for prognostication purposes.

Methodology

A search of the PubMed electronic database (National Library of Medicine, Bethesda, MD) was performed using combinations of the following keywords: traumatic brain injury, brain injury, TBI, head injury, head trauma, CT, MR, computed tomography, and magnetic resonance imaging. The search was limited to adult human studies and English-language articles. Additional articles were selected from references within the reviewed articles as well as similar articles suggested by the PubMed search engine.

Discussion of Issues

Which Patients with Traumatic Brain Injury Need Imaging?

Summary of Evidence All patients with acute moderate and severe TBI should undergo imaging to assess for conditions that require immediate intervention. Given the availability, rapidity, and evidence supporting its use in the acute setting, non-contrast head CT (NCCT) is recommended for initial imaging (strong evidence). MRI may be indicated in the acute setting if clinical findings are not explained by CT results. In particular, T2*-gradient-echo (GRE) and susceptibility-weighted

imaging (SWI) sequences are sensitive to findings of TAI, although the prognostic value of brain MRI remains undetermined.

Patients with acute mild TBI should be imaged by NCCT if they meet clinical triage guidelines as this modality has a high negative predictive value for excluding abnormalities requiring immediate surgical treatment (strong evidence). Although there is no current consensus on which clinical guideline is the most useful, the Canadian CT Head Rule (CCTH) is the most validated with multiple prospective studies demonstrating 100% sensitivity for the detection of surgical lesions (moderate evidence) [17]. Skull radiographs should not be used as a screening exam in adults with mild TBI (strong evidence). Nuclear medicine techniques, including single-photon emission computed tomography (SPECT) and positron emission tomography (PET), are also not indicated in the acute imaging of TBI (limited evidence). These recommendations are concordant with those of the ACR Appropriateness Criteria for acute head trauma [18, 19].

Supporting Evidence As noted in the Definitions section above, TBI severity is clinically evaluated by GCS score and generally separated into two groups: mild TBI (GCS 14–15) and moderate to severe TBI (GCS <14) [1]. Most evidence-based imaging recommendations incorporate moderate and severe TBI into a single group as both of these have a much higher incidence of intracranial abnormalities than mild TBI and have been studied with more methodological consistency [5]. Also noted above, evidence for imaging mild TBI is more complex to summarize as it is traditionally less well defined with alternate terms in use such as minor TBI or concussion [6]. In addition, studies of mild TBI have used different clinical inclusion and exclusion criteria.

Mild TBI

CT

Historically, the role of imaging in the triage of mild TBI has been controversial with some advocating for routine imaging of all patients and others supporting more selective criteria [20].

As CT became widely available and inexpensive, acute imaging of mild TBI patients became more common, although objective selection criteria remained lacking [21]. The prevalence of acute CT findings in mild TBI patients varies widely between studies, ranging from 6 to 29% with neurosurgical intervention required in a small percentage of cases (0.4–4.2%) [22]. This relatively high likelihood of a negative imaging exam in mild TBI led to the development of risk stratification criteria. For example, patients aged 65 years or older with mild TBI have a higher incidence of positive findings and should undergo NCCT in the acute setting (strong evidence) [23]. By an objective triage process, low-risk mild TBI patients can be safely observed, sparing radiation exposure. In addition, for some patient populations, the cost of acute imaging followed by potential discharge from the emergency department has been shown to be less expensive than admission and observation (limited evidence) [24, 25]. However, attempts to create comprehensive predictive rules have achieved high specificity rates to the detriment of sensitivity, resulting in a large number of false-negative cases [26–28]. Some authors have argued that missing nonsurgical lesions is acceptable; conversely, others have urged that a rule must have 100% sensitivity to any abnormality because of the potential morbidity incurred from an undiagnosed intracranial finding [20, 26, 29–34].

Although at least 25 decision rules have been developed to triage mild TBI patients into those that require head CT and those that may be managed without imaging, the CCTH and the New Orleans Criteria (NOC) are the two most studied and commonly used prediction rules in North America (Table 5.1) [17, 35–37]. The NOC was developed from a prospective study of patients older than 3 years who suffered a mild TBI with loss of consciousness but without a focal neurological deficit. This criteria recommends head CT in any patient with a GCS of 15 possessing any one of the following seven findings: headache, vomiting, seizure, intoxication, short-term memory loss, age >60 years, or evidence of injury above the clavicles [35]. The CCTH was prospectively developed from a cohort of patients at

Table 5.1 Canadian CT Head Rule and New Orleans Criteria

Canadian CT Head Rule	New Orleans Criteria
<i>High risk (neurosurgical intervention likely)</i>	<ul style="list-style-type: none"> • Age > 60
<ul style="list-style-type: none"> • Age > 65 	<ul style="list-style-type: none"> • Headache
<ul style="list-style-type: none"> • GCS score 15 at 2 h post-injury 	<ul style="list-style-type: none"> • Emesis
<ul style="list-style-type: none"> • Signs of skull base fracture (CSF otorrhea, Battle's sign, periorbital ecchymosis, or hemotympanum) 	<ul style="list-style-type: none"> • Anterograde amnesia (short-term memory deficits)
<ul style="list-style-type: none"> • Suspected depressed or open skull fracture 	<ul style="list-style-type: none"> • Intoxication
<ul style="list-style-type: none"> • Emesis more than once 	<ul style="list-style-type: none"> • Seizure
<i>Medium risk (abnormal CT findings likely)</i>	<ul style="list-style-type: none"> • Visible trauma of the head or neck
<ul style="list-style-type: none"> • Retrograde amnesia of >30 min 	
<ul style="list-style-type: none"> • Dangerous mechanism of trauma (fall from greater than 3 feet or five stairs, pedestrian struck, by or ejection from a vehicle) 	

least 16 years of age and with a GCS of 13–15. This rule risk stratifies patients into high-, medium-, and low-risk categories, with head CT mandated in those at high risk (strong evidence) [17]. High-risk patients demonstrate at least one of the following: GCS < 15 at 2 h after injury, signs of calvarial or skull base fracture, at least two episodes of vomiting, or age ≥ 65 . Medium-risk patients have none of the findings found in high-risk patients, but must have amnesia of greater than 30 min preceding the trauma or a dangerous mechanism (pedestrian struck by motor vehicle, motor vehicle ejection, or fall from height of >1 m or five stairs). Although NCCT is recommended in medium-risk patients, close clinical observation may be used as a safe alternative (moderate evidence). Imaging is not indicated for those patients who lack any of these findings, which are defined as low-risk individuals (moderate evidence).

A 2005 multicenter, prospective trial comparing NOC and CCTH found lower sensitivities than initial reports for the detection of CT imaging findings (98% and 87%, respectively), although both rules

showed 100% sensitivity for detection of injuries requiring surgical intervention [38]. The CCTH did outperform the NOC with a higher specificity (39%, 6%) and CT scan rate reduction (37%, 5%). A larger prospective trial comparing the NOC, CCTH, and the National Emergency X-Ray Utilization Study (NEXUS-II), a third set of predictive rules, confirmed the finding of significantly lower sensitivities for clinically important imaging findings than initial studies (75%, 91%, and 84%, respectively) [39, 40]. However, sensitivities for injuries requiring surgical intervention were also remained high in this study (100%, 100%, and 95%, respectively). Of note, NEXUS-II demonstrated the highest CT scan rate reduction but was the only rule in this study that failed to identify 100% of mild TBI patients requiring surgical intervention [39]. This high sensitivity to surgical lesions in both the CCTH and NOC has been reproduced in many studies; however, CCTH consistently demonstrates better specificity when compared to other guidelines [37, 41–45]. One of these prospective studies analyzed independent risk factors of acute intracranial lesion in mild TBI, confirming the utility of the clinical findings that had been previously used in decision rules (Table 5.2) [43]. Finally, a comprehensive meta-analysis of clinical decision rules from 2011 demonstrated CCTH to have sensitivities of 99–100% for surgical lesions and 80–100% for any intracranial injury [46]. Although this meta-analysis found similar sensitivities for NOC, the specificity was much higher with CCTH.

Table 5.2 Clinical findings predicting CT abnormalities in mild TBI

Independent risk factors for CT findings in mild TBI	
Clinical signs and symptoms	Pre-existing conditions
• GCS < 15	• Age > 65
• Loss of consciousness	• Coagulopathy
• Headache	• Hydrocephalus with a shunt
• Emesis	
• Signs of skull base fracture	
• Neurological deficits	
• Significant associated injuries	

New decision rules continue to be introduced and studied prospectively, despite multiple studies validating the utility of several of the current rules [47]. Refinement of the current and more recent rules will continue as further validation studies are performed and new data is included in an effort to reduce false negatives. For example, none of these rule systems incorporate patient demographics with the exception of age; however, a retrospective analysis of more than 80,000 patients found that male gender and African-American ethnicity were also significantly correlated with positive CT findings in mild TBI [22]. Although there is no evidence-based consensus on which mild TBI patients should get imaged, CCTH is the most validated decision rule, identifies virtually all surgical lesions, and significantly reduces imaging overutilization [46]. Despite the lack of a universally accepted imaging algorithm for mild TBI, there is consensus that CT is the preferred initial imaging exam when an intracranial abnormality is suspected (strong evidence) [48–50].

MRI

MRI should not be used in the acute setting for the routine evaluation of mild TBI according to evidence-based guidelines (moderate evidence) [48]. Although MRI is not recommended in typical cases of acute mild TBI, it may be useful when the clinical findings are not explained by the CT results, such as in the presence of persistent or progressive neurologic findings (limited evidence). MRI has consistently been shown to be more sensitive than CT for the detection of injury following mild TBI, especially parenchymal injuries such as contusion and traumatic axonal injury (TAI) [51–58]. However, this increased sensitivity may be of limited utility as the detection of additional intracranial injuries by MRI has not been shown to alter clinical management in the acute setting [59–61].

Over the past decade, there has been a near exponential increase in research using MRI to determine the presence and extent of injury in mild TBI, in particular the use of diffusion tensor imaging (DTI) [62]. This technique provides assessment of structural connectivity dysfunction

in TBI, which may contribute to post-concussion symptoms [62]. Although the changes in DTI metrics may be more uniform and validated following moderate to severe TBI, the changes observed in mild TBI are time dependent and may even demonstrate pseudonormalization in the subacute time period [63]. In addition, the magnitude and possibly the direction of TBI-associated changes in DTI metrics are dependent upon the magnet, sequence parameters, and post-processing software used. This limits cross comparisons between studies and the use of DTI for individual patient decision-making and prognostication [64]. Finally, the current acquisition times for DTI and the significant amount of time required for data post-processing limit the use of this technique in the acute setting. Therefore, while future studies and advances in software and hardware may improve the utility of MRI for acute mild TBI, currently the use of this modality remains largely in the research realm.

Moderate/Severe TBI

CT

There is strong evidence that CT is the preferred initial diagnostic imaging in acute moderate to severe TBI [48, 59, 65]. Although CT is less sensitive than MRI to abnormal findings in acute TBI patients, it is not inferior to MRI for the detection of clinically significant TBI, defined as injury requiring neurosurgical intervention or resulting in death within 7 days [17]. For example, an acute TBI study comparing modalities found that CT was overall less sensitive (63%) than MRI (96%) in detecting intracranial abnormalities, with the exception of fracture (moderate evidence) [52]. However, the additional findings detected by MRI did not alter acute surgical management. Fast, safe, and ubiquitous, CT has many advantages in the acute setting with the only significant disadvantage being radiation exposure [66]. Even if MRI becomes as fast and widely available as CT, patients would have to be screened for MRI contraindications such as ferromagnetic foreign bodies or MRI-incompatible implanted devices prior to imaging, which may be impossible due to altered patient sensorium in the setting of acute TBI.

MRI

The increasing availability and reduced cost of MRI have stimulated interest in its use in the acute setting. Generally, a TBI protocol includes T1- and T2-weighted imaging, T2*GRE, fluid attenuation inversion recovery (FLAIR), and diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) maps [66, 67]. More recently, SWI has been added to TBI imaging protocols as a more sensitive way to diagnose microhemorrhages [68]. Currently, MRI is not indicated for moderate or severe acute TBI unless there are clinical findings unexplained by the CT (moderate evidence) [69].

Many studies have directly compared the ability of MRI and CT to detect acute TBI findings. Comparisons of these modalities have consistently shown MRI to be more sensitive in detecting extra-axial hematomas, nonhemorrhagic contusions, and brainstem injuries (moderate evidence) [58, 70–76]. MRI has proven especially useful in detecting abnormalities in areas traditionally limited on CT, such as the posterior fossa and skull base (moderate evidence) [77]. Nonhemorrhagic contusions can be especially difficult to detect on CT in the acute setting. For example, studies have reported a sensitivity rate for MRI of up to 98% compared to 56% for CT for detection of nonhemorrhagic contusions [77]. MRI has reliably been shown to be more sensitive than CT in the detection of subarachnoid hemorrhage. Specifically, FLAIR sequences are more sensitive than CT in the detection of subarachnoid and small subdural blood products (moderate evidence) [74, 75, 77–81]. A recent study comparing postmortem MRI and CT to autopsy findings found almost identical accuracy, sensitivity, and specificity of the two modalities to TBI findings, although MRI was more sensitive for subarachnoid hemorrhage [70]. A prospective study comparing MRI and CT in the detection of intraventricular hemorrhage found them to be equivalent [32, 82]. However, as intracranial blood products are metabolized, their density decreases which may make detection on CT difficult. Comparison studies have also shown that the GRE sequence is more sensitive for the detection of subacute or chronic blood [58, 74]. Initial studies demonstrated no significant utility

to use of contrast-enhanced MRI for acute TBI [83, 84]. However, contrast may be used to detect the presence of active extravasation in hemorrhagic lesions and thereby predict the need for surgical intervention [85–87].

Imaging of TAI in acute TBI has been of particular interest as a means of grading injury and predicting clinical outcomes. TAI, or diffuse axonal injury, is characterized by injury to axons of the white matter tracts, and the rate of TAI increases with the severity of TBI [88, 89]. Microhemorrhages secondary to acute TBI have been correlated with the presence of TAI in both animal models and postmortem human studies [90, 91]. Although these hemorrhagic lesions are often visible on CT, MRI has demonstrated a greater sensitivity in TAI evaluation, in part because of the increased detection of nonhemorrhagic lesions. TAI lesions can be grouped into three types based on their MRI signal characteristics: type 1, hyperintense on both DWI and ADC likely representing vasogenic edema (T2 shine-through effect); type 2, hyperintense on DWI

while hypointense on ADC likely representing cytotoxic edema (diffusion restricting); and type 3, hemorrhagic [92]. Due to the sensitivity of GRE sequences to the paramagnetic effects of blood products of certain chronicities, the use of GRE results in the detection of more hemorrhagic TAI lesions than CT (Fig. 5.1a–f) [93]. SWI sequences are even more sensitive to microhemorrhages than GRE [68, 94]. A 2011 study comparing interobserver reliability on each of these sequences found that both GRE and SWI were more sensitive than standard T1 and T2 weighting in detecting hemorrhagic lesions [95]. However, hemorrhagic TAI only represents a single type, and relying solely on the characterization of these lesions will underestimate the extent of injury [96]. TBI imaging has historically utilized FLAIR sequences to detect the vasogenic edema associated with axonal injury [77, 97]. DWI and ADC were then used to detect more clinically significant cytotoxic injury seen in acute contusions and TAI [67, 92, 93, 98]. Finally, studies of other imaging methods such as DTI, MR spectroscopy, and magnetization transfer

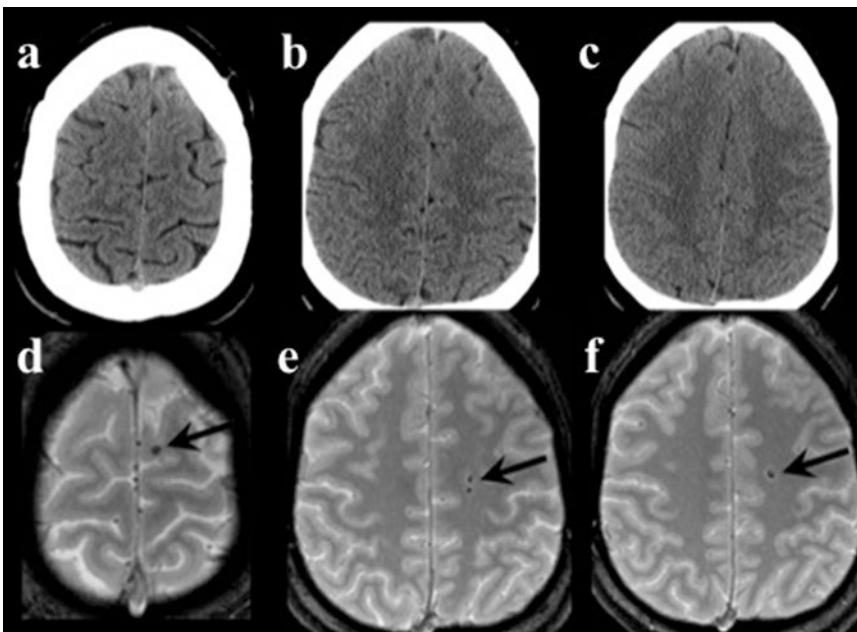


Fig. 5.1 Superiority of MRI over CT in the detection of TAI. Axial images from a NCCT (a–c) obtained at presentation in a 35-year-old man who was involved in a motor vehicle collision. Neurologic examination was normal. Follow-up MRI performed in the same patient within 24 h demonstrates several tiny foci of susceptibility on

susceptibility-weighted imaging (SWI) that are occult on NCCT (d–f, axial SWI images obtained at the same levels as NCCT) (Images courtesy of Max Wintermark, MD, MAS, MBA, Professor of Radiology, Stanford University and Medical Center.)

imaging may allow further delineation of axonal injury, although these techniques have not been fully validated and remain limited in the acute setting [66].

In spite of studies accumulating in favor of its use in acute TBI, MRI remains of limited practical application in this setting. Some of the reasons for this include longer imaging times, sensitivity to patient motion, and incompatibility with metallic foreign bodies and medical devices such as mechanical ventilators and pacemakers [18]. In addition, studies of acute TBI imaging have found that MRI rarely alters clinical management, although it may have prognostic value (moderate evidence) [60, 99–102].

Other Imaging Modalities

Before the advent of cross-sectional imaging, skull radiographs were used to screen for a fracture in even trivial scalp wounds [103]. More judicious ordering patterns developed after studies showed that patients could be risk stratified, with radiographs deferred in low-risk groups [104, 105]. Finally, a meta-analysis of skull radiography in mild TBI found that the sensitivity was only 38%, and the positive predictive value was 41% for detection of intracranial hemorrhage [106]. Given the much higher sensitivity and positive predictive value for the detection of intracranial injuries with cross-sectional imaging, skull radiographs do not play a role in the evaluation of TBI (strong evidence).

SPECT and PET imaging have also been studied in the setting of TBI. SPECT has been studied in TBI for its use in improving lesion detection over CT and MRI, prognostication, and treatment interventions. In a 2014 review of SPECT in the setting of TBI, the authors found strong evidence for its use in each of these areas [107]. While occasionally a patient with TBI may have acute symptoms not be explained by either CT or MRI findings, and this could potentially be addressed with SPECT imaging, the value of SPECT is predominantly in the subacute and chronic settings. PET has also been studied in TBI, but with more mixed results. Initially, acute areas of injury will demonstrate decreased metabolism; however, these same regions can become hypermetabolic

soon after injury [66]. The use of SPECT and PET in the acute setting is hindered by the length and cost of the examinations and, therefore, is not recommended. A 2015 review of TBI imaging found no evidence for PET use in acute TBI, although it may be used in clinical research to study its pathophysiology and treatment effects [108].

What Is the Sensitivity of CT for Detection of TBI Findings Requiring Surgical Intervention? Is There Value in Performing Serial CTs in Acute TBI?

Summary of Evidence CT is the preferred imaging in acute TBI as it has nearly 100% sensitivity for the detection of findings requiring surgical intervention (strong evidence) (Fig. 5.2a–d).

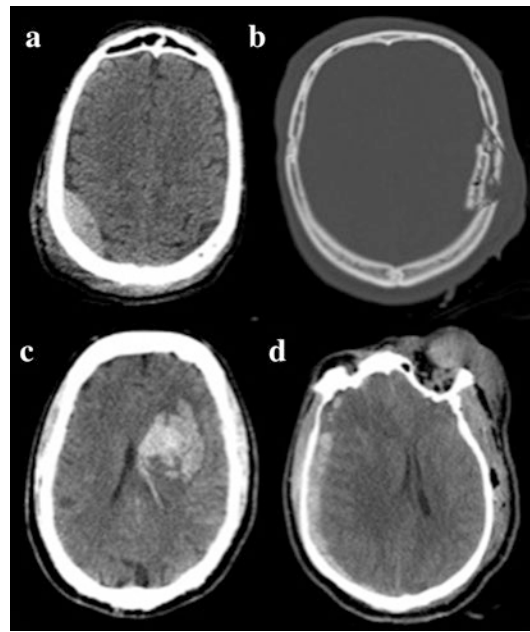


Fig. 5.2 Examples of NCCTs in patients with acute TBI requiring surgical intervention. A 69-year-old man presented after physical assault with a right parietal epidural hematoma (a). A 32-year-old man was found to have a complex left temporoparietal depressed skull fracture after assault with a blunt object (b). A large left frontal lobe intraparenchymal hematoma (> 30 cc in estimated volume) was present in a 66-year-old man after physical assault (c). A 39-year-old man suffered a large right cerebral convexity subdural hematoma after motor vehicle collision with ejection (d)

Serial CT may also increase sensitivity in the acute setting and should be performed in moderate and severe TBI patients as well as all TBI patients with neurological decline after initial imaging or those on anticoagulation (strong evidence).

Supporting Evidence The incidence of significant imaging findings increases with severity of injury; CT in moderate and severe TBI patients is more often abnormal than in mild TBI patients. Even in mild TBI patients, those with GCS less than 15 are more likely to have imaging abnormalities than those with GCS of 15 [38, 109]. However, a normal GCS score of 15 does not guarantee a normal imaging study; for example, one study reported that even among TBI patients with a GCS of 15, 18% of them had abnormal findings on CT with 4% requiring surgical intervention [30]. A 2011 systematic review of studies of mild TBI patients found a median prevalence of acute CT imaging abnormality in about 7% of patients [46]. In addition, the median prevalence of an acute lesion requiring surgical intervention was about 1%. A prospective study of moderate TBI patients found that the incidence of significant CT findings was 61% [5]. Abnormal CT findings are highest in severe TBI. A review article found that the incidence of abnormal CT in these patients ranged from 68 to as high as 94% [110].

The pathophysiology of TBI is a dynamic process. Acute imaging findings are not static and can evolve over short time intervals, occasionally requiring repeat head CT. A prospective study of CT in moderate and severe TBI patients found that the initial CT underestimated the extent of hemorrhage in almost 50% of patients and recommended routine repeat imaging in all patients with intracranial hemorrhage (strong evidence) [111]. A systematic review of repeat CT studies in TBI found that the likelihood of progression and the need for surgery were correlated with clinical severity of initial injury and also recommended repeat CT, but in a select group of risk-stratified patients [112]. A large prospective study provided additional evidence that repeat CT was most likely to show progression of acute findings in the setting of severe TBI [113].

Finally, a 2014 meta-analysis reported that approximately 10% of moderate and severe TBI patients undergo a change in management due to repeat imaging [114]. Additional factors can influence the decision to routinely repeat imaging in acute TBI patients. One retrospective study demonstrated that all TBI patients receiving anticoagulation therapy were also at significantly increased risk of progressive hemorrhage and should receive a follow-up CT in 12–18 h [115]. In addition, patients who demonstrate acute neurologic deterioration following their initial imaging should also receive repeat CT, although the exact time interval has not been studied prospectively (moderate evidence) [111, 113, 116].

The value of repeat imaging in mild TBI is less certain. A retrospective study of repeat CT in mild TBI found that although there may be interval progression of the imaging findings, significant changes were always predicated by clinical deterioration and argued against routine follow-up imaging in these patients [117]. A 2012 retrospective study of mild TBI found that subfrontal and temporal contusions as well as large hematomas (>10 ml) were more likely to worsen after initial imaging and suggested more selective use of repeat imaging [118]. However, a meta-analysis of routine repeat CT studies in mild TBI found no significant effect on clinical outcomes with only about 2% of patients having a change in clinical management [114]. Therefore, at this time, follow-up imaging in patients with mild TBI should be dictated by clinical factors, and routine repeat imaging is likely not warranted.

What Is the Prognostic Value of Imaging in TBI?

Summary of Evidence Mild TBI outcomes are not correlated with initial CT findings. When combined with clinical classification systems such as Corticoid Randomisation After Significant Head (CRASH) injury or the International Mission on Prognosis and Analysis of Clinical Trials (IMPACT), CT findings are correlated with long-term outcomes in moderate and severe TBI (moderate evidence). However, these likely cannot

be applied to individual patients and are best used in populations or research trials.

Currently, there is no definite evidence that conventional MRI sequences are correlated with outcomes in TBI; however, advanced MRI sequences have been shown to be correlated with long-term outcomes in TBI patients across the severity spectrum (moderate evidence).

Supporting Evidence Prognostication in TBI was initially studied using clinical measures such as GCS scores or physiologic markers. In fact, age, motor score, and pupillary reactivity have been consistently correlated with prognosis since the earliest models were proposed [119]. As CT and MR imaging became more prevalent in the setting of acute TBI, prognostic models were developed which also incorporated these findings. The outcomes measured vary between papers, but are often evaluated at least 6 months after the initial injury. Although multiple objective measures of outcomes have been developed, the Glasgow Outcome Scale Extended is the best studied and is recommended by multiple reviews [120, 121].

CT

Predictors of outcome in TBI have been most extensively studied for moderate and severe TBI. One of the earliest attempts at classifying CT findings to predict TBI outcomes was in a large series of severe TBI patients [122]. In this 1983 paper, initial CT findings were correlated with final outcomes by categorizing them into one of eight different patterns such as diffuse axonal injury, single brain contusion, or extra-axial hematoma. Since that time, several different classification systems have been proffered for stratification/prognostication of TBI patients by CT findings. Developed in 1991 from a larger study of moderate and severe TBI patients, the Marshall classification predicted outcomes by sorting patients into one of six different classes based on CT findings such as the presence of mass lesion or signs of elevated intracranial pressure (Table 5.3) [123]. A review of CT imaging in severe TBI outcomes found that initial CT abnormalities, Marshall CT classification, compressed basal cisterns, and traumatic subarachnoid

Table 5.3 Marshall CT classification system

Marshall CT classification system	
Category	Definition
Diffuse injury I	No abnormal CT findings
Diffuse injury II	Cisterns present, midline shift of ≤ 5 mm, and/or lesions present; no lesion >25 cm ³
Diffuse injury III	Cisterns compressed or absent and midline shift of ≤ 5 mm; no lesion >25 cm ³
Diffuse injury IV	Midline shift >5 mm; no lesion >25 cm ³
Evacuated mass lesion (V)	Any surgically evacuated lesion
Non-evacuated mass lesion (VI)	Any lesion >25 cm ³ not surgically evacuated

hemorrhage each demonstrated 70% or greater positive predictive value (moderate evidence) [110]. One of the drawbacks to the Marshall classification is that it requires a priori knowledge of whether or not a mass lesion was surgically resected. While this requirement does not hinder TBI research, it does limit the clinical utility of the classification system in real time. In addition, the volume of the largest mass lesion is required for the Marshall classification, and measurements may be difficult for nonuniform lesions, such as subdural hematomas. The Rotterdam score is a CT-based scoring system more recently developed in an attempt to improve upon the Marshall classification, which allows for greater discrimination by parsing out individual CT findings (moderate evidence) (Table 5.4) [124]. This score was developed retrospectively using recursive partitioning and logistic regression analysis from a database of more than 2000 patients enrolled in an international TBI drug therapy trial. Rather than a classification, a patient's CT findings are scored based on independent findings such as midline shift, subarachnoid hemorrhage, or compression of the basal cisterns. In contradistinction to the Marshall classification, the Rotterdam score does not require lesion volumes or knowledge of surgical intervention. In addition, this scoring system takes into account the more favorable outcomes associated with epidural hematomas as compared to other types of intracranial hemorrhages [110]. Most recently, a third classi-

Table 5.4 CT scoring systems—Rotterdam and Helsinki

Rotterdam score		Helsinki score	
Finding	Score	Finding	Score
Basal cisterns		Mass lesion	
<i>Normal</i>	0	<i>Subdural hematoma</i>	2
<i>Compressed</i>	1	<i>Intracerebral hematoma</i>	2
<i>Absent</i>	2	<i>Epidural hematoma</i>	−3
Midline shift		Mass lesion size >25 cm ³	2
≤ 5 mm	0	Intraventricular hemorrhage	3
> 5 mm	1	Suprasellar cisterns	
Epidural mass lesion		<i>Normal</i>	0
<i>Present</i>	0	<i>Compressed</i>	1
<i>Absent</i>	1	<i>Obliterated</i>	5
Intraventricular blood or SAH			
<i>Absent</i>	0		
<i>Present</i>	1		
Total (add 1)	1–6	Total	−3 to 14

fication scheme, the Helsinki CT score, has been described, which combines variables from the Marshall classification and Rotterdam score [125, 126]. Similar to the Marshall classification, the Helsinki CT score does require lesion volume measurements, although surgical intervention is not included in the final score (Table 5.4). It remains to be seen if the Rotterdam or Helsinki CT scores outperform the more validated Marshall classification in TBI prognostication.

The classification/scoring systems described above represent a small handful of the more than 100 published TBI prognostic models, the majority of which were generally not validated on other populations and were of overall poor quality [127, 128]. In an attempt to create more robust, validated outcome models, two newer classification schemes incorporating both clinical and CT findings were developed based on large patient groups—IMPACT and CRASH [119, 129, 130]. The IMPACT model was developed from moderate and severe TBI patients in wealthier nations, whereas the CRASH model was developed from mild, moderate, and severe TBI patients in less wealthy nations and includes major extracranial

injury as a predictor. These models have been externally validated in large datasets and were found to be equivalent (moderate evidence) [131]. However, IMPACT and CRASH are not considered accurate enough for application to individual patients' outcomes and instead should be applied to populations and clinical research, describing overall probabilities [132, 133].

In contrast to moderate and severe TBI, there is no consensus currently on the significance of CT findings in mild TBI, limiting the development of prognostic models [134]. Although clinically similar in the acute setting, mild TBI is a heterogeneous disease process, and subgroups of these patients have significantly different long-term outcomes [134, 135]. Mild TBI is generally subdivided into uncomplicated and complicated types, with uncomplicated subtype demonstrating normal CT and conventional MRI imaging whereas complicated subtypes have abnormal imaging [136]. Even within the uncomplicated subtype, post-concussive symptoms may persist in some patients with negative CT exams, and more advanced imaging may be required to predict outcomes [34, 137].

MRI

MRI performed early in acute TBI may have prognostic value and is the subject of ongoing studies [138]. Early investigators found that conventional FLAIR, DWI, and ADC sequence abnormalities were not correlated with initial GCS or outcomes [61, 139]. Subsequent studies specifically looking at TAI lesions have demonstrated correlation with GCS scores as well as clinical outcomes (moderate evidence) [95, 100, 140, 141]. These routine sequences have been used to quantitatively assess TAI and predict functional outcomes [142]. A study by Moen et al. investigated TAI lesions detected acutely after injury and reported vasogenic lesions that resolved spontaneously were correlated with better clinical outcomes [143]. A 2014 prospective study of TAI lesions found that the number, volume, and location of these lesions correlated with clinical outcomes in severe TBI (strong evidence) [144]. Abnormal DTI metrics have also been demonstrated to be correlated with TAI and allow

more sensitive, quantitative evaluation of white matter tract disruption [145]. Studies of DTI have found correlation with initial GCS scores as well as long-term outcomes (moderate evidence) [146–150]. A prospective trial of mild TBI patients found that combining clinical factors with acute MRI findings using only conventional sequences significantly improved outcome prediction [134]. A prospective trial in severe TBI patients using the IMPACT score alone versus IMPACT combined with DTI found significantly increased accuracy in 1-year outcomes (moderate evidence) [151]. Nonetheless, given the current disadvantages associated with acquiring MRI in the acute setting detailed above, as well as the lack of standards for DTI metrics across different magnet vendors and post-processing software and the complex time course of TBI-associated changes in DTI metrics, the use of advanced diffusion imaging in the emergency department cannot be currently recommended (limited evidence).

Take-Home Tables

Tables 5.1 through 5.4 highlight various criteria, classifications, and scoring systems, as well as clinical findings.

Take-Home Points

- TBI is a heterogeneous group of disorders, and classifications of TBI (e.g., mild, moderate, and severe) are controversial and not universally applied.
- Non-contrast head CT remains the modality of choice in the acute setting, particularly for moderate to severe TBI.
- Brain MRI is likely more sensitive and specific for the sequelae of TBI than CT; however, the use of MRI is limited by multiple factors, and the detection of additional abnormalities has not been demonstrated to alter acute patient management. MRI may be more useful for long-term prognostication, particularly for mild TBI, although supporting evidence is currently lacking.

Imaging Case Studies

The advantages and limitations of CT and MRI in the imaging of TBI are highlighted by the cases below.

Case 1

Figure 5.1a–f demonstrates the superiority of MRI over CT for establishing TAI, using the case of a 35-year-old man who experienced a motor vehicle accident.

Case 2

Figure 5.2a–d gives examples of NCCTs in various patients needing surgical intervention for acute TBI.

Suggested Imaging Protocols

- CT: axial 5-mm images reconstructed in standard and bone algorithms.
- MR: sagittal and axial T1-weighted, and axial T2-weighted, FLAIR, T2*-weighted GRE or SWI, and DWI.

Future Research

- Despite decades of research investigating the diagnosis and prognostication of TBI using imaging, clear consensus views are few, particularly for mild TBI. This is in part related to the heterogeneous nature of TBI itself, which is influenced by multiple variables such as mechanism of injury and patient age. In addition, clinical definitions of TBI are lacking, in particular for mild TBI or concussion, and entry into TBI studies is frequently based upon clinical parameters. Standardization of clinical and imaging definitions, as well as of imaging reporting, will facilitate the multi-institutional large studies that are required to overcome individual heterogeneity in TBI.

- Given the increasing availability and speed of MRI, further study in the use of this modality in head-to-head comparison with NCCT in the acute setting is warranted.
- Further investigation of the utility of advanced MRI techniques, such as DTI, in the diagnosis and prognostication of TBI needs to be performed. This is particularly true for mild TBI, in which conventional imaging may be normal but patients may have significant clinical symptoms. In order for DTI to be clinically useful, obstacles such as differences between scanners and post-processing vendors need to be overcome so that uniform guidelines may be established.
- Prognostication algorithms need to be developed that encompass both clinical and imaging findings. These then need to be validated in large, multi-institutional studies.

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Pediatric Accidental Traumatic Brain Injury: Evidence-Based Emergency Imaging

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Key Points

- The PECARN decision rule can help identify children in whom imaging after TBI is unnecessary (strong evidence).
- In the acute TBI setting, CT is the imaging modality of choice because of availability, speed, and importance in deciding emergent neurosurgical approach (moderate evidence).

- MRI is the preferred imaging modality in children with TBI who need additional imaging and in children with subacute or chronic TBI (moderate evidence).
- Advanced neuroimaging techniques are emerging as a potential tool for diagnosis, to guide management and to predict prognosis in pediatric patients with TBI (limited or insufficient evidence).

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Definitions and Pathophysiology

The definition of TBI used by the Centers for Disease Control is a disruption in the normal function of the brain that can be caused by a bump, blow, or jolt to the head or a penetrating head injury [1].

The pathomechanism in TBI relates to primary and secondary brain injury. Primary brain injury refers to effects that result directly from transfer of external mechanical forces to the contents of the brain. These include diffuse axonal injury (Fig. 6.2a–c), focal contusions (particularly in frontal and temporal lobes), and extra-axial hemorrhages (epidural, subdural, subarachnoid) (Fig. 6.3) [2]. Secondary brain injury is the result of a cascade of molecular mechanisms that are

initiated at the time of initial trauma and continue for hours or days, such as excitotoxicity, oxidative stress, mitochondrial dysfunction, apoptosis, and inflammation [2]. In mild TBI, the underlying mechanism is usually an acceleration-deceleration event, not direct impact [3].

TBI can be classified based on clinical severity, mechanism of injury, and pathophysiology, each of which may impact prognosis and treatment. Most commonly TBI is classified based on the Glasgow Coma Scale (GCS) score, where a GCS of 9–12 is moderate TBI and a GCS of <9–12 is severe TBI [2]. Mild TBI is defined as a GCS of 13–15, loss of consciousness <30 min, and post-traumatic amnesia <24 h [4].

Computed tomography signs of focal injury (epidural and subdural hematomas, parenchymal contusions) or diffuse injury (axonal injury, diffuse cerebral edema) can be used as predictors for mortality after moderate or severe TBI. The two most commonly used systems for outcome prognostication are the Marshall classification [5] and the more recent Rotterdam scale [6]. The Marshall classification is a set of injury classes with fixed definitions, while the Rotterdam score accounts for individual patient differences in signs of cerebral edema, degree of midline shift, presence of epidural mass effect, and presence of intraventricular or traumatic subarachnoid blood [6]. The majority of patients with clinical criteria of mild TBI have no CT imaging findings, but it has been shown that a subset of 6–10% of these patients are CT positive [7] and another subset of 27% of these patients are CT negative and MRI positive [8].

Epidemiology

In the United States in 2010, there were 2.5 million patients with TBI; approximately 87% of these patients came to the emergency department, 11% were admitted, and approximately 2% died. These statistics likely underestimate the occurrence rate of TBI because outpatient visits and TBI in patients who did not seek medical care were not captured [1]. In a large European study, the incidence of TBI was reported as 235 per 100,000 per year [9].

Worldwide data show peak incidences in children, young adults, and in the elderly population [10].

Mild TBI totals 80–90% of all TBI cases, and it has been reported that one third of these patients experience prolonged physiological or neuropsychological complications and commonly take long times off work [11].

In the United States, the following etiologies are most commonly the cause of TBI: motor vehicle accidents (20–45%), falls (30–38%), occupational accidents (10%), recreational accidents (10%), and assaults (5–17%) [11]. TBI can also occur in contact sports, such as American football, ice hockey, soccer, boxing, and rugby.

Male gender doubles the risk for TBI. 50% of patients with TBI are between 15 and 34 years old, and age <5 years or >60 years are considered a moderate risk for TBI.

Other risk factors are lower socioeconomic status, lower cognitive function, and a history of hospital admissions for intoxications [11].

Overall Cost to Society

For the year 2000, it was reported that the cost for hospitalization of children with TBI was over \$1.0 billion, ranking fifth of most expensive hospital diagnoses for children in 2000 [12]. The CDC reports that in 2010 estimated direct and indirect medical costs of TBI were approximately \$76.5 billion [1].

Goals of Imaging

Neuroimaging is important for detecting and delineating extent of traumatic brain injury in children. Its main role is the timely detection of brain injuries that require further management. Advanced neuroimaging is used in the study of primary and secondary brain injuries and their relationship to outcomes after TBI.

In children it is particularly important to identify those with TBI who are at low risk and do not need to undergo CT brain imaging in order to avoid unnecessary radiation exposure to this vulnerable population.

Methodology

Information on definition, pathophysiology, risk factors, epidemiology, and goals of imaging were retrieved from the Centers for Disease Control 2015 Report to Congress “Traumatic Brain Injury in the United States: Epidemiology and Rehabilitations” and from UpToDate.

The remaining information was obtained through a comprehensive Medline search (United States National Library of Medicine database) for original articles published between January 1, 2005 and May 24, 2015 using the PubMed search engine. The search was limited to English-language articles and human studies. Additional relevant articles were selected from the references of reviewed articles and published guidelines. The following search terms were used: “pediatrics,” “brain injuries,” “traumatic brain injury,” “TBI,” “costs and cost analysis,” “costs,” “analysis,” “costs and cost analysis,” “guideline,” “guidelines [as topic],” “decision rule,” “PECARN,” “CATCH,” “CHALICE,” “applicability,” “implementation,” “compliance,” “research,” “CT protocol,” and “MRI protocol.”

Discussion of Issues

What Clinical Practice Guidelines Are Available to Determine Which Children Do Not Need Imaging After Traumatic Brain Injury (TBI)?

Summary of Evidence The PECARN (Pediatric Emergency Care Applied Research Network) guideline has the highest sensitivity (100%) in identifying children with TBI who are at low risk for brain injury and do not need to undergo CT brain imaging (strong evidence). The use of this guideline reduces CT utilization, which may result in a decrease of radiation-induced malignancy rates, cost of care, and lower net quality-adjusted life-year loss (strong evidence). The CATCH (Canadian Assessment of Tomography for Childhood Head injury) and CHALICE (Children’s Head injury Algorithm for the predic-

tion of Important Clinical Events) decision tools also demonstrated very high sensitivities (98 and 98.1%) in identifying high-risk children who require brain CT imaging (strong evidence).

Supporting Evidence

PECARN (Pediatric Emergency Care Applied Research Network)

The PECARN guidelines (Fig. 6.1) were published in 2009 [13] and are the results of a prospective cohort study performed in patients <18 years old across 25 emergency departments. The goal of this study was to determine a set of predictive criteria for clinically important TBI (ciTBI) and to identify children at low risk for ciTBI in whom CT imaging could be avoided. The PECARN rule was shown to have a 99.95–100% negative predictive value [13, 14], 100% positive predictive value [15], and 100% sensitivity [16]. Children with a GCS <14 are not included in this rule.

Two studies compared PECARN, CHALICE, and CATCH [17, 18]. It was shown that PECARN had the highest sensitivity (100%) and that CHALICE was most specific (84–85%) [17, 18]. CHALICE was applicable to most patients (97%), followed by PECARN (76%) and CATCH (26%) [19].

A study using decision analytic modeling in a hypothetical cohort of 1000 children with minor blunt head trauma, the PECARN strategy missed slightly more children compared to hypothetical “usual” care, but there was decreased utilization of cranial CT scans. This could theoretically cause fewer radiation-induced malignancies and cost less, and there could be a lower net quality-adjusted life-year loss (strong evidence) [20].

There is variability in adherence rates to the PECARN rule. An Italian tertiary care academic pediatric emergency department implemented the PECARN rule and achieved a 93.5% adherence [15], while an implementation across four hospital emergency departments in Spain showed that only one hospital achieved compliance in >50%, of patients, and the other hospitals complied in <50% [21].

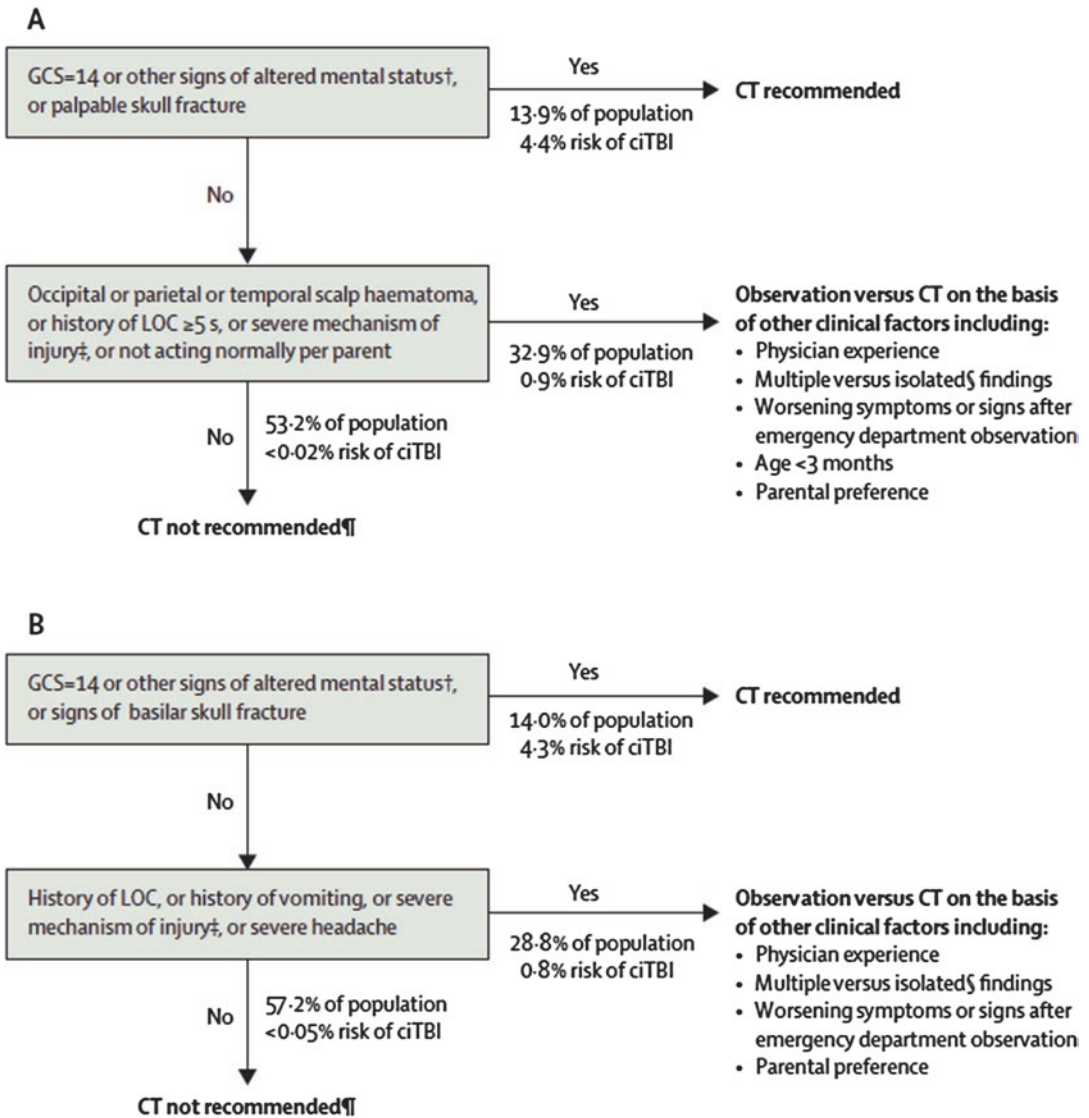


Fig. 6.1 PECARN criteria for TBI in children <2 years of age. (Used with permission from Kuppermann N, Holmes JF, Dayan PS, et al. Identification of children at very low risk of clinically important brain injuries after head trauma: a prospective cohort study. *Lancet*. 2009 Oct 3;374(9696):1160–70). †Altered mental status: other signs of altered mental status: agitation, somnolence, repetitive questioning, or slow response to verbal communication. ‡Severe mechanism of injury: motor vehicle crash with patient ejection, death of another passenger, or rollover;

pedestrian or bicyclist without helmet struck by a motorized vehicle; falls of more than 0.9 m (3 feet); or head struck by a high-impact object. ***CT not recommended: risk of ciTBI exceedingly low, generally lower than risk of CT-induced malignancies. Therefore, CT scans are not indicated for most patients in this group. ****Patients with certain isolated findings such as isolated LOC, isolated headache, isolated vomiting, and certain types of isolated scalp hematomas in infants older than 3 months have a risk of ciTBI substantially lower than 1%

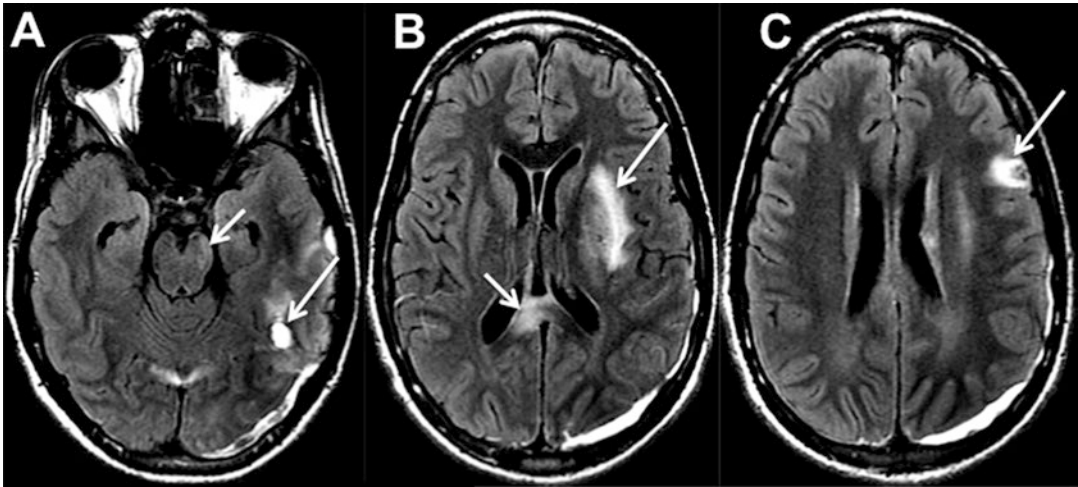


Fig. 6.2 (a–c) Grading of diffuse axonal injury (DAI). Axial FLAIR images in a 14-year-old girl with TBI after rollover motor vehicle accident. DAI is graded based on regional involvements: Grade 1 is used for injuries of the gray-white matter junction (a, b, c, *long arrows*). Grade 2 involves the corpus callosum (b, *short arrow*) in addition

to the gray-white matter junction. Grade 3 refers to brainstem involvement (a, *short arrow*) in addition to the gray-white matter junction and the corpus callosum. This patient has DAI grade 3. In addition, this patient has a left subdural hemorrhage



Fig. 6.3 Extra-axial hemorrhage. Axial non-contrast CT in a 4-year-old boy with traumatic brain injury after fall from a balcony. Note the mixed density, crescentic extra-axial collection on the left (*long arrows*). There is associated mass effect with diffuse sulcal effacement and midline shift (*short arrows*)

CATCH (Canadian Assessment of Tomography for Childhood Head Injury)

The CATCH guidelines were published in 2010 [22] and are the results of a prospective multicenter cohort study performed in patients <16 years with a GCS of 13–15. The goal of this study was to develop a decision tool for identifying children with minor TBI who should undergo CT imaging [22]. The CATCH rule was shown to have a sensitivity of 98.1% [22]. A validation study is pending [16].

CHALICE (Children's Head Injury Algorithm for the Prediction of Important Clinical Events)

The CHALICE guidelines were published in 2006 [23] and are the results of a prospective multicenter cohort study in England, performed in patients <16 years. The goal of this study was to derive a decision rule to aid in identification of children at high risk who should undergo CT imaging of the brain. The rule was applied to

children, regardless of GCS, and was shown to have a sensitivity of 98% [23]. A validation study is pending [16].

Which Imaging Modality Should Be Used in Children with TBI?

Summary of Evidence The benefits of non-contrast brain CT imaging include availability and speed of imaging, its ability to detect hemorrhages, mass effects, and fractures. The major disadvantage is radiation exposure. In children of any age with minor head injury, with a GCS of 14–15, and without neurologic signs or high-risk factors, the PECARN rule (Fig. 6.1) can be applied to determine who can safely be observed and who needs to undergo CT brain imaging (strong evidence).

In children <2 years of age, axonal injury is more common, and therefore brain MRI plays a greater role, although non-contrast CT brain remains the modality of choice in the initial evaluation (moderate evidence). In children of any age with minor head injury who are symptomatic or in children with moderate and severe head injury, non-contrast CT brain is most appropriate in detection of any acute traumatic injuries that require monitoring or treatment interventions (strong evidence). In this patient population, it is unlikely that MRI will detect neurosurgically relevant lesions, but MRI may detect axonal injury that could be missed by CT [24].

MR imaging is useful in patients with acute TBI and neurological findings and negative CT. MR imaging is superior in the detection of brain pathology in patients with mild, subacute, and chronic TBI (moderate evidence). CT criteria in patients with moderate and severe TBI play a role in predicting mortality (moderate evidence) [6].

In children of any age with subacute or chronic TBI, MRI is the imaging modality of choice (moderate evidence).

The use of various imaging modalities in pediatric traumatic TBI should be in agreement with the American College of Radiology (ACR) Appropriateness Criteria® Head Trauma – Child, last updated in 2014 [24].

Supporting Evidence The American College of Radiology (ACR) Appropriateness Criteria® Head Trauma – Child, last updated in 2014, give an overview of study results on which recommendations are based upon [24].

In non-accidental head injury, there is considerable debate regarding the selection of appropriate imaging techniques. More details can be found in Chap. 34 on non-accidental injury of infants and children.

What Is the Role for Advanced Neuroimaging in Pediatric TBI?

Summary of Evidence Magnetic resonance spectroscopic (MRS) imaging can help in predicting outcome after TBI. Single-photon emission computed tomography (SPECT) hypoperfusion abnormalities may be an indicator of a worse outcome in children (limited evidence). Brain positron emission tomography (PET) metabolic abnormalities may also predict outcome (limited to moderate evidence). Data about functional MRI (fMRI), MR perfusion, and diffusion tensor imaging (DTI) are limited in the adult population, even more so in the pediatric population. Susceptibility weighted imaging is helpful in detecting microhemorrhages related to shearing injury (or diffuse axonal injury) not seen on conventional MRI. DWI has been shown to improve detection of non-hemorrhagic shearing lesions, although there are only a few small studies describing sensitivity in adults; please see Chap. 5 on acute traumatic brain injury in adults for more details. The role of advanced neuroimaging in pediatric patients is not entirely clear for many of its applications, but some prognostic information is obtained as will be described below. Large studies are required with these advanced imaging modalities to determine the role and outcome after TBI.

Supporting Evidence

MR Spectroscopy (MRS)

MRS can detect subtle cellular abnormalities that may more accurately estimate the extent of brain injury, particularly in diffuse axonal injury (DAI)

(limited to moderate evidence). Makoroff and colleagues studied 11 children with TBI and documented elevated lactate and diminished N-acetylaspartate (NAA) in several brain regions, in four children with global ischemic injury (limited evidence) [25]. Holshouser and colleagues performed MRS in 40 children with TBI 1–16 days after injury and correlated this with neurologic outcome 6–12 months after TBI [26]. A logistic regression model demonstrated a significant decrease in the NAA/creatinine and increase in the choline/creatinine ratios in normal-appearing ($P < 0.05$) and visibly injured brain ($P < 0.001$). In normal-appearing brain, NAA/creatinine decreased more in patients with poor outcomes (1.32 ± 0.54) than in those with good outcomes (1.61 ± 0.50) (limited evidence). Babikian and colleagues studied 20 children and adolescents and demonstrated a moderate to strong correlation of decreased NAA and worse cognitive scores (limited evidence) [27]. Ashwal and colleagues demonstrated in 38 children with TBI that the occipital glutamate/glutamine in the short-echo MRS was significantly increased in TBI when compared with controls (limited evidence) [28]. They also demonstrated that occipital gray matter myoinositol in 38 children with TBI was increased (4.30 ± 0.73) compared with controls (3.53 ± 0.48 ; $P = 0.003$). In addition, patients with poor outcomes 6–12 months after injury had higher myoinositol levels (4.78 ± 0.68) than patients with good outcomes (4.15 ± 0.69 ; $P = 0.05$) (moderate evidence) [29], indicating that myoinositol elevation after pediatric TBI is associated with a poor neurologic outcome. Ashwal and colleagues also demonstrated significant decreases in NAA-derived ratios and elevation of Cho/Cre measured in occipital gray matter within 13 days of neurological insult. These metabolite changes correlated with poor neurological outcome at 6–12 months after injury ($n = 52$) (limited evidence) [30]. In a subgroup of these patients ($n = 24$), neuropsychological evaluations were performed at 3–5 years after neurological insult. It was found that these metabolite changes strongly correlated with below average functioning in multiple areas including full-scale IQ, memory, sensorimotor, and attention/executive functioning (limited evidence) [31].

Diffusion Tensor Imaging (DTI)

DTI requires special software that maps the degree and direction of water diffusion along major fiber bundles based on diffusion-weighted imaging (DWI). DTI can detect the impaired connectivity of white matter tracts, even in normal-appearing tissue. Few studies have studied the role of DTI in pediatric patients with TBI. Treble and colleagues studied 74 children with TBI and 49 controls with DTI tractography of eight callosal subregions in relation to measures of verbal and visuospatial working memory [32]. They found that lower fractional anisotropy (FA) and higher radial diffusivity in callosal subregions connecting anterior and posterior parietal cortical regions predicted poorer verbal working memory. Additionally, higher radial diffusivity in callosal subregions connecting the anterior and posterior parietal as well as temporal cortical regions predicted poorer visuospatial working memory. They concluded that reduced microstructural integrity of the corpus callosum might act as a neuropathological mechanism contributing to long-term working memory deficits in TBI. This may help early identification of children at higher risk of working memory deficits and earlier intervention (limited evidence). Oni and colleagues examined DTI in 46 children with moderate-to-severe TBI and 47 children with orthopedic injury 3 months post-injury [33]. Significant group differences in frontal lobe white matter DTI metrics (FA, apparent diffusion coefficient, and radial diffusivity) were identified that were predictive of later Glasgow Outcome Scale (GOS) ratings (limited evidence). Therefore, DTI could serve as an index of white matter integrity in TBI and as a potential biomarker for the outcome. Levin and colleagues studied DTI in 32 children with moderate-to-severe TBI, compared to 36 children with orthopedic injury [34]. They found that fractional anisotropy and apparent diffusion coefficient (ADC) values differentiated the groups and that both cognitive and functional outcome measures were related to DTI findings. Dissociations were present wherein the relation of FA to cognitive performance differed between the TBI and OI groups. A DTI composite measure of white matter integrity was related to global outcome in

children with TBI (limited evidence). McCauley et al. evaluated incentive effects in prospective memory after TBI with DTI in 40 children with TBI and 37 children with orthopedic injury [35]. Children underwent an event-based prospective memory test under two motivational enhancement conditions (low and high motivation) and had concurrent DTI 3 months after injury. The FA of the left cingulum bundle, left orbito-frontal white matter, and bilateral uncinate fasciculi predicted performance in the high-motivation condition. They concluded that these white matter structures are important in mediating event-based prospective memory responses following moderate-to-severe TBI in children (moderate evidence).

Mayer et al. examined FA, axial diffusivity, and radial diffusivity in 15 pediatric patients with mild TBI and in 15 healthy controls [36]. Results showed that patients with TBI had increased anisotropic diffusion and a higher number of clusters with increased anisotropy. Measurements of increased anisotropy differentiated TBI patients from controls with 95% accuracy but were not associated with neuropsychological deficits (limited evidence). Wozniak and colleagues studied 14 children with TBI and 14 controls aged 10–18 years who had DTI studies and neurocognitive evaluations at 6–12 months [37]. The TBI group had lower FA in three white matter regions: inferior frontal, superior frontal, and supracallosal. Supracallosal FA is correlated with motor speed and behavior ratings (limited evidence). Parent-reported executive deficits were inversely correlated with FA. A few other small studies (insufficient to limited evidence) have shown decreased anisotropy in brain parenchyma of TBI patients [38–40].

Functional MRI (fMRI)

Functional MRI (fMRI) can provide noninvasive serial mapping of brain activation, such as with memory tasks. This form of imaging can potentially assess the neurophysiological basis of cognitive impairment, with better spatial and temporal resolution than SPECT or PET. However, it is susceptible to motion artifact and requires extremely cooperative subjects and

therefore is more successful in mildly injured rather than moderate or severely injured patients as well as in older children and adolescents. There have only been a few small studies (insufficient evidence) with adults and even less with pediatric patients, attempting to correlate fMRI with outcomes. Fourteen pediatric subjects with mild TBI who underwent fMRI to investigate its effects on auditory orienting had decreased activation within the bilateral posterior cingulate gyrus, thalamus, basal ganglia, midbrain nuclei, and cerebellum, with spatial topography of hypoactivation similar to previous studies in adults [41]. These patients showed no significant deficits in other measures of attention. The findings suggest that fMRI could potentially serve as a biomarker for subtle injury caused by mild TBI and documenting the course of recovery (limited evidence).

A pilot study by Krivitzky et al. examined 13 children with symptomatic mild TBI using fMRI during tasks of working memory and inhibitory control [42]. Children with mild TBI showed greater activation in the posterior cerebellum and addition of a demand for inhibitory control in comparison with the control group (limited evidence). These findings suggest that children with mild TBI may experience disrupted neural circuitry. Newsome and colleagues studied eight children with moderate-to-severe TBI and eight matched, uninjured control children with fMRI using an N-back task to test effects of TBI on working memory performance and brain activation [43]. Two patterns in TBI patients were seen: Patients whose criterion performance was reached at lower memory loads than control children demonstrated less extensive frontal and extrafrontal brain activation than controls; patients who performed the same highest memory load as controls demonstrated more frontal and extrafrontal activation than controls (limited evidence). These were small series, and further longitudinal studies are needed.

Susceptibility Weighted Imaging (SWI)

Susceptibility weighted imaging (SWI) is a modified gradient echo (GRE) high-spatial resolution 3D MR technique that accentuates the paramag-

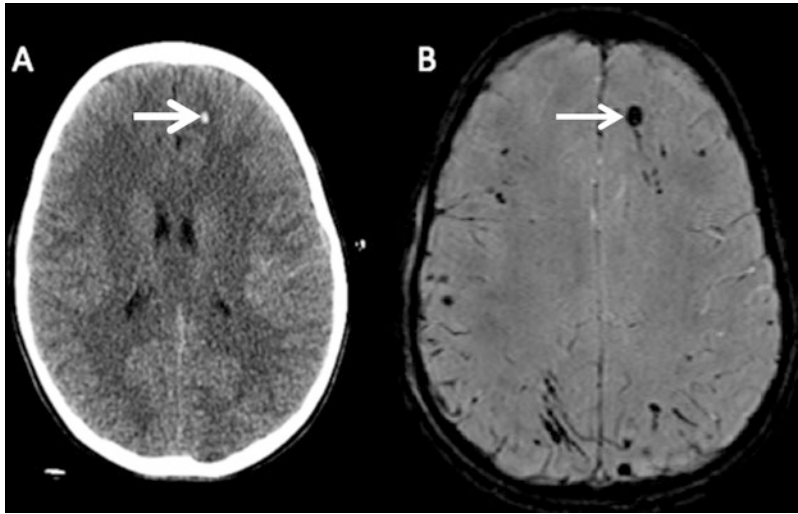


Fig. 6.4 DAI in CT versus SWI; both exams were performed the same day. An 11-year-old female with altered mental status after motor vehicle accident, thus fulfilling PECARN criteria for imaging. Axial head CT (**a**) shows a hyperattenuating focus at the gray-white matter junction in the left frontal lobe in keeping with a focus of hemorrhagic axonal shearing injury (*black arrow*). Axial MRI using susceptibility weighted imaging (**b**) shows the focus with low signal intensity representing susceptibility artifact. This sequence proves that this dominant focus is only

the tip of the iceberg as there are several other hypointense foci representing bilateral microhemorrhages related to diffuse axonal injury. For the astute viewer, linear areas of hyperattenuation in the left subarachnoid space on CT have no hypointense correlate in susceptibility weighted imaging and are thus favored to represent vascular congestion rather than subarachnoid hemorrhage. DAI diffuse axonal injury, SWI susceptibility weighted imaging

netic properties of blood products, which disturb the magnetic field and result in a loss of MRI signal. This technique is particularly helpful in detecting cerebral microhemorrhages related to DAI that are not seen on CT or conventional MRI, and SWI has been shown to detect more hemorrhagic lesions than GRE (Figs. 6.4a, b and 6.5a, b) [44–46].

Microhemorrhages can cause long-term deficits, and detecting them is important for the treatment and prognosis in patients with TBI, particularly in those who have no ominous findings with conventional imaging (moderate evidence). Tong et al. studied 40 children with TBI using SWI to detect hemorrhage (moderate evidence) and found that children with lower GCS scores (≤ 8 , $n = 30$) or prolonged coma (>4 days, $n = 20$) had a greater average number ($P = 0.0007$) and volume ($P = 0.008$) of hemorrhagic lesions [47]. Beauchamp et al. evaluated the relationship

of SWI to the outcome after TBI in 106 children with varying levels of TBI who underwent SWI [48]. Subjects completed an assessment of intellectual functioning, processing speed, and behavioral and adaptive skills 6-month post-injury. The number and volume of SWI lesions were significantly correlated with clinical outcome variables including GCS, surgical intervention, length of hospital stay, and length of intubation, as well as with intellectual functioning. SWI and GCS accounted for significant proportion of the variance in IQ. They concluded that SWI shows promise in the prediction of cognitive outcomes in the initial stages post-injury (moderate evidence) [48]. Babikian and colleagues studied 18 children and adolescents 1–4 years after injury using susceptibility weighted imaging showing negative correlations between lesion number and volume with neuropsychological functioning (limited evidence) [49].

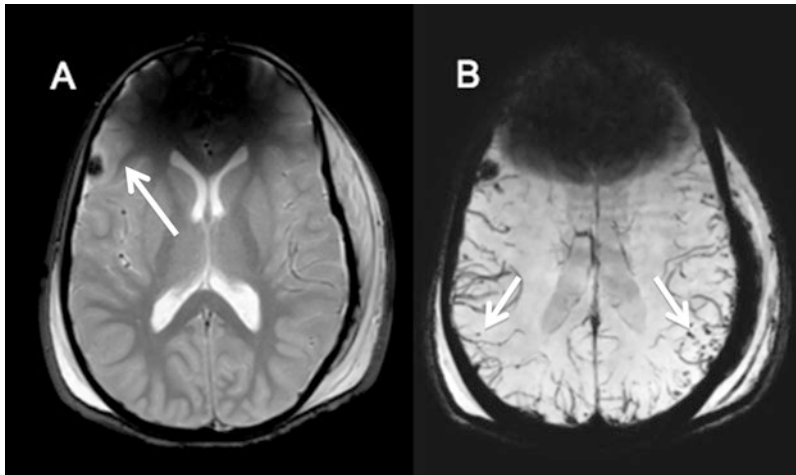


Fig. 6.5 DAI in MRI: GRE versus SWI in a 14-year-old male following a motor vehicle accident. Axial GRE sequence (a) shows a hypointense focus in the periphery of the right frontal lobe (*white arrow*) representing hemorrhage of diffuse axonal injury. Axial SWI (b) shows sev-

eral other foci of microhemorrhage (*white arrows*) that were not seen in the conventional GRE sequence, thus better depicting the severity of injury. *DAI* diffuse axonal injury, *GRE* gradient recalled echo, *SWI* susceptibility weighted imaging

Positron Emission Tomography (PET)

Positron emission tomography (PET) can measure regional glucose and oxygen utilization, cerebral blood flow (CBF) at rest, and CBF changes related to performances of different tasks. Spatial and temporal resolution is limited, although better than with SPECT. PET is not widely available, uses high ionizing radiation, and requires patient cooperation. A few PET studies evaluating patients of different ages have reported various areas of decreased glucose utilization, even without visible injury. Bergsneider and colleagues prospectively studied 56 patients with mild to severe TBI, evaluated with ^{18}F fluorodeoxyglucose (FDG)-PET within 2–39 days of injury, 14 of which had subsequent follow-up studies. They found that TBI patients demonstrate a triphasic pattern of glucose metabolism changes that consist of early hyperglycolysis, followed by metabolic depression, and subsequent metabolic recovery (after several weeks) (limited to moderate evidence) [50]. Wu and colleagues evaluated gray and white matter with PET in 14 TBI patients, and 19 normal volunteers studied with a quantitative FDG PET, a quantitative H_2 ^{15}O -PET,

and MRI acutely following TBI [51]. The gray to white matter ratios for both FDG uptake rate and changes of glucose metabolic rate were significantly decreased in TBI patients ($P < 0.001$) (limited evidence). The changes of glucose metabolic rate decreased significantly in gray matter ($P < 0.001$) but not in white matter ($P > 0.1$). The glucose to white matter ratios of changes in glucose metabolic rate correlated with the initial GCS of TBI patients with $r = 0.64$. Patients with higher changes in glucose metabolic rates (>1.54) showed good recovery 1 year after TBI. Another study by Lupi and colleagues examining PET in 58 consecutive patients (age range 14–69 years), with 44 having TBI, demonstrated a relative hypermetabolic cerebellar vermis as a common finding in the injured brain regardless of the nature of the trauma (limited evidence) [52]. A recent clinical validation study of FDG PET and fMRI in disorders of consciousness was performed by Stender and colleagues in 126 patients (48 of whom had TBI) with unresponsive wakefulness syndrome (vegetative state), locked-in syndrome, or in a minimally conscious state [53]. The validation of cerebral FDG PET and fMRI used the

Coma Recovery Scale-Revised (CRS-R) as a reference for diagnostic accuracy. Outcome after 12 months was assessed using the GOS-Extended. FDG PET was more sensitive for identification of patients in a minimally conscious state than fMRI (95% versus 45%, respectively). In addition, FDG PET had higher congruence with behavioral CRS-R scores than fMRI (85% versus 63%, respectively). FDG PET correctly predicted outcome in 74% and fMRI in 56% of the patients. Therefore, they concluded that FDG PET could be used to complement bedside examinations and predict long-term recovery of patients with unresponsive wakefulness syndrome (moderate evidence).

Cost-Effectiveness Analysis

The advanced imaging modalities are not readily available in many of the clinical settings. Additionally, they can be expensive and time-consuming and require patient cooperation. At present, the role of advanced imaging modalities in evaluating pediatric patients with TBI is uncertain from an evidence-based standpoint. More data is necessary in order to define what contribution these modalities can add to the diagnosis, management, and/or prognosis of the patients.

Take-Home Figure

Figure 6.2a–c presents PECARN criteria to be used for TBI in children less than 2 years old.

Imaging Case Studies

Case 1

Figure 6.3 presents the grading of a diffuse axonal injury (DAI) in a 14-year-old girl with TBI.

Case 2

Figure 6.1 presents an extra-axial hemorrhage in a 4-year-old boy with traumatic brain injury.

Case 3

In Fig. 6.4a, b, a diffuse axonal injury is presented in CT and SWI images of an 11-year-old girl who experienced a motor vehicle accident and altered mental status thereafter.

Case 4

Figure 6.5a, b presents diffuse axonal injury as imaged by MRI (GRE and SWI) in a 14-year-old male who experienced a motor vehicle accident.

Case 5

Figure 6.6a, b presents a parietal skull fracture as imaged by CT 3D skull reconstruction and maximum intensity projection.

Suggested Imaging Protocols

CT Brain

When using CT imaging in children, in order to decrease radiation exposure, (1) the kVp and mA should be adjusted for each size and age group, (2) the area should only be scanned once, and (3) only the area of interest should be included in the field of view [Image Gently: CT]. A typical trauma head CT acquisition includes helical 5 mm axial images with axial 2.5 mm reformatted images in bone and soft tissue algorithm, 2.5 mm coronal soft tissue reformats, and 3D bone reconstruction and maximum intensity projections (MIPs) of the skull (Fig. 6.6a, b) [54, 55].

MRI Brain

The use of brain MR imaging in children may require procedural sedation. Access to MRI in the emergency setting may be difficult, and image acquisition times are long. The major benefits of

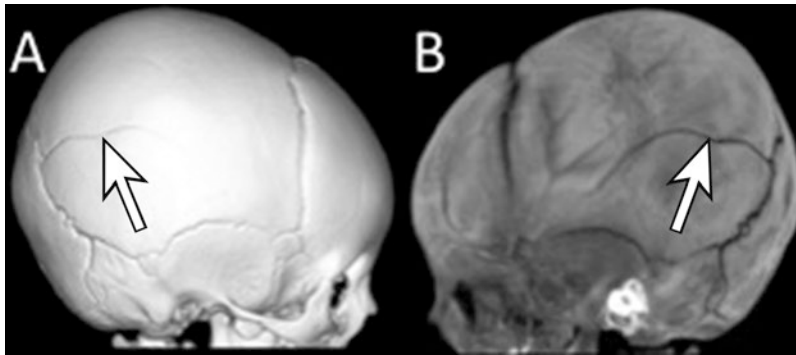


Fig. 6.6 Computed tomography: 3D skull reconstruction and maximum intensity projection (MIP) of a parietal skull fracture. This right parietal skull fracture in a 9-month-old patient was not identified on axial CT images

due to its orientation parallel to the axial imaging plane. 3D reconstruction (**a**) and MIP (**b**) were instrumental in identification of this fracture (*arrows*)

MRI are (1) the lack of radiation exposure and (2) the ability to detect axonal injuries and small bleeds with higher sensitivity compared to CT. For children the routine brain imaging protocol includes sagittal T1 (5 mm or isometric 1.5 mm with multiplanar reconstructions), 5 mm axial T2 with fat saturation, 5 mm axial FLAIR, 3 mm axial DWI, 5 mm axial susceptibility weighted imaging, and 5 mm coronal T2.

Research Imaging

Advanced imaging techniques that have been used in the study of TBI include susceptibility weighted imaging (SWI), diffusion tensor imaging (DTI), diffusional kurtosis imaging (DKI) cerebral perfusion/permeability MR imaging, MR spectroscopy, resting-state functional MR imaging, positron emission tomography, and magnetoencephalography. These techniques allow for quantitative rather than qualitative imaging assessments and may facilitate statistical correlations to enhance knowledge of TBI and its prognosis [56].

Future Research

- Validation of PECARN in abusive head trauma
- Determination of actual cost savings related to the use of PECARN criteria

- Multicenter studies to assess prognostic value of various advanced neuroimaging methods
- Imaging predictors of outcomes after TBI
- Define the role of advanced neuroimaging techniques in pediatric patients with TBI

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Traumatic Extracranial Vascular Injury in Adults: Evidence-Based Emergency Imaging

7

Jessica Warsch, Gary H. Danton,
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Key Points

- Screening for vascular injuries in high-risk patients decreases morbidity and may be cost-effective (moderate evidence).
- Multidetector CT (MDCT) has variable sensitivity and specificity for diagnosing vascular injury in patients with blunt neck trauma; however, results from recent studies bolster its clinical utility (moderate evidence).
- MDCT has high sensitivity and specificity for diagnosing vascular injury in patients with penetrating trauma (moderate evidence).
- Digital subtraction angiography remains the gold standard for diagnosing vascular injury following trauma (moderate evidence).

Definition and Pathophysiology

Blunt trauma injuries most often occur in the setting of motor vehicle accidents but can happen with any direct blow to the craniocervical region, strangulation, in sports-related incidents, and as a result of spinal manipulation. The majority of penetrating neck injuries involve guns and knives, with motor vehicle accidents and industrial and household accidents comprising the remainder. Injury of the carotid and/or vertebral arteries of the neck in blunt and penetrating trauma can occur through a variety of mechanisms, from direct transection, to shearing of blood vessels from hyperextension of the cervical spine, to disruption by fractures, and is an important cause of morbidity and mortality in trauma patients.

Epidemiology

Traumatic injury is the leading cause of death and disability for young adults, accounting for 1 in every 8 male deaths and 1 in every 14 female deaths [1]. Blunt and penetrating neck injuries comprise 5% and 5–10% of adult trauma cases, respectively [2, 3]. In the pediatric population, blunt injuries are much more common, accounting for 90% of all pediatric trauma admissions [4]. While the majority of significant vascular injuries to the neck are seen in victims of penetrating

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trauma, the morbidity and mortality related to blunt cerebrovascular injuries is significantly higher—one-third to one-half of blunt trauma victims develop permanent neurologic complications due to brain ischemia from vascular compromise, and the mortality rate from blunt injuries is 20–30% versus 2–6% for penetrating injuries [3]. And the annual nationwide incidence of the diagnosis of blunt traumatic extracranial cerebrovascular injury is increasing, according to a study using the Nationwide Inpatient Sample Database, likely secondary to the increasing use of aggressive CT angiography (CTA) screening protocols and advancements in CT technology [5]. Indeed, while early studies estimated the incidence rate of blunt cerebrovascular injury (BCVI) to be as low as 0.08% in all blunt trauma cases, higher incidence rates ranging from 0.3% to 1.60% have been reported more recently [6].

Overall Cost to Society

Comprehensive screening for vascular injuries in blunt and penetrating neck trauma patients is likely to be cost saving in terms of hospital and rehabilitation costs through earlier diagnosis and prompt treatment [7]. For instance, CTA was found in a recent decision analysis to be the most cost-effective screening strategy for patients at high risk for BCVI, with the lowest cost (\$3737 per patient screened) and stroke rate (1%) [8].

Goals of Imaging

Performing diagnostic imaging of the neck in high-risk trauma patients will rapidly identify extracranial vascular injury in time to apply evidence-based treatments and decrease risk of morbidity and mortality.

Methodology

A MEDLINE search was performed using PubMed (National Library of Medicine, Bethesda, Maryland) for original research publications

discussing the use of imaging modalities in blunt and penetrating neck injuries. The search strategy employed different combinations of the following terms: blunt or penetrating, neck trauma or neck injury, radiography or imaging or computed tomography and/or angiography or CTA or MDCT, and cerebrovascular or vascular or carotid and/or vertebral. The search covered the period from January 1980 to June 2015 and was limited to studies in humans and publications in the English language. The authors reviewed the full text of all articles identified from the literature search and included additional publications identified from their reference lists.

Discussion of Issues

How Are Patients Selected for CT Screening Following Trauma?

Summary of Evidence The current approach to the evaluation of patients with penetrating neck injuries is one of selective surgical management based on clinical examination and the results of MDCT angiography (limited evidence).

In cases of blunt injury, the use of CTA as a screening tool has been more controversial, due to variability in its diagnostic accuracy in the current literature. However, several recent studies have supported the use of CTA, especially in patients with a high pretest probability of BCVI (moderate evidence). The Denver classification and Denver modifications are the most often cited criteria in identifying those patients for whom screening is most appropriate [9].

Supporting Evidence

Blunt Trauma

There are no consistent recommendations for standardized screening algorithms to rapidly and accurately detect BCVIs. The majority of studies, including those by Biffi et al. [10–12], have advocated for the screening of patients based on mechanism of injury (e.g., closed head injury, rapid deceleration, and hyperextension as occur during motor vehicle accidents; direct cervical

blow; strangulation; or chiropractic manipulation), patterns of injury, including concomitant head and chest injury, and clinical exam findings including cervical hematoma, Battle's sign, chest wall contusion, altered mental status, lateralizing neurologic signs, and stroke or transient ischemic attack (limited evidence) [10, 13–16]. However, while a greater number of these risk factors are associated with a higher likelihood of BCVI, these vascular injuries have been found to occur in approximately 20% of patients without any of the known risk factors [17, 18]. Additional indicators including mandibular fractures, basilar skull fracture, complex frontal skull fractures with orbital involvement, and combined traumatic brain injury and thoracic injury may increase the sensitivity for BCVI [19]. Restricting the use of CTA to Denver protocol screen-positive trauma patients was found in one registry-based study of 30 blunt trauma patients in Auckland City Hospital to decrease the use of CTA as a pre-emptive screening tool by 95–97% [20]. Berne et al. developed multivariate logistic regression models to explore the relative roles of a number of clinical factors in determining which patients should be screened with MDCT (moderate evidence) [21]. The factors that were found to be most predictive of the presence of BCVI, and may therefore justify imaging, were cervical spine fracture (odds ratio (OR) = 7.46, 95% confidence interval (95% CI) = 4.87–11.44) and mandible fracture (OR = 2.59, 95% CI = 1.30–5.15). Other clinical parameters did not demonstrate a clear increase risk including high injury severity score (OR = 1.05, 95% CI = 1.04–1.07) and low Glasgow Coma Scale score (OR = 0.93, 95% CI = 0.89–0.97). In their prospective cohort study, Lohrer et al. recently developed a screening and management protocol applicable for both mild and severely injured patients and feasible in a level I trauma center setting; trauma patients who met inclusion criteria modeled after the Denver criteria underwent CTA as part of standard diagnostic procedure upon admission [22]. After screening for the inclusion criteria, their BCVI detection rate improved from 2.75% to 36.3%, and they were successful in preventing any strokes in patients without primary thromboembolic

Table 7.1 Screening criteria for BCVI

<i>Modified Denver Screening Criteria^a</i>
Infarction demonstrated by brain CT
Lateralizing or central fixed neurologic deficit (not explained by imaging findings)
Nonexpanding cervical hematoma
Massive epistaxis
Anisocoria/Horner's syndrome
Glasgow Coma Scale score < 8
Cervical spine fracture
Basilar skull fracture
Severe facial fracture (LeFort II or III)
Seatbelt sign above clavicle
Cervical bruit or thrill
<i>Other proposed criteria^b</i>
Scalp degloving
Complex skull fractures
Mandibular fractures
Traumatic brain injury with thoracic injuries
Thoracic vascular injuries

^aModified Denver Screening Criteria for BCVI as described by Eastman et al. [9] and based on data from Biffi et al. [10]

^bData from Burlew et al. [58]

Adapted from Danton GH, Warsch JRL, Munera F. Traumatic Extracranial Vascular Injury: Evidence-Based Neuroimaging. In Medina LS et al. (eds): Evidence-Based Neuroimaging Diagnosis and Treatment. New York: Springer Science + Business Media; 2013

neurological deficits (moderate evidence). A summary of traditional and proposed screening criteria for BCVI can be found in Table 7.1.

Penetrating Trauma

Patients with hard clinical signs including active hemorrhage, expanding or pulsatile hematoma, bruit or thrill, massive hemoptysis or hematemesis, or shock refractory to fluid resuscitation most often undergo emergent operative exploration for both diagnosis and treatment. However, evidence suggests that those patients with a history of penetrating neck trauma but who are hemodynamically stable and either without clinical signs or with soft signs, such as non-expanding non-pulsatile hematoma, venous oozing, subcutaneous emphysema, minor hemoptysis, dysphonia, or dysphagia, can safely undergo CTA as the initial diagnostic examination. CT angiography is also

useful in delineating wound trajectory, in assessing the aerodigestive tract in order to determine the need for additional evaluation with laryngoscopy, endoscopy, and esophagography, and in evaluating the cervical spine [23].

What Is the Recommended Modality and Protocol for Screening for Vascular Injury in Blunt Neck Trauma?

Summary of Evidence Digital subtraction angiography (DSA) continues to be the reference standard as both a screening and diagnostic test for blunt and penetrating neck trauma but has significant drawbacks in terms of resource demands and risks associated with its invasiveness (strong evidence). Results from CT in the literature are highly variable depending on such factors as the vessel studied, the type of scanner utilized, and the outcome measure reported, though CTA is largely supplanting DSA in many institutions given that it is less invasive, less expensive, and less resource intensive (limited to moderate evidence). In a survey conducted in 2011 among trauma surgeons, neurosurgeons, and radiologists in North America, for instance, 60% report using CTA for screening and diagnosis of BCVI, while only 15% continue to use DSA [24]. Additionally, these screening exams can be performed as part of a dedicated neck exam or a whole-body scan. Interest is growing in MRI as an alternative screening test, as it is noninvasive and does not require contrast administration; however, its use is not yet well established (limited evidence). Color duplex sonography has also been evaluated; however, it is not recommended for stand-alone use given its low sensitivity of 38.5% (moderate evidence) [25].

Supporting Evidence

Digital Subtraction Angiography

Digital subtraction angiography has been the traditional gold standard diagnostic tool for blunt and penetrating neck trauma since the late 1960s owing to its high sensitivity and specificity and its ability to provide flow analysis [26]. However,

DSA is relatively expensive and requires skilled personnel and specific equipment to perform and can also therefore result in prolonged time to diagnosis compared to other less-invasive modalities [27]. It also is associated with a 1.3% complication rate, including thrombosis, arterial dissection, and contrast-induced nephropathy [28]. And, in contrast to CTA, DSA does not provide any information on other vital structures that would be helpful in the management of poly-trauma patients.

CT Angiography

The utility of screening CTA has been assessed with a number of studies, with sensitivities ranging from 29 to 100% [27, 29, 30]. Specificity has been much more consistent, though, with most modern studies showing rates above 90% [31]. Most of the evidence in support of CTA has been moderate or limited, and variance among study design and techniques has traditionally limited the conclusions that can be drawn. While DSA therefore presently remains the gold standard, MDCT angiography is a noninvasive, rapid, readily accessible, and cost-efficient modality and is capable of detecting associated injuries throughout the body; these practical advantages have led to its adoption over DSA in many institutions. Advances in technology laid the foundation for this shift in management. The development of MDCT allows for more rapid image acquisition, with higher resolution and decreased motion artifact. Post-processing tools enable the creation of multiplanar reformats for easier visualization and quantitative analysis of the vessel wall and lumen, and iterative reconstruction has demonstrated an ability to reduce radiation dose while maintaining image quality [32, 33]. As technology continues to improve and radiologists gain experience in diagnosing BCVIs, it is hoped that the accuracy of CTA will soon approach that of DSA. Descriptive analysis of CTA for diagnosing blunt trauma based on recent studies can be found in Table 7.2.

Duplex Sonography

Duplex sonography is commonly used in the trauma setting, given its noninvasiveness, lack of ionizing radiation, portability, and low cost.

Table 7.2 Descriptive analysis of CTA for diagnosing blunt trauma based on recent studies using 16-MDCT or higher

Reference	Year	CT scanner	Prot	Vess	Sen	Spec	PPV	NPV	G.S.	Level
[27]	2006	16-MDCT	Neck	C, V	98	100	100	99	A	2
[59]	2007	16-MDCT	Neck	C, V	74	86	65	90	A	2
[44]	2007	16-MDCT	WB	C extra	69	82	74	78	A	2
[44]	2007	16-MDCT	WB	V extra	74	91	74	91	A	2
[44]	2007	16-MDCT	WB	C intra	60	95	28	98	A	2
[44]	2007	16-MDCT	WB	V intra	0	99	0	99	A	2
[44]	2007	16-MDCT	Neck	C extra	64	94	84	84	A	2
[44]	2007	16-MDCT	Neck	V extra	68	100	100	87	A	2
[44]	2007	16-MDCT	Neck	C intra	25	94	40	89	A	2
[44]	2007	16-MDCT	Neck	V intra	n/a	100	n/a	100	A	2
[48]	2009	16-MDCT	Both	C, V	29	97	67	85	A	2
[48]	2009	64-MDCT	Both	C, V	54	97	73	92	A	2
[60]	2011	32-MDCT	Neck	C, V	51	97	43	98	A	2
[30]	2014	64-MDCT	Both	C, V	68	92	36	98	A	3

Adapted from Danton GH, Warsch JRL, Munera F. Traumatic Extracranial Vascular Injury: Evidence-Based Neuroimaging. In Medina LS et al. (eds): Evidence-Based Neuroimaging Diagnosis and Treatment. New York: Springer Science + Business Media; 2013

Prot type of protocol, *Neck* dedicated CTA of the neck, *WB* neck studies as part of the whole-body scan, *Vess* vessels studied, *C* carotid, *V* vertebral, *extra* extracranial only, *intra* intracranial only, *Sen* sensitivity, *Spec* specificity, *PPV* positive predictive value, *NPV* negative predictive value, *G.S.* gold standard used as a comparison, *A* angiography, *Level* level of evidence

Though it has high specificity, the sensitivity of duplex sonography for BCVI is low, ranging from 39 to 86% [25]. The skull base cannot be assessed by ultrasound, and vertebral arteries, too, are difficult to examine due to overlying bony foramina. Ultrasound is also inherently operator dependent. As a result, it is not considered an adequate screening modality for BCVI, and the Eastern Association for the Surgery of Trauma (EAST) guidelines favor CTA instead (moderate evidence) [26, 34].

MRI and MR Angiography

Though recent advances have decreased acquisition times while preserving image quality, the use of MRI for the detection of traumatic cerebrovascular injuries has been limited by accessibility and logistical limitations in the acute trauma setting, along with contraindications such as the presence of metallic foreign bodies [35]. Evidence is therefore limited, with substantial variability in study designs and test performance characteristics. Studies comparing MRA to DSA have found sensitivity and specificity values for MRA ranging from 50 to 100% and 29 to 100%, respectively [6].

What Is the Recommended Modality and Protocol for Screening for Vascular Injury in Penetrating Neck Trauma?

DSA remains the reference standard for the evaluation of nonoperative penetrating vascular injuries of the neck, as with blunt traumas (strong evidence). However, studies comparing the accuracy of CTA with DSA have prompted a shift in the assessment of penetrating vascular neck injuries toward MDCT angiography as the primary modality of choice (moderate evidence) [36]. CTA has shown more reliability for penetrating injuries than blunt injury—though fewer studies have been conducted of CTA for penetrating neck injury, many are prospective and well designed, and diagnostic sensitivities for CTA in penetrating trauma studies tend to be higher than what is reported for blunt injury (moderate evidence). This may reflect the higher pretest probability for injury and of the diagnostic utility of the trajectory of the injury and its proximity to the vasculature.

Patient stratification on presentation begins by physical examination of depth of injury, with viola-

tion of the platysma generally regarded as defining a superficial or deep injury. Diagnostic evaluation of superficial injuries often stops at the physical exam. In the past, most deep injuries were explored operatively, leading to a high rate of unnecessary explorations, with one study finding that no vascular injuries were detected in 67% of asymptomatic patients [2]. While unstable patients continue to be explored surgically, asymptomatic patients may be sent for screening exam. CTA provides accurate and resource-sparing vascular injury screening (moderate evidence). One prospective study of 60 patients with injuries in various neck zones compared CTA to DSA and found sensitivity and specificity of 90% and 100%, respectively [37]. Another prospective study of 175 patients comparing CTA, DSA, surgery, and clinical outcomes found 100% sensitivity and 98.6% specificity [38]. In 2006, a prospective study of 91 patients measured outcomes using an aggregate gold standard including final discharge diagnosis, all imaging studies, surgical procedures, and clinical follow-up, demonstrating 100% sensitivity and 93.5% specificity for the diagnosis of vascular injury [39]. And by directing targeted surgical exploration, and thereby minimizing non-therapeutic surgery, and by reducing or even eliminating the need for additional diagnostic tests, CTA streamlines the workup and management of patients and reduces costs. For instance, in a study comparing the number of negative neck explorations in patients who did or did not receive a CTA, the explorations were negative 48% of the time in those who did not receive a CTA, while those who had a CTA had no negative neck explorations [40].

How Important Is the Number of CT Detectors?

With respect to penetrating neck trauma, even early studies with single-detector CT reported high sensitivities and specificities as compared to DSA [37, 38, 41, 42]. The diagnostic sensitivity of CTA in the screening of blunt neck trauma on the other hand is marginal, though as CT technology is improving, particularly with regard to the number of detectors, so too is the ability of CT to diagnose BCVI [43]. For instance, in a study by

Paulus et al. 64-channel CTA demonstrated significantly improved sensitivity over 32-channel CTA (68% versus 51%), with 62% of false-negative findings occurring with low-grade injuries [30]. Based on the available evidence, CTA with a 64-MDCT or greater to screen for BCVI is preferred and has largely supplanted DSA, given that the speed and accessibility of CTA provide additional advantages and will ultimately likely reduce mortality and morbidity (moderate evidence) [19].

What Is the Recommended CTA Protocol for Vascular Injury Screening in Traumatic Neck Injury?

There is no data separately considering blunt or penetrating injury, and no controlled studies comparing specific CT acquisition techniques and parameters have been performed. The majority of articles instead describe the techniques used at their institution, which may vary by technologies and manufacturers. Post-processing tools allow for various types of reconstructed images including maximum intensity projections and three-dimensional and curved planar reformats, which are believed to improve detection of subtle vascular injuries. Their use is commonplace and recommended, despite a paucity of evidence affirming any value in increasing sensitivity, specificity, or confidence of interpretation.

Should Screening CTA Be Performed as Part of a Whole-Body Trauma Scan or Is a Dedicated CTA Required?

A more controversial yet more formally studied aspect of CTA screening is the question of whether a dedicated CTA neck timed to optimize the extracerebral vasculature with the arms adducted is needed or if the CTA neck can be performed in the same acquisition of a “trauma scan,” which includes the CT neck along with the cervical spine, chest, abdomen, pelvis, thoracic, and lumbar spine exam with the arms abducted. In 2008, Sliker et al. compared patients who underwent both screening CT and DSA, demonstrating

similar sensitivities and specificities for carotid and vertebral injuries among an MDCT group that had CT neck as part of a body trauma protocol and a second group that underwent a dedicated CTA neck [44]. Langner et al. followed a protocol consisting of a CT brain, followed by a CTA neck with one contrast bolus, and then scanning of the chest, abdomen, and pelvis using a second contrast bolus, concluding that a dedicated CTA could be incorporated easily into a whole-body trauma scan (limited evidence) [16]. Bonatti et al., too, recently affirmed that CTA neck included as part of a whole-body MDCT protocol is an adequate means of screening for BCVIs in poly-trauma patients [45].

Special Considerations for Pediatric Patients

Thankfully, vascular injury is a rarity in the pediatric trauma population. Similar to adult trauma cases, when hard signs of a vascular injury are present on physical examination, immediate surgical intervention is warranted. In the pediatric patient with soft signs of vascular trauma, CTA appears to be the diagnostic tool of choice (limited evidence). Observational studies support the use of imaging in clinically stable pediatric patients with penetrating neck trauma, particularly those sustaining projectile injuries [46]. In a recent study assessing the value of CTA in neck and extremity pediatric vascular trauma, CTA was 100% sensitive and 93% specific in penetrating trauma and 88% sensitive and 100% specific for blunt trauma, with accuracy for penetrating and blunt trauma of 95% and 97%, respectively [47]. There are no standard screening guidelines to evaluate BCVI in children, though, and given the heightened lifetime risk of malignant tumors associated with the increased radiation exposure from MDCT, judicious use of this screening modality is warranted. While one review of the available literature by Desai et al. showed that, aside from Glasgow Coma Scale (GCS) score, no single risk factor was statistically significant in predicting BCVI, another identified fracture of the petrous temporal bone or through the carotid canal, focal neurological deficit, stroke, and GCS

score <8 as independent risk factors for BCVI [48, 49]. A review of the National Pediatric Database attempted to examine the usefulness of ultrasound in pediatric blunt carotid injuries, but due to the low incidence of only 0.035% in 57,659 patients, an assessment could not be performed [50].

What Is the Imaging Impact on Outcome?

Penetrating Trauma

As high clinical suspicion for vascular injury almost always mandates immediate operative intervention, studies of penetrating neck trauma typically compare CT results to findings from surgical exploration. Clinically stable patients in whom suspicion for injury exists from location of injury only have been studied with CTA as the screening exam, with the primary outcome being the avoidance of unnecessary surgical exploration. CTA has performed well in this setting and is recommended as a screening tool in patients with low suspicion (moderate evidence) [2, 34, 37, 38, 40, 46, 51–53]. Long-term evaluation of patient outcomes is not well studied.

Blunt Trauma

The greatest concern regarding BCVIs is the risk of stroke. Stein et al. reported a decrease in stroke rate from 26% to 4% in patients who were treated for blunt extracranial vascular injury regardless of diagnostic method, illustrating the importance of prompt diagnosis and treatment [17]. Scott et al. found the risk of post-traumatic stroke to be highest in grade 3 (greater than 50% stenosis of the vessel or the development of a pseudoaneurysm) or grade 4 (complete vessel occlusion) BCVI, at approximately 7%, with follow-up imaging showing progressive worsening without radiographic improvement only in a small number of patients, findings which alone did not correlate with adverse clinical outcome [54]. They reported a stroke rate of only 1% in lower-grade BCVI, with a 14% rate of radiographic worsening on follow-up imaging, albeit with no adverse clinical outcomes associated with these radiographic changes [55].

Take-Home Tables

Tables 7.1 highlights screening criteria for BCVI, and Table 7.2 gives a descriptive analysis of CTA for diagnosing blunt trauma based on recent studies using 16-MDCT or higher.

Imaging Case Studies

Case 1

In Fig. 7.1a, b, a 20-year-old man presents following a motor vehicle accident in which he was an unrestrained passenger.

Case 2

In Fig. 7.2a–c, a 25-year-old man presents following a motorcycle crash in which he was a helmeted rider.

Case 3

In Fig. 7.3a, b, a 77-year-old man presents who was a restrained driver in a motor vehicle accident.

Suggested Imaging Protocols

See Table 7.3 for CTA protocols for 64-MDCT or higher typical of those reported throughout the literature.

Future Research

Large trials comparing CTA to DSA would be time-consuming and expensive and put patients at potential risk of catheter-related injury. And designing prospective, blinded studies is difficult due to the relatively low incidence of vascular injuries and the already widespread acceptance of CTA as an effective screening tool for blunt

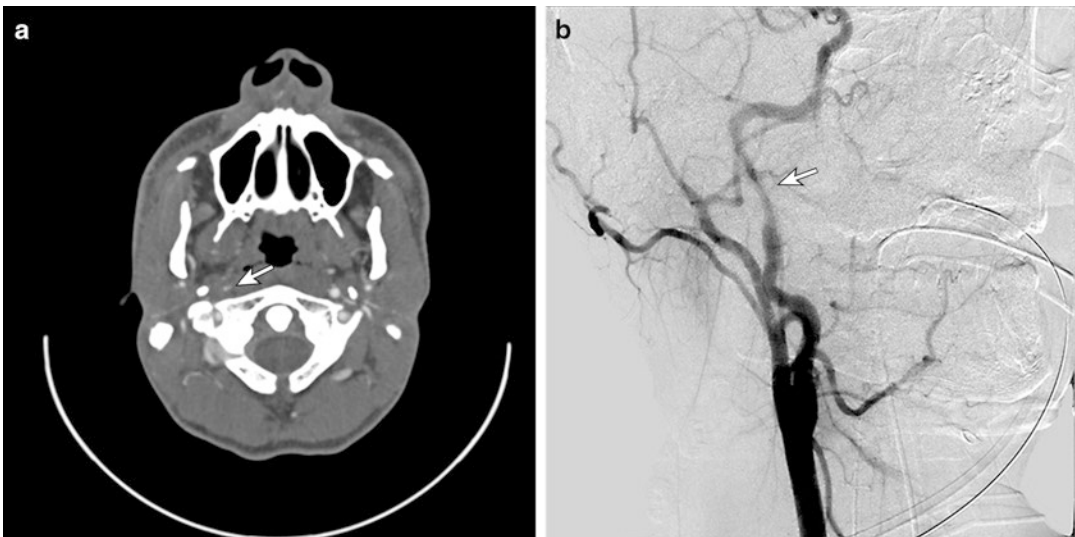


Fig. 7.1 A 20-year-old man who was an unrestrained passenger in a motor vehicle crash was found on initial whole-body CT scan to have a right extracranial internal carotid artery dissection at the level of C1, which was subsequently confirmed on angiogram. The patient was

started on aspirin 81 mg daily. (a) Axial CTA image demonstrating near complete occlusion of the high cervical right internal carotid artery (arrow). (b) Angiogram showing right intimal flap in the cervical ICA with 50% narrowing of the vessel

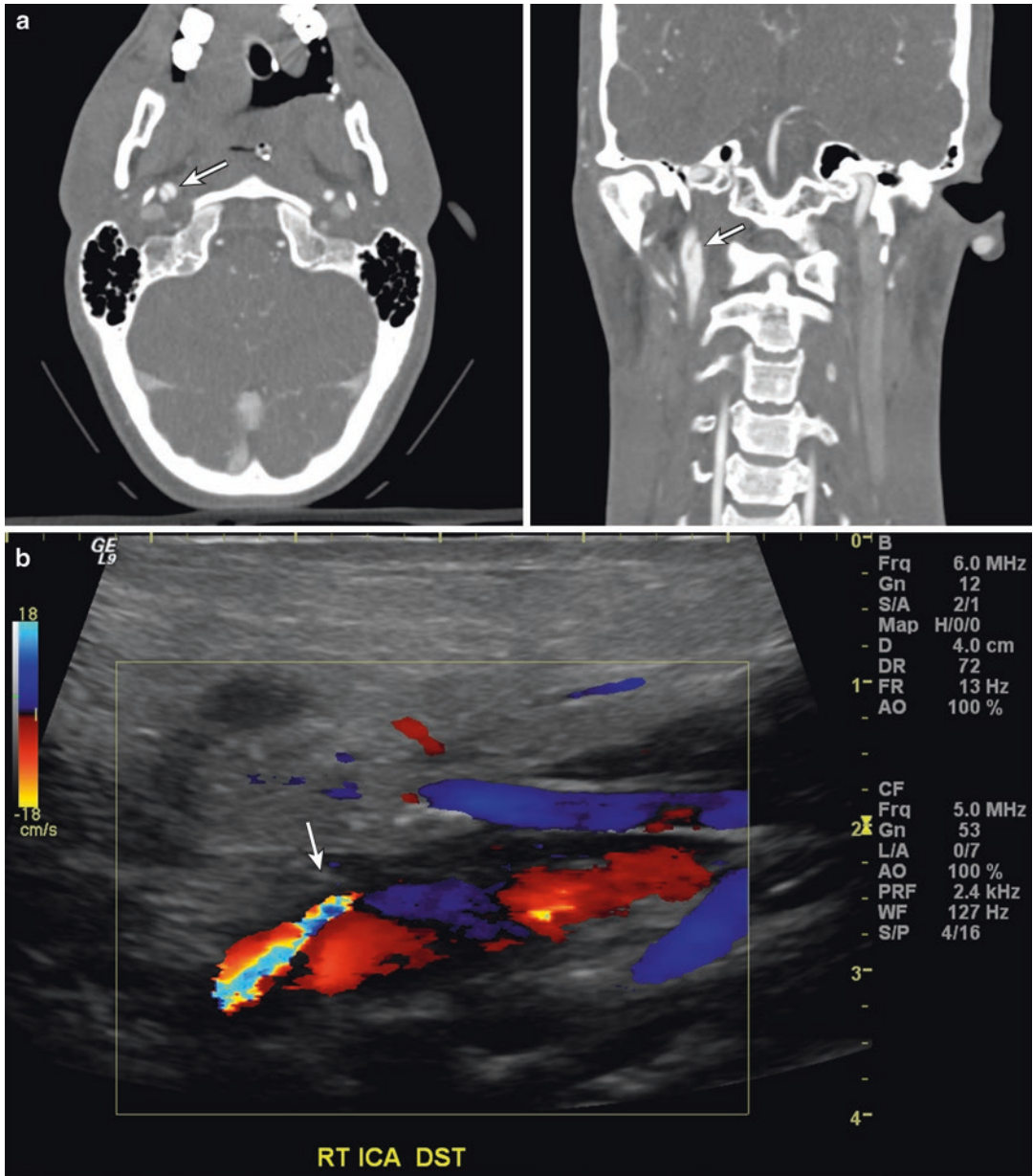


Fig. 7.2 A 25-year-old man who was a helmeted rider involved in a motorcycle crash was found on initial whole-body CT scan to have polytrauma including a focal dissection of the high right cervical internal carotid artery at the level of C1 with intimal flap. The patient was started on aspirin 81 mg daily and Coumadin 5 mg daily. (a) Axial and coronal CTA images showing the focal dissec-

tion with intimal flap (arrows), resulting in approximately 60% stenosis of the true lumen. (b) Color-flow Doppler ultrasound of the distal right internal carotid artery showing turbulent flow in the area of the dissection. (c) 3D reconstruction from 6-month follow-up MRA redemonstrating the dissection (arrow)

Fig. 7.2 (continued)



Fig. 7.3 A 77-year-old man who was the restrained driver in a motor vehicle crash was found on initial whole-body CT scan to have polytrauma including a right extracranial vertebral artery dissection/pseudoaneurysm. The patient was started on aspirin 81 mg daily. (a) Sagittal CTA image showing the vertebral artery dissection (*arrow*) and (b) axial CTA image showing a tiny pseudoaneurysm (*arrow*)

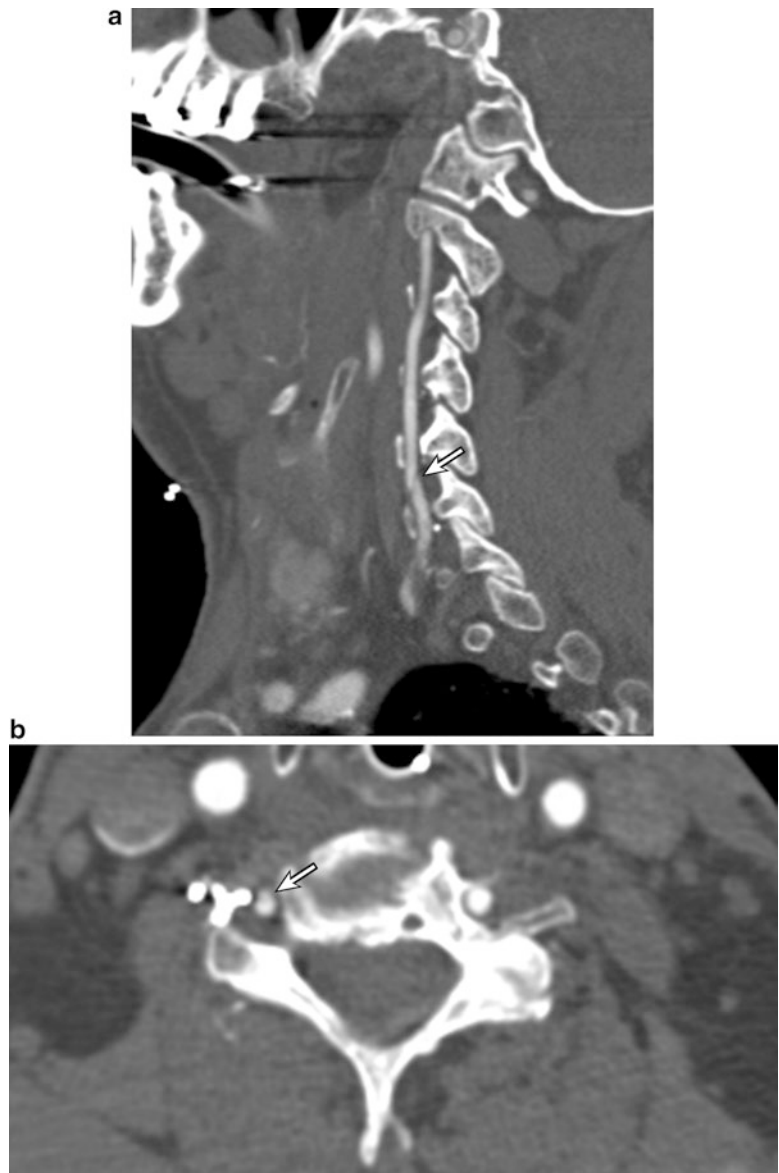


Table 7.3 CTA protocols for 64-MDCT or higher typical of those reported throughout the literature

References	[57]	[61]	[30]
CT detector	64-MDCT	64-MDCT	64-MDCT
Collimation	0.6 mm	0.625 mm	
Slice thickness		1.25–3.75 mm	1.0 mm
Pitch		0.984	0.5
Recons	2D, 3D, MIP	2D, 3D	2D
Contrast agent		350–370	
Injection rate	5 ml/s	4–5 ml/s	5 ml/s
Vol. 1st bolus	50–100	100–120 ml	60–75 ml for neck only; 120 ml for WB
Vol. 2nd bolus		30–50 ml saline	
Timing technique	Bolus tracking	20-s delay	Bolus tracking
ROI location	Ascending aorta	n/a	Origin of carotids
Scan type	Neck	WB	Neck, neck w/WB

Blank fields indicate the information was not provided. *MDCT* multidetector CT, *Recons* reconstructions reported to be performed and used in analysis, *Contrast agent* concentration of iodine reported, *Vol* volume of first and second boluses when reported. If saline is not listed, the bolus was contrast. Scan type is neck, neck only, or WB, part of a whole-body scan where there is one acquisition. Neck w/WB is a scan where the neck was separate but scanned immediately before the scan for the body

and penetrating traumatic injuries. Therefore, in order to affirm the clinical utility of CTA, more, longer-term follow-up studies of patients who have undergone initial screening with CTA should be performed. As well, as CT technology continues to improve, comparison of 64-, 128-, and 320-MDCT and dual-source scanners may demonstrate either continued improvement in sensitivity or reach a plateau. Finally, the added value of reconstructed images in the analysis of CTA data has not been adequately elucidated—making interpretation of images more efficient in the acute trauma setting has been anecdotally shown to be useful, and individual sensitivities and specificities for curved planar and multiplanar reformats, and 3D images, should be further studied [56, 57].

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Hyperacute Ischemic Stroke in Adults: Evidence-Based Emergency Imaging

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Key Points

- Noncontrast head CT should be performed expeditiously in all patients with hyperacute ischemic stroke to evaluate for intracranial hemorrhage (ICH) [Strong Evidence]. Magnetic resonance imaging (MRI) is equivalent to CT in the detection of intracranial hemorrhage for patients <6 h from onset [Strong Evidence] but typically takes longer to perform, potentially delaying time-sensitive therapies which can worsen outcomes [Strong Evidence].
- Magnetic resonance diffusion-weighted imaging (DWI) is superior to CT for the detection of ischemic stroke within the first 24 h of symptom onset [Strong Evidence]. However, MRI may confirm a clinical diagnosis of ischemic stroke *without* influencing outcomes and

potentially delaying time-sensitive therapies, though may remain useful when the clinical diagnosis is unclear [Limited Evidence]. Patients at high risk for hemorrhagic conversion and poor outcome regardless of intravenous thrombolysis can be predicted with noncontrast head CT and MRI [Moderate Evidence], but such high-risk patients still may marginally benefit from intravenous thrombolysis despite overall increased risk of worse outcomes [Limited Evidence].

- CT angiography (CTA) should be performed expeditiously in hyperacute stroke patients who are potential candidates for endovascular thrombectomy (EVT) to evaluate for large vessel occlusion (LVO) [Strong Evidence]. CTA is generally safe and can be performed without first evaluating renal function [Moderate Evidence].
- The net benefit of EVT in severe ischemic strokes may be modestly predicted by determining the size of an ischemic core, with CT and Alberta Stroke Program Early CT (ASPECTS) scoring [Moderate Evidence] CT perfusion [Moderate Evidence] or MRI and DWI [Moderate Evidence]. However, the interrater variability of ASPECTS scoring and time

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delays arising from MRI or advanced imaging need to be weighed carefully against the utility of avoiding EVT.

- Identification of “salvageable tissue” by either identifying a “penumbra” or collateral flow with advanced imaging techniques predicts outcomes in hyperacute stroke patients after intravenous thrombolysis and EVT [Strong Evidence] but does so for untreated patients also [Strong Evidence]. Selection of patients based on the presence of a penumbra with perfusion imaging or collateral flow with multiphase CTA identifies patients more likely to benefit from EVT within 6 h though might exclude patients who could have benefited from EVT in this time window [Moderate Evidence]. However, beyond 6 h CT perfusion, imaging and multiphase CTA may help select patients that could still benefit from EVT [Strong Evidence, pending publication of trial results at the time of this writing].
- Time to intravenous thrombolysis and EVT highly influences outcomes [Strong Evidence], and reducing the time of imaging and interpretation expedites treatment delivery to hyperacute stroke patients [Strong Evidence]. Improving systems of stroke care, including imaging in the hyperacute setting, is thus likely to improve neurological outcomes.

Definitions and Pathophysiology

Stroke is a clinical term that refers to an acute neurological deficit arising from disruption of focal blood supply to the brain [1]. Stroke may be due to an occlusion or stenosis of an artery or arteries (ischemic stroke), rupture of an artery leading to hemorrhage in or around the brain (intracranial hemorrhage), or from occlusion of a cerebral vein or dural sinus. The vast majority of strokes are ischemic (~85%) [2], and etiologies

are protean and include arterioarterial emboli from large vessel atherosclerosis, small-vessel atherosclerosis, cardiogenic or other systemic emboli, and arterial dissection, among other more uncommon etiologies.

This chapter focuses on the imaging of ischemic stroke patients within the first several hours after stroke onset, i.e., *hyperacute* ischemic stroke. We do not use this term to refer to a specific time interval after stroke onset but rather for patients who stand to benefit from emergently applied therapies including intravenous thrombolysis or EVT. Thus, the time interval from stroke onset might be as short as 4.5 h for patients who are not candidates for EVT to as long as 24 h for imaging-selected patients. Imaging may have utility beyond this hyperacute period, for example, in identifying the etiology of a stroke or predicting the need for hemicraniectomy in a patient with “malignant” ischemic stroke. However, these issues are typically dealt with after the patient has left the Emergency Department, which is beyond the scope of this chapter.

Epidemiology

It is estimated that approximately 795,000 ischemic strokes occur in the United States annually [3]. In the United States, stroke is now the fifth leading cause of death and the second leading cause of adult disability, down from the third and first leading causes, respectively, due to improvements in stroke prevention and treatment, yet remains the second leading cause of death worldwide [4, 5]. In the emergency room, cerebrovascular disease accounts for over 700,000 visits (0.5% of all Emergency Department visits) in the United States annually.

Costs to Society

The estimated direct and indirect costs of stroke in the United States in 2010 were 74 billion dollars [6]. Acute inpatient hospitalization accounts for 70% of the first-year costs after stroke, and diagnostic testing represents approximately 20% of this cost.

Goals of Imaging

Here, we take the approach that imaging and its interpretation should be driven solely by its ability to improve neurological outcomes, which inherently relies on its ability to help select patients for *proven* therapies. In the hyperacute setting, the principal goals of imaging are to (1) identify candidacy for intravenous thrombolysis and (2) identify candidacy for EVT. While imaging may have a role in predicting outcomes without or with treatment, it is important to note that the goal may include selecting patients that might benefit from therapy even when prognosis is generally (though not universally) poor. For example, patients above the age of 80 are likely to have worse outcomes after ischemic stroke than those below the age of 80 but receive the same benefit from intravenous thrombolysis [7] and even further benefit from EVT regardless of their age [8, 9].

It is also important to note that the incremental benefit of an imaging modality must be weighed against the additional time required to obtain this imaging. For every 15 min saved in administering intravenous alteplase, nearly 1 month of disability-free life is gained, and the number needed to treat to achieve good outcomes significantly improves [10]. The value of providing endovascular treatment more quickly has an even larger benefit [11, 12]. The additional time added by an imaging modality must thus account for patient transfer, preparation, scan time, post-processing, image transfer, and interpretation. Conversely, minimizing these times is likely to improve the benefit of the imaging modality in improving neurological outcomes.

Methodology

The evidence and literature cited here were identified through several search strategies including keyword searches via PubMed and Google Scholar, references contained within review articles and other key references, and personal collection of key literature on stroke imaging, updated to the time of this writing (March 2017).

Discussion of Issues

Should This Patient Receive Intravenous Thrombolysis?

In 1995, the Food and Drug Administration approved intravenous tissue plasminogen activator (IV-tPA) for the treatment of acute ischemic stroke after two randomized controlled trials (RCT) demonstrated its efficacy in improving neurological disability at 3 months when intravenously administered within 3 h of stroke onset [13]. A subsequent RCT showed that IV-tPA improved neurological outcomes in patients presenting within 4.5 h of stroke onset [14]. After IV-tPA an additional one in ten patients remains independent in their daily activities, and one in three to six patients, depending on time to treatment, shows some improvement in their disability, as compared to those treated with a placebo [15].

Despite the strong evidence supporting this treatment, only a minority of potentially eligible patients receives IV-tPA, largely due to patients arriving beyond the 4.5 h time window [16]. Several other factors limit candidacy for IV-tPA, particularly those that herald an increased risk for hemorrhagic complication, which include the presence of acute intracranial hemorrhage and a particularly large ischemic stroke more likely to hemorrhage. Head imaging thus plays a critical role in this evaluation (Question 1.1).

It may seem intuitive to use imaging to confirm the diagnosis of ischemic stroke prior to IV-tPA (Question 1.2). However, treatment of stroke mimics with intravenous thrombolysis has been found to be safe [17–19] [Strong Evidence], and the desire to improve diagnostic certainty of stroke may introduce delays in administering treatment, which is known to worsen outcomes [15, 20, 21] [Strong Evidence]. Establishing the diagnosis of acute ischemic stroke with imaging may yet continue to have a role in patients with unknown time of symptom onset or in patients who are unlikely to have a stroke but could receive thrombolysis if proven otherwise.

A third concern is whether treatment with IV-tPA in a patient with a particularly large ischemic stroke will lead to hemorrhagic conversion

and thereby worsened outcomes (Question 1.3). No such criteria were used in the initial National Institute of Neurological Disorders and Stroke (NINDS) trials demonstrating efficacy of IV-tPA in the first 3 h after symptom onset [13]; subsequent subgroup analyses have shown that while hemorrhagic conversion and poor outcomes increase in patients with very large ischemic strokes, there is persistent benefit for IV-tPA in these patients [7] [Moderate Evidence]. On the other hand, the European Cooperative Acute Stroke Study (ECASS) III trial, which demonstrated efficacy of IV-tPA in the 3–4.5 h window, specifically excluded patients with a large middle cerebral artery (MCA) stroke (defined as greater than 1/3 of the MCA territory) [14]. Thus, determining the presence of a large stroke that is likely to hemorrhage remains standard practice for patients being treated within the 3–4.5 h time window, though no study has proven that excluding such patients affects outcomes [Limited Evidence].

Does This Patient Have an Acute Intracranial Hemorrhage?

Summary of Evidence Noncontrast head CT (NHCT) is widely accepted as the gold standard for detection of acute intracranial hemorrhage [Moderate Evidence] and is the modality of choice for exclusion of intracranial hemorrhage in evaluation for thrombolytic candidacy, based on its successful use in several RCTs [Strong Evidence]. MRI can replace NHCT, as it is nearly as sensitive in detecting acute intracranial hemorrhage [Strong Evidence]. However, when compared to NHCT, MRI may cause a delay in treatment [Moderate Evidence], which is known to worsen outcomes [Strong Evidence]. No other method, imaging based or otherwise, has demonstrated superior or equivalent efficacy to NHCT.

Supporting Evidence

- (i) *Noncontrast head CT (NHCT)* Acute hemorrhage appears hyperdense on NHCT for several days due to the high concentration of hemoglobin in compressed blood and then becomes progressively isodense and then hypodense over a period of weeks to months.

Hyperacute hemorrhage can rarely be isodense in the acute period in severely anemic patients [22]. No rigorous prospective study has been performed to validate the sensitivity and specificity of noncontrast head CT in detecting intracranial hemorrhage (ICH). In an early single autopsy series of 79 patients, CT did not detect 4 out of 17 patients with ICH—all brainstem hemorrhages [23]. However, this study was performed using a first-generation CT scanner, and experience with NHCT was just beginning. More recent studies evaluate the role of NHCT in diagnosing subarachnoid hemorrhage as compared to cerebrospinal fluid analysis. The overall sensitivity of NHCT for subarachnoid hemorrhage is 91–92% but is time dependent such that the sensitivity is nearly 100% within the first 6 h [24–26]. RCTs demonstrating the efficacy of IV-tPA nearly always used NHCT to exclude patients with ICH [13, 14]; in these trials, subsequent hemorrhage typically occurred in the setting of very large ischemic strokes suggesting that an underlying missed ICH was very unlikely to account for subsequent hemorrhagic complication. Thus, NHCT is widely accepted as the gold standard for detection of acute ICH, particularly when evaluating patients for thrombolytic candidacy.

- (ii) *Magnetic resonance imaging (MRI)* The appearance and identification of ICH on MRI depend on the age and location of the hemorrhage, the strength of the magnetic field, and the type of MR sequence [27]. As the hematoma ages, oxyhemoglobin breaks down sequentially into several paramagnetic products: first deoxyhemoglobin, then methemoglobin, and finally hemosiderin. Iron exposed to surrounding water molecules in the form of deoxyhemoglobin creates signal loss on susceptibility-weighted and T2-weighted (T2 W) sequences [28, 29]. Thus, the earliest detection of hemorrhage depends on the conversion of oxyhemoglobin to deoxyhemoglobin which was believed to occur after the first 12–24 h [27].

However, this early assumption had been questioned with reports of ICH detected by MRI within 6 h and as early as 23 min from symptom onset [30, 31].

More recently, studies have assessed MRI (diffusion-, T2-, and T2*-weighted images) for the evaluation of ICH within 6 h of onset. One study evaluated 62 ICH patients and 62 nonhemorrhagic stroke control patients, with three experienced readers (two stroke neurologists and one neuroradiologist) utilizing CT as the reference standard [32]. The readers, blinded to clinical and CT results, identified all acute hemorrhages on MRI yielding 100% sensitivity and specificity compared to CT. Subsequently, prospective studies compared MRI and CT for detection of ICH. In the first study, 4 of 25 acute ICH patients were not identified by MRI including three cases in which “acute” ICH was classified as “chronic” and one case of subarachnoid hemorrhage associated with ischemic stroke [33]. Interestingly, CT also missed four hemorrhages, though all were identified as foci of hemorrhage within an acute ischemic infarct on MRI—the relevance of which remains uncertain in the context of hyperacute stroke treatment. A following prospective study from the same group confirmed that MRI is similar to CT in the diagnosis of intracranial hemorrhage in patients suspected to have acute ischemic stroke [34]; in this study the sensitivity of MRI and CT were 81% and 89%, respectively, and both were found to be 100% specific. Therefore, it appears that rare cases of early ICH may be missed on either MRI or CT, though hemorrhage missed on CT is typically either chronic or related to an ischemic infarct. Studies with tissue confirmation, allowing for measurement of the exact accuracy of both modalities, are lacking.

- (iii) *Miscellaneous* Multiple attempts to obviate the need for imaging to exclude intracranial hemorrhage have failed, including clinical scores and lumbar puncture [35]. A few studies have explored transcranial ultrasound

as an alternative to NHCT for identifying intracerebral hemorrhage, which may be a promising alternative in low-income countries without available access to a CT scanner, but this requires patients with an adequate acoustic window and an experienced sonographer [36, 37].

Does This Patient Have Hyperacute Ischemic Stroke?

Summary of Evidence NHCT is poor at identifying acute ischemic stroke [Strong Evidence]. CT perfusion imaging (CTP) and angiography (CTA) both modestly improve the accuracy of ischemic stroke diagnosis [Moderate Evidence]. MRI (diffusion-weighted imaging) is far superior to CT for identifying ischemic stroke within the first 12 h of symptom onset [Strong Evidence], but has not been shown to improve clinical outcomes and typically requires additional time relative to CT [Moderate Evidence], and thus cannot yet be recommended prior to IV-tPA in patients with suspected stroke presenting within 4.5 h of symptom onset. MRI helps to predict time of symptom onset [Moderate Evidence], and the safety of using MRI to treat patients with thrombolysis on this basis is established [Strong Evidence], but the efficacy remains unknown [Limited Evidence]. MRI may also be helpful in patients clinically unlikely to have a stroke but who would be thrombolytic candidates if proven otherwise [Limited Evidence].

Supporting Evidence

- (i) *Computed tomography (CT)* NHCT images are commonly normal during the acute phase of ischemia. At times, patients may present with stroke-like symptoms due to non-stroke etiologies including postictal state following seizure, “complicated” migraine, brain tumor, toxic-metabolic conditions, acute peripheral vertigo, subdural hematoma, herpes encephalitis, demyelinating disease, or conversion disorder. Based purely on history and physical examination alone without confirmation by NHCT, stroke mimics may account for up to 13–19% of cases initially diagnosed with stroke [38, 39]. Diagnostic

accuracy improves when NHCT is used, but approximately 5% of cases are still misdiagnosed as stroke [40], which may improve to less than 2% at experienced academic centers treating patients with intravenous thrombolysis [19].

Increased scrutiny of hyperacute NHCT scans, especially following the early thrombolytic trials, suggests that some patients with large areas of ischemia may demonstrate subtle early signs of ischemia, even when imaged less than 3 h after symptom onset [41]. These early NHCT signs include parenchymal hypodensity, loss of the insular ribbon, obscuration of the lentiform nucleus, loss of gray and white matter differentiation, visualization of hyperdense clot in the region of the proximal middle cerebral artery (MCA) known as the “hyperdense MCA sign,” subtle effacement of the cortical sulci, and local mass effect. Early changes are found in only 31% of NHCTs performed within 3 h of ischemic stroke, precluding its reliability as a positive sign of ischemia [42]. Early CT signs, however, are often subtle and difficult to detect even among experienced readers, though experience and expertise improve accuracy [43, 44].

Advanced CT imaging, including CT perfusion imaging (CTP) and CT angiography (CTA), may have increased sensitivity for ischemic stroke. CTP can detect areas of ischemic stroke by demonstrating either increased mean transit time or decreased cerebral blood flow in a vascular territory of the brain. A pooled analysis of 15 studies found a sensitivity of 80% and specificity of 95% for CTP as compared to DWI or follow-up MRI or CT as the reference standard [45]. False negatives were mostly due to lacunar infarcts or limited coverage. At one institution, the incremental benefit in diagnosing acute ischemic stroke with CTP over CTA and NHCT was found to be 12.4% and 18.2% over NHCT only [46]. Drawbacks of CTP include the requirement for contrast administration, increased radiation dosage, and limited coverage of the brain. CTA also

improves the sensitivity for large ischemic stroke, either by identifying a large vessel occlusion or through a geographic paucity of vessels demonstrated on source images [47] but remains insensitive to small strokes.

- (ii) *MRI diffusion-weighted imaging (DWI)* Unlike NHCT, DWI is capable of detecting very early physiologic changes during cerebral ischemia, demonstrating changes within minutes of ischemia in rodent stroke models [48–50]. Moreover, the sequence detects lesions as small as 4 mm in diameter [51]. The cause of signal alteration in DWI after acute ischemia is not entirely understood but is thought to reflect diffusion restriction predominantly in the intracellular space [52]. As duration of ischemia increases, a DWI lesion becomes progressively brighter with the added contribution of hyperintense T2 W signal known as “T2 shine through” [53]. To differentiate between true restricted diffusion and “T2 shine through,” a bright DWI lesion should also show hypointense signal on the corresponding apparent diffusion coefficient (ADC) map, which is a more quantitative and direct measure of restricted diffusion.

The relatively high sensitivity and specificity of DWI for the detection of ischemia makes it an ideal sequence for positive identification of hyperacute stroke. Two studies evaluating DWI within 6 h of stroke onset reported 88–100% sensitivity and 95–100% specificity, using final clinical diagnosis as the reference standard [54, 55]. In another study, 50 patients were randomized to DWI or NHCT within 6 h of stroke onset and subsequently received the other imaging modality with a mean delay of 30 min [56]. Sensitivity and specificity of ischemia detection among blinded expert readers were significantly better with DWI (91% and 95%, respectively) compared to NHCT (61% and 65%). A recent large prospective study including 190 ischemic stroke patients assessed the accuracy of DWI compared to NHCT as a function of time from symptom onset [34]. As time from symptom onset increased, the sensitivity of DWI for

final diagnosis of ischemic stroke increased: 73%, 81%, and 92% for <3 h, 3–12 h, and >12 h, respectively, whereas NHCT had only 12%, 20%, and 16% sensitivity at these three respective time intervals [Strong Evidence].

Although DWI is the optimal test for imaging acute ischemia, the highest level data suggests that the sensitivity for detection within 6 h of onset is 81–91%; therefore, the absence of a DWI lesion does not rule out ischemia. False negatives have been reported in small subcortical and brainstem infarctions and in patients with low National Institutes of Health Stroke Scale (NIHSS) scores [34, 55, 57–59]. Furthermore, within the first 6 h of stroke onset, DWI demonstrates delayed signal evolution after changes in perfusion [60]. Restricted diffusion has been reported with other nervous system pathologies such as brain abscesses [61], herpes encephalitis [62], Creutzfeldt-Jakob disease [63], highly cellular tumors such as lymphoma or meningioma [64], seizures [65], and hypoglycemia [66]. However, the clinical history and appearance of these lesions on the remaining standard MR sequences should allow for diagnosis of these different pathologies. Diagnosis of ischemic stroke with DWI should be interpreted in conjunction with conventional MR sequences and within the proper clinical context.

Regarding CT versus MRI for first-line imaging in patients with suspected acute ischemic stroke, several critical factors have not been adequately studied. These factors include practicality (including scanner, technician, and radiologist/neurologist access round the clock, patient eligibility and tolerability, and scan duration), cost-effectiveness, and effect on clinical decision-making and patient outcomes. A large study assessing CT vs. MRI for diagnosis of acute ischemic stroke excluded 11% of patients due to issues such as patient intolerability and claustrophobia in the MR scanner, MR contraindications such as pacemaker placement, and medical instability [34]. One study compared the cost-effectiveness of immediate vs. delayed NHCT for all patients compared with a subset of

acute stroke patients and found that an immediate NHCT in all patients was more cost-effective than delayed NHCT in a subset of patients [67]. However, similar studies have not yet been performed for MRI and are greatly needed.

Recent advances have shown that MRI fluid-attenuated inversion recovery (FLAIR) sequences can determine whether an ischemic stroke identified by DWI is <4.5 h in age or not. Ischemic strokes that demonstrate diffusion restriction but no correlate on FLAIR imaging were typically <4.5 h in age, while those with a correlate on FLAIR imaging were typically >6 h in age [68–70], though an exact cut-off value for subtle FLAIR hyperintensity relative to the contralateral normal parenchyma remains to be determined. A large safety trial in the United States [71] demonstrated that using MRI to identify hyperacute stroke patients for intravenous thrombolysis results in a hemorrhage rate less than that identified in ECASS III [72]. At the time of this writing, another trial in Europe [73] is underway to evaluate the efficacy of this approach in improving neurological outcomes.

In some circumstances, patients may present with symptoms clinically unlikely to be due to stroke, but the possibility of stroke cannot be completely excluded. MRI can occasionally be performed quickly enough to leave time for IV-tPA in case an acute ischemic stroke is identified [21, 74]. No trial has yet determined whether administering IV-tPA in this setting improves outcomes or not.

Is This Ischemic Stroke Likely to Hemorrhage After Intravenous Thrombolysis?

Summary of Evidence The risk of hemorrhage and poor outcomes after intravenous thrombolysis increases in the presence of early CT signs of infarction and low ASPECTS score [Strong Evidence]. Nevertheless, within the 3 h window, IV-tPA continues to benefit these patients at higher risk [Moderate Evidence]. Patients with a large MCA stroke may not benefit from IV-tPA in the 3–4.5 h window due to increased risk of

hemorrhagic conversion [Limited Evidence]. Novel imaging techniques with CT and MRI improve our ability to predict hemorrhagic conversion, but none is proven to identify patients that will not benefit from IV-tPA [Limited Evidence].

Supporting Evidence

- (i) *Computed tomography (CT)* Early CT signs of infarction, especially involving more than one-third of the MCA distribution, have been reported to be associated with severe stroke, increased risk of hemorrhagic transformation [75–77], and poor outcome [78]. Recently, ECASS-3, which demonstrated efficacy of intravenous tPA administration within 3–4.5 h after stroke onset, excluded patients with early signs of stroke in greater than 1/3 of the MCA territory [14]. In contrast to ECASS-3, the National Institute of Neurological Disorders and Stroke tPA trial [13] did not exclude patients with early CT signs, and subgroup analysis has shown that IV-tPA continues to benefit patients with early CT signs of ischemic stroke [7]. Therefore, early CT signs should not be used to exclude patients who are otherwise eligible for thrombolytic treatment within 3 h of stroke onset.

The Alberta Stroke Program Early CT Scores (ASPECTS), a 10-point semiquantitative scoring system, was developed as a tool for detection of early ischemic changes on noncontrast head CT that would be more reliable and prognostic than simple visual inspection of the MCA territory [41, 79]. A normal ASPECT score is 10 with 1 point subtracted for each abnormal brain region (of 10, 7 cortical and 3 subcortical) within the affected hemisphere. Both methods (visual inspection and ASPECTS) require training to ascertain subtle ischemic changes, and ASPECTS remains vulnerable to inter-rater variability [80].

- (ii) *Magnetic resonance imaging (MRI)* Compared to NHCT, DWI is highly sensitive to acute ischemic stroke and can delineate the ischemic core that is likely to represent

the final infarct as defined by follow-up MRI [34]. Large infarcts are more likely to develop hemorrhagic transformation and result in poor outcomes [77, 81, 82]. The volume of a stroke with very low apparent diffusion coefficient (ADC) values also predicts hemorrhagic transformation [81]. Novel techniques, such as measurement of parenchymal enhancement [83], permeability imaging [84], or perfusion imaging [85], may be better able to predict which strokes are likely to develop hemorrhagic transformation after thrombolysis. The number of microbleeds detected on susceptibility-weighted sequences (T2* and SWI) also predicts the risk of hemorrhagic transformation [86–90]. However, no study demonstrates that patients identified to be at heightened risk based on MRI will not benefit from IV-tPA, neither within the 3 h nor the 3–4.5 h windows. Thus, the role of MRI in determining whether to continue with IV-tPA or not in an otherwise eligible patient remains in question.

Applicability to Children

No prospective clinical trial to date has investigated the use of intravenous thrombolysis in children under the age of 16. An attempt to perform a randomized evaluation of thrombolysis in pediatric stroke was halted due to poor accrual [91]. Thus, none of the recommendations above may apply to children. Pediatric stroke is further complicated by protean etiologies, many different than those typically seen in adults, an immature fibrinolytic system, and a far lower prevalence that resists establishment of efficient rapid systems of care.

Should This Patient Undergo Endovascular Thrombectomy?

In October 2014, the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) trial had completed and announced significantly improved outcomes in patients treated

with endovascular thrombectomy (EVT) and IV-tPA as compared to IV-tPA alone [8]. Subsequently, other similar RCTs were halted, including the trials: Endovascular Treatment for Small Core and Anterior Circulation Proximal Occlusion with Emphasis on Minimizing CT to Recanalization Times (ESCAPE), Solitaire with the Intention for Thrombectomy as Primary Endovascular Treatment (SWIFT-PRIME), Extending the Time for Thrombolysis in Emergency Neurological Deficits (EXTEND-IA), and Randomized Trial of Revascularization with Solitaire FR Device versus Best Medical Therapy in the Treatment of Acute Stroke Due to Anterior Circulation Large Vessel Occlusion Presenting within Eight Hours of Symptom Onset (REVASCAT). These all showed significant or nearly significant improvements in outcomes with EVT, establishing EVT as the new standard of care for hyperacute stroke patients with large vessel occlusion (LVO) [92–95] [Strong Evidence]. EVT was shown to be highly efficacious and consistent, demonstrating an absolute risk reduction of poor outcome ranging from 14% to 33% across the five different trials. The time window for these trials (stroke onset to anticipated time to endovascular treatment) varied from 6 h to 12 h, though the vast majority of patients were enrolled within the 6 h time window. Nearly all patients first received IV-tPA prior to EVT, unless specifically contraindicated. In contrast to prior neutral RCTs evaluating EVT (IMS-3, SYNTHESIS Expansion, and MR RESCUE) [96–98], a stent retriever device was used in the vast majority of cases, sometimes supplemented with clot aspiration.

Another critical departure between the prior neutral RCTs and the recent positive RCTs for EVT was that the positive RCTs required patients to have LVO demonstrated by noninvasive imaging, nearly always with CTA. Given that the presence of LVO is a prerequisite for endovascular thrombectomy and that the majority of hyperacute stroke patients will not have an LVO [99], determining the presence of LVO in a hyperacute stroke patient is a critical step in evaluating patients for EVT candidacy [Strong Evidence] (Question 2.1).

The recent RCTs varied greatly according to inclusion and exclusion criteria. A key exclusion criterion in three of the trials (ESCAPE, SWIFT-PRIME, and EXTEND-IA) was the presence of a large ischemic “core” [92, 93, 95] (Question 2.2). Though conceptually a large ischemic core is meant to reflect a large completed infarct that could not be salvaged, the definition of how to measure the ischemic core varied across the three trials. MR CLEAN also evaluated the presence of a large ischemic core using ASPECTS scoring of NHCT but did not require exclusion of any patients on this basis [8]. Subgroup analysis of the MR CLEAN data shows that when ASPECTS score was very low (0–4), EVT (with IV-tPA) provided no statistically significant benefit as compared to IV-tPA alone (odds ratio for good outcome 1.09), though the number of patients in this subgroup was low. A pooled analysis of the five positive RCTs similarly found insufficient evidence to support EVT in treating patients with a low ASPECTS [9]. Further, trials that excluded patients with a large ischemic core (ESCAPE, SWIFT-PRIME, and EXTEND-IA) had overall improved outcomes compared to those that did not. While the exact role of measuring an ischemic core prior to EVT remains to be determined, it is likely of consequence as an important tool to limit “futile” EVT [Moderate Evidence].

Another commonly held hypothesis is that EVT may only improve outcomes in patients who have “salvageable” parenchyma that is vulnerable to infarct, frequently conceptualized as a “penumbra” around an ischemic core (Question 2.3). Both CT and MRI perfusion imaging attempts to directly measure a penumbra by establishing thresholds for particular perfusion parameters for an ischemic core and subtracting this from surrounding oligemia to determine a “penumbra” or “mismatch volume”; in some cases, the ischemic core may also be compared to the clinical status of the patient, i.e., “clinical imaging mismatch.” Identifying the adequacy of collateral flow to an affected territory has also been used to identify potentially salvageable parenchyma. The underlying assumption here is that adequate collaterals will help protect vulnerable tissue from infarct long enough for EVT to

remain effective. One RCT explicitly tested the efficacy of penumbra evaluation with perfusion-diffusion mismatch MRI in patients subsequently undergoing EVT [98]. While this trial found no benefit for EVT in either group undergoing or not undergoing penumbra evaluation [Strong Evidence], this trial did not use stent retrievers and thus is not adequately informative for current practice. Another trial evaluated the use of a new thrombolytic agent (tenecteplase) versus IV-tPA after only including patients with a penumbra as assessed with CTP; this trial found improved outcomes with the new thrombolytic agent, but since it did not randomize patients to no CTP, it does not directly test the use of penumbra imaging to select patients for tenecteplase [100] [Limited Evidence].

The more recent positive RCTs for EVT varied widely in both their use and definition of salvageable tissue for patient inclusion and exclusion. A meta-analysis of these results demonstrated that in patients selected by having adequate or good collaterals on multiphase CTA or small ischemic core/adequate penumbra on perfusion imaging, EVT likely improved outcomes in patients beyond 6 h and up to 7.3 h [12] [Moderate Evidence]. Finally, at the time of this writing, a trial using a “clinical imaging mismatch” paradigm to select patients beyond the 6 h window was stopped early following a prespecified interim analysis due to strong efficacy [101]; along with DEFUSE-3, another stopped trial that used imaging mismatch to select patients for EVT beyond 6 h, these trials now strongly support the use of perfusion imaging to select patients beyond 6 h for EVT [evidence level pending publication of results].

Does This Patient Have a Large Vessel Occlusion?

Summary of Evidence CTA is an accurate and highly efficient method to evaluate for LVO in hyperacute stroke patients [Strong Evidence], which is critical in determining which patients may benefit from EVT [Strong Evidence]. The risk of permanent contrast nephropathy in stroke patients is sufficiently low that the delay imposed by evaluating renal function prior to CTA is not routinely warranted [Moderate Evidence]. MRA

without contrast (i.e., time-of-flight MRA) is equivalent to CTA in evaluating for intracranial LVO [Moderate Evidence], and MRA with contrast is equivalent or superior to CTA in evaluating the extracranial vasculature [Strong Evidence], but MRA often imposes additional delays to treatment, which can worsen outcomes [Strong Evidence]; thus MRA should be reserved for patients who absolutely cannot undergo CTA or who are already undergoing MRI. Other techniques such as transcranial Doppler imaging or clinical assessment is not yet sufficiently accurate to replace CTA [Limited Evidence].

Supportive Evidence

(i) *Digital subtraction catheter-directed angiography (DSA)* The gold standard for assessing large vessel occlusion is currently DSA. Given the high spatial and temporal resolution of DSA as compared to other techniques, occlusion and stenosis of both large and small vessels are readily demonstrated (however, for note of controversy, see [102]). The dynamic images from DSA also help in evaluating collateral flow. The major drawbacks of DSA are that it requires (1) groin puncture to access the femoral artery subjecting the patient to potential groin complications including hemorrhage and pseudoaneurysm; (2) the use of intra-arterial wires and catheters to select target vessels for angiography, which may result in stroke or arterial injury; and (3) availability of experienced operators, technologists, and nurses to perform the procedure. On the other hand, DSA is a prerequisite to EVT and, if positive, can lead directly to EVT.

Most patients in the IMS-3 trial were evaluated with a “DSA-first” approach, whereby patients suspected to have LVO based on clinical assessment were taken directly to the angiography suite for DSA and then EVT if LVO was detected [96]. The IMS-3 trial showed no benefit for EVT with this approach, though older-generation thrombectomy devices (and not stent retrievers) were used in the vast majority of these patients. In contrast, the recent RCTs that

were positive for EVT all required noninvasive evidence of LVO prior to EVT [8, 92–95]. It is difficult to determine how much noninvasive LVO detection contributed to the success of the recent RCTs, as compared to use of stent retrievers and improved systems of care. However, while the evidence does not fully prove that non-DSA-based LVO detection itself leads to improved outcomes, the preponderance of evidence strongly supports noninvasive LVO detection in hyperacute stroke patients as a prerequisite to EVT. As discussed further below, noninvasive LVO detection also improves systems of care that involves more hospitals without local access to neuro-interventional services.

(ii) *Computed tomographic angiography (CTA)*

While a hyperdense vessel on NHCT is suggestive of thrombus in the M1 segment or basilar artery, this sign is variably present and not sensitive nor entirely specific to the presence of LVO [103]. Ongoing efforts to improve LVO detection with thin-section NHCT may improve the accuracy of this sign in the future [104, 105]. Given improvements in CT scanners over the past decade, largely due to multidetector row technology, it is now possible to evaluate the cerebral vasculature highly accurately with CT and high-rate intravenous contrast administration. With proper technique, CTA delineates the course and caliber of the carotid and vertebral arteries in the neck, the internal carotid and basilar arteries intracranially, and the proximal portions of the anterior, middle, and posterior cerebral arteries [106]. When an occlusion of one of these vessels is present, contrast opacification of the vessel is absent, providing evidence for the occlusion.

One advantage of CTA is that it can be performed immediately following the prerequisite noncontrast CT for all stroke patients. The entire examination can be completed within a few minutes using 75–100 mL of nonionic intravenous contrast. CTA has been found to be both sensitive and

specific in identifying a large vessel occlusion (defined as A2, M2, P2, or more proximal) in comparison to catheter angiography [102, 106], including several small case series [107–113]. CTA is also accurate in measuring large vessel stenosis. One study with two blinded raters comparing CTA to DSA measured 475 short segments of intracranial arteries in 41 patients [114]. For detection of $\geq 50\%$ stenosis, CTA had 97.1% sensitivity and 99.5% specificity. A meta-analysis of eight high-quality studies and 864 patients compared carotid stenosis as measured by CTA to DSA [115]. For 70–99% internal carotid artery (ICA) stenosis, the overall sensitivity and specificity were 85% and 93%, respectively. For detection of ICA occlusion, the sensitivity and specificity were 97% and 99%, respectively. Analysis of the recent RCTs for EVT regarding CTA accuracy is pending but is widely expected to demonstrate similar or better accuracy. The accuracy of CTA interpretation increases with the training and experience of the physician [116]. In our experience, 3D reconstructions using maximum intensity projections (MIPs) and volume rendering both improve the accuracy of CTA interpretation, though the use of these techniques in the hyperacute period should be balanced against the additional delay incurred by performing these reconstructions.

There are several pitfalls in the use of CTA for identifying LVO [106, 117, 118]. Flow in an affected vessel may be slowed sufficiently for contrast opacification to be absent proximal to the occlusion, leading to inaccurate determination of the length of occlusion and possible incorrect interpretation of an occlusion arising from a proximal trunk such as the common carotid artery; this can be overcome in many instances with delayed or multiphase CTA [119, 120], but the diagnostic yield and effect on outcomes of performing delayed or multiphase CTA remain uncertain [121]. Also, incorrect contrast bolus timing can lead to poor opacifica-

tion of the cerebral arteries when too early or excessive venous contamination when too late. Identifying occlusion of smaller branches, such as M3 vessels or the anterior inferior cerebellar artery (AICA), is also difficult due to the limited resolution of CTA imposed by radiation dose limits.

One concern regarding CTA is the risk of contrast-induced nephropathy (CIN). Several studies have addressed this by measuring the rate of CIN in acute ischemic stroke patients following CTA. Despite varying definitions of CIN, these consistently demonstrate a very low rate of CIN (2–5%) in patients undergoing CTA for stroke and virtually no patient requiring hemodialysis as a result of CIN [122–126]. A recent study further compared patients undergoing contrast-enhanced CT for any reason to those undergoing noncontrast-enhanced CT [127, 128]. This study found that the rate of acute renal failure was not significantly different between the two groups. No study has prospectively randomized patients to contrast administration versus no contrast, so definitive evidence regarding the risk of CIN specifically (as compared to any cause acute renal failure) is lacking. The time required to evaluate for pre-existing risk factors for CIN, including serum creatinine, diabetes, and heart failure, will vary across hospitals but is likely to require at least a few additional minutes of time prior to performing the CTA. Thus, there is no evidence to support checking a serum creatinine prior to CTA in the hyperacute setting and in fact at least moderate evidence to the contrary.

(iii) *MR angiography (MRA)* MRA is capable of imaging the intracranial vasculature without contrast using a time-of-flight technique and also via contrast-enhanced MRA. For proximal ICA lesions, the sensitivity and specificity of contrast-enhanced MRA are high when compared to DSA. In a meta-analysis of 41 studies in 2541 patients looking at ICA lesions of 70–99% stenosis on DSA, contrast-enhanced MRA was found to be

the most sensitive (94%) and specific (95%) of four modalities: enhanced MRA, non-enhanced MRA, Doppler ultrasound, and CTA [115]. While MRA appears to be a useful tool for measuring stenosis in large vessels, its sensitivity decreases for smaller caliber intracranial vessels. Although contrast-enhanced MRA of the extracranial arteries appears to be better at defining the degree of stenosis than time-of-flight MRA [129, 130], assessment of the intracranial vessels with contrast is limited due to venous contamination and poor spatial resolution. In the study of intracranial disease discussed above comparing CTA and MRA to DSA, in 28 patients (in 672 vessel segments) time-of-flight MRA had a sensitivity of 70% and 81% and specificity of 99% and 98% for intracranial stenosis and intracranial occlusion, respectively [102]. The Stroke Outcomes and Neuroimaging of Intracranial Atherosclerosis (SONIA) trial was a prospective, multicenter study comparing the diagnostic accuracy of transcranial Doppler (TCD) and MRA to DSA [131]. The SONIA study found that both TCD and MRA have high negative predictive values (86% and 91%, respectively) but low positive predictive values (36% and 59%, respectively). Sensitivity and specificity could not be obtained since not every patient had DSA. As noted previously, the major limitation to MRA is the increased time required to perform MRI compared to CT in most institutions. However, MRA may be useful in select circumstances where patients are already undergoing brain MRI in the hyperacute stroke period.

(iv) *Miscellaneous* As noted above, TCD was evaluated in the SONIA study and was found to have a modestly high negative predictive value, but a low positive predictive value for detecting intracranial atherosclerosis [131]. As for MRA, the diagnostic performance of TCD may improve in the more limited clinical context of attempting to detect LVO. However, TCD requires an adequate temporal acoustic window to evaluate

for MCA occlusion, which may not be present in approximately 20% of patients. Thus, TCD cannot be recommended currently as a replacement for CTA. Clinical assessment with the National Institutes of Health Stroke Scale (NIHSS) has been investigated as a tool to predict which patients may or may not have LVO. Interestingly, LVO is found variably in patients with NIHSS ranging from 2 to 20 [99]. Thus the NIHSS cannot be recommended as a surrogate for LVO detection. Usage of a NIHSS cutoff to determine which patients to screen for EVT is beyond the scope of this chapter but should be determined based upon the clinical inclusion and exclusion criteria for EVT rather than its predictive value for LVO.

Does This Patient Have a Large Ischemic Core?

Summary of Evidence The size of an ischemic core as defined by DWI accurately predicts a final infarct size and outcomes in acute stroke patients [Strong Evidence]. A low ASPECTS score on NHCT also predicts larger final infarct size and worse outcomes, though not as robustly as DWI [Strong Evidence]. A large ischemic core identifies patients unlikely to benefit from EVT, when defined by either a very low ASPECTS score (0–4) [Moderate Evidence] or by a large DWI lesion [Limited Evidence]; however, performing MRI may also introduce delay to therapy. Other methods to define the ischemic core, including CTA source images (CTA-SI) and CT or MR perfusion imaging, may also be accurate in predicting final infarct size and outcomes, in particular using relative cerebral blood flow maps with CT perfusion imaging [Strong Evidence].

Supporting Evidence

- (i) *Computed tomography (CT)* While NHCT remains poorly sensitive to hyperacute ischemic stroke, early signs of ischemia when present predict larger final infarct size and worse outcomes [75–78]. Among other trials, the positive ECASS-3 trial, which showed efficacy of IV-tPA in improving outcomes within the 3–4.5 time window, excluded

patients with NHCT signs of ischemic stroke that involved greater than 1/3 of the MCA territory [14]. However, while this criterion predicts worse outcomes overall, it does not necessarily negate the benefit of IV-tPA [7].

ASPECTS was devised as an ordinal scoring method to more reliably determine the extent of early signs of ischemic stroke on NHCT [41, 47, 79]. As noted above, the score ranges from 0 to 10, with a point lost for each of ten MCA territory regions demonstrating features of ischemic stroke including loss of gray-white matter distinction and hypodensity. In the ESCAPE trial, an ASPECTS <6 was used as a criterion to exclude patients from enrollment [93]. Subsequent analysis found that of the patients enrolled, 3.6% had an ASPECTS <6 based on core lab review, suggesting that using a cutoff of <6 may be reliable, though it is unknown what percentage of patients excluded from the trial due to a low ASPECTS would have been included if their ASPECTS was determined by a core lab. SWIFT-PRIME and REVASCAT also excluded patients with a low ASPECTS score (<7). MR CLEAN included patients with any ASPECTS score, at the discretion of the treating physicians, including 28 patients with an ASPECTS of 0–4 [8]. Subgroup analysis found benefit of EVT in patients with ASPECTS 8–10 (odds ratio for good outcome favoring EVT [OR] 1.61) and 5–7 (OR 1.97), but no benefit when ASPECTS was 0–4 (OR 1.09). However, the number of patients in the last group was small resulting in large confidence intervals (OR 95% CI 0.14–8.46). A subsequent pooled analysis of five of the positive RCTs comparing stent retriever-based EVT versus best medical therapy also found no significant benefit for EVT in patients with ASPECTS of 0–5, though again with small sample size ($n = 121$, OR 1.24, 95% CI 0.62–2.49) [9].

The size of an infarct can also be predicted using the CTA-SI, by measuring the region of hypodensity and hypovascularity in

the affected territory, as compared to DWI [132, 133], but may overestimate infarct core depending on the protocol used [134, 135]. CTP may also be used to predict infarction by setting a low perfusion threshold below which tissue is presumed to represent the ischemic core. Studies vary greatly in terms of the perfusion parameter and threshold used to determine an ischemic core. For example, a large series of 130 patients found good accuracy (AUC = 0.927) for an absolute CBV threshold of $2.0 \text{ mL} \times 100 \text{ g}^{-1}$ [136]. More recent efforts have demonstrated that a relative cerebral blood flow (CBF) of less than 30–34% or CBV of less than 32–34% is [137] highly accurate of ultimate infarct volume; this latter threshold has further validity in that it was used to select patients in the recently halted DAWN and DEFUSE-3 trials (see Question 2.3).

- (ii) *Magnetic resonance imaging (MRI)* When tissue infarcts, it results in increased diffusion restriction both intracellularly and extracellularly, resulting in marked decreased apparent diffusion coefficients (ADC) and hyperintensity on the trace DWI images. Several studies have confirmed that the resulting region of diffusion restriction represents infarcted tissue demonstrated on subsequent follow-up MRI [34, 53, 54, 138–141]. Patients with an initial DWI lesion $>70 \text{ mL}$ demonstrate a very high rate of poor outcomes [142]. Prior to the recent RCTs but after the introduction of stent retrievers, DWI was used in one study to exclude patients from EVT with a large infarct $>70 \text{ mL}$ [143]. They investigated outcomes before and after introducing this exclusion criterion and found that outcomes improved significantly after they began using DWI for this purpose. EXTEND-IA and initially SWIFT-PRIME both used DWI definitions of ischemic core to exclude patients with large completed infarcts but do not provide independent evidence that using DWI in this fashion appropriately excludes patients from futile EVT [92, 95]. It is thus probable, but not certain,

that DWI can identify patients in whom EVT will be futile. As with any MR-based method, a drawback of DWI is that it may delay treatment [144].

Does This Patient Have “Salvageable” Tissue?

Summary of Evidence Methods to define salvageable tissue vary widely and include perfusion-based techniques as well as assessment of collateral flow to the affected territory, with no clearly defined gold standard. The presence of salvageable tissue based on perfusion imaging does not identify patients more likely to benefit from older-generation EVT methods [Strong Evidence]. Selection of patients based on the presence of a penumbra with perfusion imaging or adequate collaterals with multiphase CTA may help to identify increased benefit from stent retriever-based EVT but may not be necessary and could possibly exclude patients who would otherwise benefit from EVT within 6 h of stroke onset [Moderate Evidence]. A trial that explicitly randomizes patients with *unfavorable* penumbra/collateral imaging (i.e., no or little mismatch or poor collaterals) for EVT or not would be required to determine whether or not it is necessary to apply such imaging in the first 6 h. On the other hand, growing evidence indicates that patients with *favorable* penumbra/collateral imaging might benefit from EVT beyond 6 h [Strong Evidence, pending publication of results].

Supporting Evidence

- (i) *Penumbra-based methods* When arterial flow is severely disrupted, a portion of the brain parenchyma in the affected arterial territory may experience ischemia. The depth and length of this ischemia determine whether the tissue will experience irreversible infarction. The idea of a penumbra defines a region surrounding or adjacent to infarcted tissue that is ischemic and thus vulnerable to future infarction but also potentially salvageable if the ischemia is reduced or abated within a certain time period. Thus,

the goal of therapy is to save this penumbra from subsequent infarction through recanalization or other methods.

Early studies used PET-based oxygen and blood flow tracer imaging to identify thresholds of oxygen metabolism and blood flow that identified tissue destined to infarct versus tissue that was ischemic but that did not necessarily infarct (i.e., penumbra) [145]. Since then, both CT- and MR-based perfusion imaging have been used in a similar fashion [136, 146–148]. Taking advantage of the blood oxygenation level-dependent (BOLD) relaxation effect, MR-based CMRO₂ measurements have also been recently used for similar purpose [149, 150]. A common feature of all of these methods is to define one threshold to represent ischemic tissue and to either define another threshold to define the ischemic core or to use another measure (e.g. DWI) to define the ischemic core. The mismatched area between ischemic tissue and the infarcted core is then used to define the penumbra.

In a prospective study, MR perfusion-diffusion mismatch identified patients more likely to experience a good outcome following reperfusion, suggesting that this method is effective at least as a prognostic indicator [151]. Another study randomized patients to MR perfusion-diffusion mismatch-based penumbra imaging versus no MR imaging to determine whether the former selected patients would uniquely benefit from EVT [98]. This study found no evidence that penumbra detection with MR perfusion-diffusion mismatch would select patients appropriately for EVT. However, this study was performed before stent retrievers were widely used and is thus limited to EVT performed with older-generation devices. Subsequently, no similar study has been performed. A few of the recent RCTs proving the efficacy of EVT employed perfusion-based penumbra imaging as an inclusion criteria, two with perfusion imaging (EXTEND-IA and SWIFT-PRIME) [92,

93, 95]. While these trials showed increased efficacy of EVT compared to trials that did not require penumbra imaging (MR CLEAN and REVASCAT), the multiple differences between the trials preclude distinction of which factors resulted in different effect sizes among the trials. Also, efficacy of EVT was sustained in trials that did not require penumbra imaging, suggesting that penumbra imaging might inappropriately exclude patients who could benefit from EVT. Interestingly, SWIFT-PRIME changed their inclusion/exclusion criteria after enrolling several dozen patients, creating an opportunity to see how penumbra imaging might affect outcomes [95]; however the sample size for this analysis may be underpowered due to the trial being halted early after the announcement of the MR CLEAN results.

Another trial used advanced CT imaging, CTA and CTP, to select patients for a prospective randomized controlled trial of intravenous tenecteplase versus alteplase for intravenous thrombolysis within 6 h of symptom onset [100]. This trial found benefit for tenecteplase. A subsequent similar prospective randomized controlled trial of intravenous tenecteplase versus alteplase found no benefit, suggesting that the advanced imaging was important in realizing the added benefit of tenecteplase [152]. Unfortunately, it cannot be determined based on these trials whether the difference in trial outcomes was due to selecting patients on the basis of CTA for LVO, CTP for a small ischemic core, CTP for an adequate penumbra, or a combination of these factors.

More recent trials, including the “DWI or CTP Assessment with Clinical Mismatch in the Triage of Wake-Up and Late Presenting Strokes Undergoing Neurointervention” (DAWN) trial and the “Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3” (DEFUSE-3) trial, aim to determine the efficacy of EVT in stroke patients presenting beyond 6 h of stroke onset. The DAWN trial applies a “clinical imaging mis-

match” paradigm that includes measurement of an ischemic core with MRI-DWI or CTP (relative cerebral blood flow <30%) and compares this to NIHSS score and age; patients presenting 6–24 h after onset with high NIHSS relative to the size of their ischemic core are then randomized to EVT or not. Though not yet published at the time of this writing, the trial was stopped early following a prespecified interim analysis due to efficacy [101]; if confirmed positive, this will strongly support the use of perfusion imaging to select patients beyond 6 h for EVT [evidence level pending publication of results]. The also halted RCT DEFUSE-3 similarly aimed to determine the efficacy of EVT in patients presenting between 6 and 16 h of stroke onset, selected using CTP- or MRI-based penumbra imaging.

- (ii) *Collateral flow-based methods* In order for tissue to remain viable despite parent artery occlusion, there must be blood flow from a collateral source—most frequently from arteries in adjacent territories [145, 153]. A brain with large collaterals is therefore more likely to have salvageable tissue than one without. This forms the basis of collateral flow imaging. Several methods have been employed to assess collateral flow in stroke patients, including DSA, PET, MRA, and FLAIR imaging which may show hyperintense pial collaterals in the affected territory and CTA [145, 154–156]. The presence of good collateral vessels has been a strong predictor of good outcomes, independent of treatment. In one of the recent positive RCTs for EVT (ESCAPE), a multiphase CTA technique was used to determine the presence of collateral vessels over the affected territory [93]. The presence of collaterals was graded as good or poor based on a visual grading system. Patients were included in the trial if collaterals were deemed to be good. A meta-analysis of 5 of the positive RCTs for EVT found that patients with good collaterals on multiphase CTA or adequate penumbra on perfusion

imaging might benefit from EVT up to 7.3 h after onset [12]. Thus, these techniques are appropriate to select for patients between 6 and 7.3 h. However, as patients were not randomized to multiphase CTA/penumbra imaging versus no such selection criteria, using this advanced imaging to select patients for EVT within 6 h of onset remains in question.

Applicability to Children

As for intravenous thrombolysis, no prospective and/or controlled study to date has evaluated the safety nor efficacy of endovascular therapy for ischemic stroke in children. Thus, none of the recommendations above necessarily nor sufficiently apply for pediatric stroke.

How Can We Improve Systems of Stroke Care and Imaging to Expedite Treatment of Hyperacute Stroke Patients?

Summary of Evidence Time to intravenous thrombolysis and EVT greatly influences outcomes [Strong Evidence]. Improving systems of stroke care, including imaging in the hyperacute setting, is thus likely to improve neurological outcomes. Value stream analysis (VSA) and mapping techniques may improve door-to-needle [Moderate Evidence] and door-to-groin puncture [Limited Evidence] times. Performing initial evaluation and intravenous thrombolysis in the CT scanner room significantly improves door-to-needle times [Moderate Evidence]. Ambulatory stroke units that include mobile CT scanners may also improve door-to-needle times and are safe [Moderate Evidence]. New multidisciplinary approaches to stroke care are likely needed to improve outcomes from intravenous thrombolysis and EVT [Limited Evidence].

Supporting Evidence Time to intravenous thrombolysis from symptom onset is a significant predictor of both 3-month outcomes and the relative benefit derived from IV-tPA [20].

Similarly, time to reperfusion by EVT was recently shown to be a significant predictor of outcomes and the relative benefit from EVT, perhaps with an even larger effect than that shown for IV-tPA [8, 11]. Hence, minimizing the time to treatment is of paramount importance to optimize stroke outcomes.

There are many elements to the evaluation and treatment of stroke patients, involving a variety of health-care professionals (including but not limited to physicians, nurses, technicians, radiology technologists, emergency medical transport personnel, and pharmacists), a variety of settings (the patient's home, ambulance or other vehicle, the CT or MR scanner, the emergency room, and the angiography suite), and a variety of assessments and decisions. Establishing door-to-needle and door-to-groin puncture guidelines, particularly those tied to accreditation, may help reduce the time to treatment in these settings [157]. Protocols for rapid thrombolysis in the Emergency Department have been developed and appear to be transferrable to other institutions [158–160]. Value stream analysis (VSA) is a technique originally developed to improve the efficiency of industrial manufacturing processes and has since been applied to the evaluation and treatment of hyperacute stroke patients leading to significant decreases in door-to-needle times. Based on these findings, guidelines from the American Stroke Association encourage direct admission of patients to the CT scanner with intravenous thrombolysis provided in the scanner suite if the patient is eligible [161].

Another method to decrease door-to-needle time is to employ a mobile stroke unit that includes a CT scanner [162–164]. The patient and a NHCT can be assessed in this unit via telemedicine methods. This method has been successfully deployed in Europe and the United States. A randomized trial suggests that this technique is safe and reduces time to intravenous thrombolysis [165]. More evidence is required to see how this approach affects time to EVT.

Table 8.1 Diagnostic performance for patients presenting with acute neurological deficits

	Sensitivity (%)	Specificity (%)	Evidence
Acute intraparenchymal hemorrhage (<6 h)			
CT	89–100 ^a	100 ^a	a
MRI	81–100	100	Strong
Acute subarachnoid hemorrhage (<12 h)			
CT	98–100	100	Strong
MRI (FLAIR)	92–100	100	Limited
Acute ischemic infarction (<6 h)			
CT	31–61	65	Moderate
MRI	88–100	95	Strong
Large vessel occlusion (intracranial)			
CTA	97	99	Strong
MRA	81	98	Moderate

Adapted from Vo KD, Lin W, Lee J-W. Neuroimaging in Acute Ischemic Stroke. In Medina LS, Blackmore CC (eds): *Evidence-Based Imaging: Optimizing Imaging in Patient Care*. New York: Springer Science + Business Media, 2006, with kind permission of Springer Science + Business Media

^aAlthough the exact sensitivity or specificity of CT for detecting intraparenchymal hemorrhage is unknown (limited evidence), it serves as the gold standard for detection in comparison to other modalities

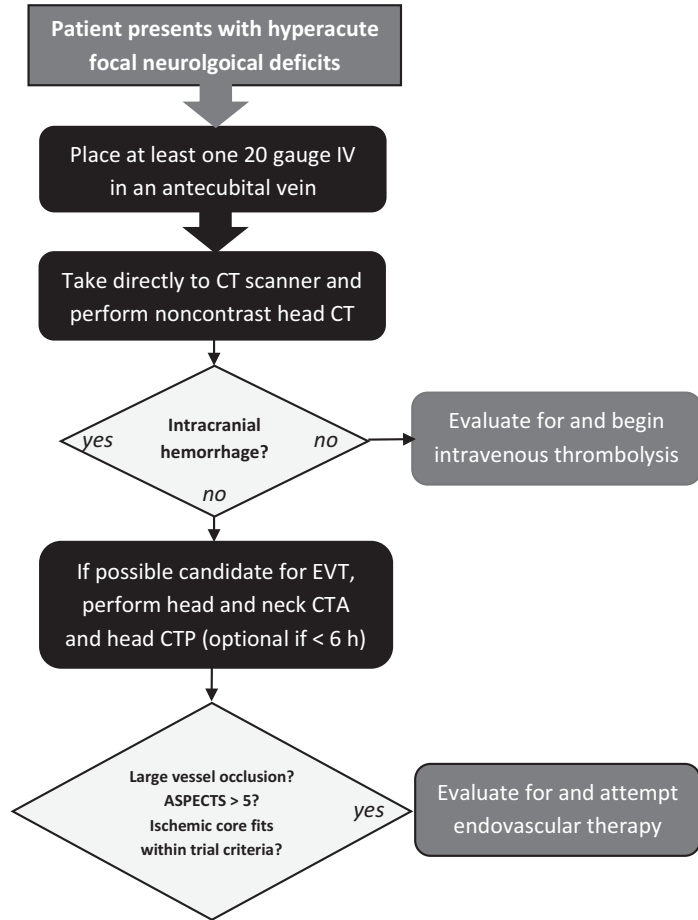
Take-Home Table and Figure

Table 8.1 highlights the diagnostic performance of imaging for acute neurological deficits. Figure 8.1 is an imaging algorithm for patients with suspected hyperacute ischemic stroke.

Take-Home Points

Imaging of patients with hyperacute ischemic stroke should be driven by its ability to enable and direct subsequent therapies that are *proven* to improve outcomes—namely, intravenous thrombolysis and endovascular thrombectomy. The choice of imaging must also weigh its utility against time delays to treatment in order to optimize patient outcome. For most Emergency Departments, CT represents the best balance of

Fig. 8.1 Suggested simplified imaging pathway for patients with suspected hyperacute ischemic stroke



accuracy and availability, allowing detection of intracranial hemorrhage, large vessel occlusion, and very large ischemic cores to permit rapid decisions on whether to proceed with intravenous thrombolysis and/or endovascular thrombectomy. MRI is essentially equivalent in these tasks but typically introduces unnecessary delays to treatment. Advanced techniques, including perfusion and collateral imaging, will likely soon have an evidence-based role particularly beyond 6 h since stroke onset and will also need to be incorporated into the armamentarium of the radiologist.

Imaging Case Studies

Case 1

In Fig. 8.2a–c, a patient presents with sudden-onset left-sided weakness, confusion, and neglect within 2 h of onset. Large vessel occlusion with hyperacute stroke is established.

Case 2

In Fig. 8.3a–c, acute or hyperacute infarct in the left corona radiata is discovered after a patient presents with sudden-onset right hemiparesis.

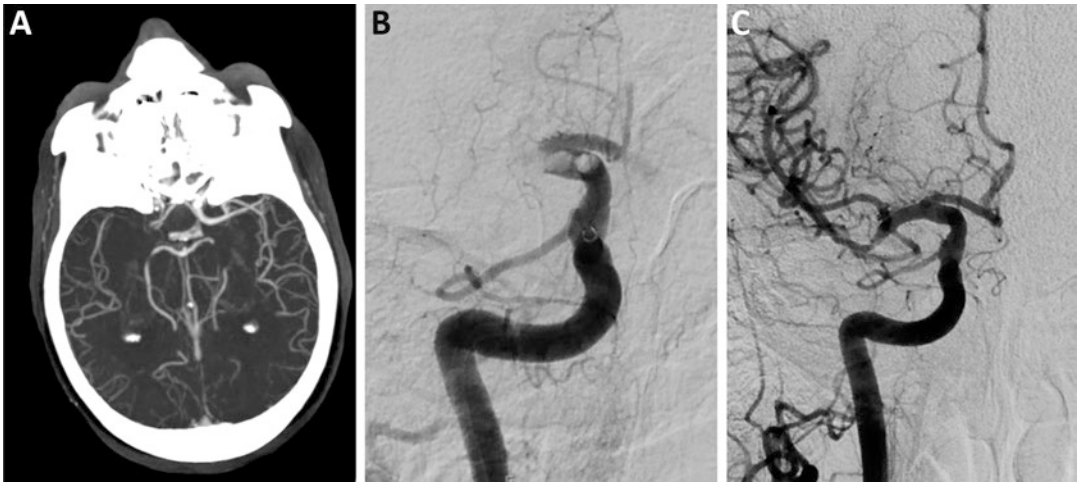


Fig. 8.2 CTA is highly accurate in identifying large vessel occlusion noninvasively in patients with hyperacute stroke, allowing selection for subsequent EVT. This patient presented with sudden-onset left-sided weakness, confusion, and neglect within 2 h of onset. (a) CTA demonstrated a

right ICA terminus occlusion extending into the right M1 and A1 segments. (b) Angiography confirmed the presence of thrombus and subsequent mechanical thrombectomy resulted in (c) recanalization of the arteries and reperfusion of the right MCA and ACA territories

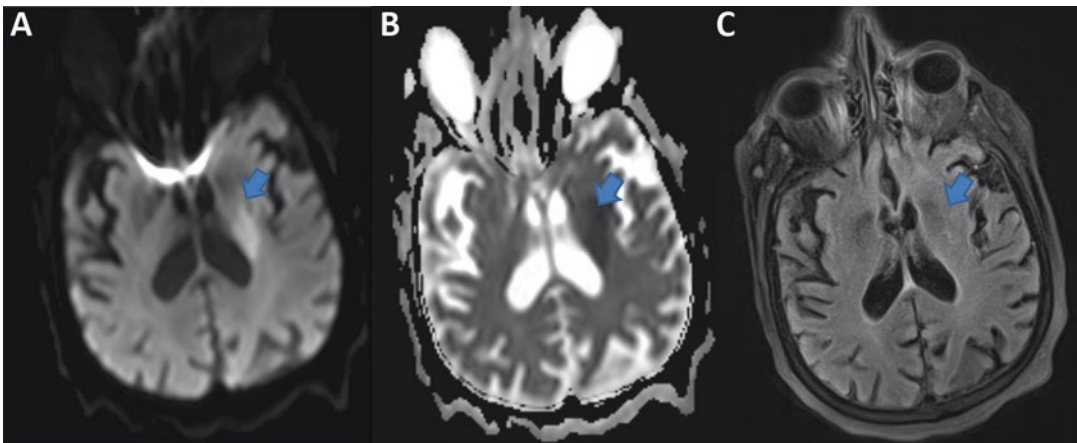


Fig. 8.3 MRI with diffusion-weighted imaging is highly sensitive to acute ischemic stroke. In this patient with sudden-onset right hemiparesis, (a) hyperintensity on a DWI sequence and (b) matching hypointensity on the ADC map confirm the presence of an acute or hyperacute infarct in

the left corona radiata. (c) The absence of hyperintensity in this region on the FLAIR sequence suggests that this imaging was performed within 4–5 h of stroke onset. *ADC* apparent diffusion coefficient, *DWI* diffusion-weighted imaging, *FLAIR* fluid-attenuated inversion recovery

Suggested Imaging Protocols

There are many factors which determine the optimal imaging protocol, including the CT or MR scanner vendor, age, and equipment. The imag-

ing protocol should also take into consideration patient motion and cooperation as well as technologist training and availability. The following represent imaging protocols that are reasonable for most Emergency Departments.

Noncontrast Head CT

- Spiral or conventional CT (the former may be better for moving patients, while the latter typically provides better gray-white matter differentiation).
- Volume of acquisition should include the vertex to the craniocervical junction, parallel to the inferior orbitomeatal line.
- kVp and mAs should be adjusted to provide sufficient gray-white matter differentiation with a radiation dose that is as low as reasonably achievable.
- 3–5 mm thick slices with 3–5 mm intervals, axial brain soft kernel reconstructions to evaluate for intracranial hemorrhage; note that 5 mm thick slices are preferred for ASPECTS rating, but thinner slices might be superior for subtle hemorrhage detection.
- Equivalent size axial bone kernel reconstructions.

CT Angiography

- Serum creatinine evaluation should not delay CTA in patients who are potential candidates for endovascular thrombectomy (as discussed in detail above).
- Spiral or helical CT is preferred, ideally on scanners with higher numbers of multidetector rows.
- Volume of acquisition should include the vertex to the aortic arch.
- kVp and mAs should be adjusted to provide sufficient vascular definition with a radiation dose that is as low as reasonably achievable.
- Bolus tracking from the aorta; if a single phase is obtained, an arterial-to-arteriovenous phase is preferred with the option to obtain a more delayed phase if needed.
- 1 mm thick slices with 0.5 mm intervals, soft tissue reconstructions to evaluate for large vessel occlusion.
- 10–30 mm MIPs in the axial and coronal planes to evaluate for large vessel occlusion.

Hyperacute Stroke MRI

Stroke MRI protocols vary greatly among institutions. The following protocol is reasonable to rapidly identify/confirm stroke, exclude hemorrhage, and evaluate for large vessel occlusion:

- MRI safety screening per institutional policy or skull, neck, and chest radiography if unable to obtain
- DWI and ADC map
- FLAIR sequence
- Blood-sensitive sequence (T2* or SWI)
- Time-of-flight noncontrast MRA to evaluate for large vessel occlusion

Future Research

Research in stroke imaging is advancing rapidly—so much that a portion of what is written here will almost certainly be outdated by the time of publication. Many important questions remain, such as the role of advanced penumbra and collateral imaging if any, more accurate determination of ischemic core using CT, whether imaging evaluation can be performed completely in the angiography suite with new tomographic techniques, methods to improve systems of stroke care beyond single hospitals to networks of hospitals, the applicability of any of this to pediatric stroke, and the applicability if any in underdeveloped nations where health-care resources are severely limited. Cost-effectiveness analyses must now also be updated given the recent positive RCTs for endovascular thrombectomy and were therefore not discussed here. Finally, while intravenous thrombolysis 20 years ago and now endovascular thrombectomy represent revolutionary advances in the treatment of hyperacute ischemic stroke, many stroke patients remain disabled; developing effective imaging and treatment methods for these patients remains a critical goal for future research in stroke imaging.

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Acute Headache Disorders in Adults and Children: Evidence-Based Emergency Imaging

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Key Points

- CT imaging remains the initial test of choice for (1) new onset of headache in high-risk adults and (2) headache suggestive of subarachnoid hemorrhage (limited evidence).
- MRI is recommended in adults with non-acute headache and unexplained abnormal neurologic examination (moderate evidence).
- In adults with headache and known primary neoplasm suspected of having

brain metastatic disease, MR imaging with contrast is the neuroimaging study of choice (moderate evidence).

- Although most headaches in children are benign in nature, a small percentage is caused by serious diseases, such as brain neoplasm.
- MRI is recommended in children with headache and an abnormal neurologic examination or seizures (moderate evidence).
- Sensitivity and specificity of MR imaging are greater than CT for non-subarachnoid hemorrhagic intracranial lesions. For intracranial surgical space-occupying lesions, however, there is no difference in diagnostic performance between MR imaging and CT (limited evidence).
- Conventional CT angiography (CTA) and MR angiography (MRA) have sensitivities greater than 85% for detection of aneurysms greater than 5 mm. Multi-detector row CT (MDCT) sensitivity and specificity are greater than 90% for aneurysms greater than 4 mm (moderate evidence).
- MDCT angiography and digital subtraction angiography (DSA) have similar sensitivities and specificities for detec-

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(continued)

tion of aneurysms greater than 4 mm (moderate evidence).

- Advanced brain imaging may help differentiate the different types of primary headache disorders. Migraine disorders have a brain stem, primarily pontine, origin (limited evidence). In contrast to migraine disorders, there is no brain stem activation during acute cluster headache episodes compared with the resting state (limited evidence). These initial studies suggest that, although primary headaches such as migraine and cluster headaches may share a common pain pathway—the trigeminovascular innervation—their underlying pathogenesis differs significantly.

Definition and Pathophysiology

Headaches can be divided into primary and secondary (Table 9.1). Primary causes include migraine, cluster, and tension-type headaches, while secondary etiologies include neoplasms, arteriovenous malformations, aneurysms, infections, trauma, and hydrocephalus. Diagnosis of primary headache disorders is based on clinical criteria as set forth by the International Headache Society [1]. A detailed history and physical examination help distinguish between primary and secondary headaches. Neuroimaging should aid in the diagnosis of secondary headache disorders.

Secondary headaches in children are more likely to present as acute headache, sudden onset in an otherwise healthy child, or as a chronic progressive headache, with gradual increase in frequency and severity. Acute recurrent headaches in an otherwise healthy child most often represent migraine or episodic tension-type headaches [2]. Sinus disease is a common cause of acute headache. Chapter 13 on sinus disease provides a comprehensive discussion on this topic.

Table 9.1 Common causes of primary and secondary headache

Primary headaches
Migraine
Cluster
Tension type
Secondary headaches
Intracranial space-occupying lesions
Neoplasm
Arteriovenous malformation
Abscess
Hematoma
Cerebrovascular disease
Intracranial aneurysms
Occlusive vascular diseases (such as dissections, vasculitis, venous stenosis, and thrombus)
Infection
Acute sinusitis
Meningitis
Encephalitis
Inflammation
Vasculitis
Acute disseminated encephalomyelitis
Increased intracranial pressure
Hydrocephalus
Idiopathic intracranial hypertension (pseudotumor cerebri)

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More than 15 studies have reported white matter abnormalities in patients with migraine headaches, ranging from 12% to 63% [3–5]. White matter abnormalities were reported more frequently in the frontal region of the centrum semi-ovale. Six of the eight studies using controls found a higher incidence of white matter abnormalities in migraineurs [6]. The cause of white matter abnormalities in migraine is uncertain but may be related to increased platelet aggregability with microemboli, abnormal cerebrovascular regulation, repeated attacks of hypoperfusion during the aura, and presence of antiphospholipid antibodies [7–10].

Epidemiology

Adults

Headache is a very common symptom among adults, accounting for 18 million (4%) of the total outpatient visits in the USA each year [11]. In any given year, more than 70% of the US population has a headache [12]. An estimated 23.6 million people in the USA have migraine headaches [13, 14].

In the elderly population, 15% of patients 65 years or older, compared to 1–2% of patients younger than 65 years, presented with secondary headache disorders such as neoplasms, strokes, and temporal arteritis [13, 15]. In a prospective study by Vazquez et al. [16], 8% of patients with intracranial tumors presented with headache as their first and isolated clinical manifestation. However, headache can be present in 50% to 60% of patients with brain neoplasms [17], with most of them meeting the international headache society criteria for tension headache [18]. Although unknown at the moment of this publication, the percent brain neoplasms presenting with secondary acute headache is felt to be low as most of the current literature regarding headaches describe subacute or chronic symptomatology in these patients. Brain metastases are the most common intracranial tumors, far outnumbering primary brain neoplasms [19]. Approximately 58% of primary brain neoplasms in adults are malignant, such as astrocytoma and glioblastoma multiforme [19]. Benign brain tumors account for 38% of primary brain neoplasms [19]. Despite their “benign” name, they may have aggressive characteristics causing significant morbidity and mortality [19]. The meningioma is the most common type [19].

Children

Pediatric headache is a common health problem in children, with a significant headache reported in more than 75% by the age of 15 years [20]. In approximately 50% of patients with migraines, the headache disorder starts before the age of

20 years [13]. In the USA, adolescent boys and girls have a headache prevalence of 56% and 74% and a migraine prevalence of 3.8% and 6.6%, respectively [11]. Recurrent headache in children is common and has significant medical comorbidity as it is commonly seen in patients with other medical conditions such as asthma, hay fever, and frequent ear infections [21]. A small percentage of headaches in children are secondary in nature. A primary concern in children with headache is the possibility of a brain tumor [22, 23]. Although brain tumors constitute the largest group of solid neoplasms in children and are second only to leukemia in overall frequency of childhood cancers, the annual incidence is low at 3 in 100,000 persons [23]. Approximately 1.3% of pediatric patients with headaches will have an intracranial tumor when evaluated by neuroimaging [24]. However, most of the pediatric patients with brain tumors, about 62%, experience chronic or frequent headaches prior to hospitalization [23]. Only 2.6% of pediatric patients with brain tumors present to the emergency department with acute headache [25]. Primary brain neoplasms are far more prevalent in children than they are in adults [26]. They account for almost 20% of all cancers in children but only 1% of cancers in adults [13]. Central nervous system (CNS) tumors are the second cause of cancer-related deaths in patients younger than 15 years [27].

Overall Cost to Society

Headache is the most common and one of the most disabling types of chronic pain among children and adolescents [28, 29]. The incidence of migraine peaks in adolescence, but the prevalence of migraine continues to increase and is highest in the most productive years of life between the ages of 25 and 55 years [30, 31]. The direct and indirect annual cost of migraine in the USA has been estimated at more than \$5.6 billion [32]. A recent US study showed that migraine families incur far higher direct and indirect health-care costs (70% higher than non-migraine families) with most of the difference concentrated in outpatient costs [33].

Of interest, in families where the sole migraineur was a child versus a parent, the total health-care costs per family were about \$600 higher and almost \$2500 higher than when both a parent and child were affected [28]. Work absence days, short-term disability, and workman's compensation days all were higher among migraine families than among families without a migraineur [33].

Goals of Imaging

- Diagnose secondary causes of headache (Table 9.1) for initiation of appropriate treatment.
- Exclude secondary etiologies of headache in patients with atypical primary headache disorders.
- Decrease the risk of brain herniation prior to lumbar puncture by excluding intracranial space-occupying lesions.
- Differentiate between the types of primary headache disorders using advanced imaging techniques.

Methodology

MEDLINE search using Ovid (Wolters Kluwer US Corporation, New York, NY) and PubMed (National Library of Medicine, Bethesda, MD) was used. Systematic literature review was performed from 1966 through January 2015. Keywords included (1) headache, (2) cephalgia, (3) diagnostic imaging, (4) clinical examination, (5) practice guidelines, and (6) surgery. The Cochrane Collaboration had no reviews of imaging for headache.

Discussion of Issues

Which Adults with New-Onset Headache Should Undergo Neuroimaging?

Summary of Evidence The most common causes of secondary headache in adults are brain neoplasms, aneurysms, arteriovenous malforma-

Table 9.2 Suggested guidelines for neuroimaging in adult patients with new-onset headache

“First or worst” headache (thunderclap headache)
Increased frequency and increased severity of headache
New-onset headache after age 50
New-onset headache with history of cancer or immunodeficiency
Headache with fever, neck stiffness, and meningeal signs
Headache with abnormal neurologic examination or nonfocal as decreased level of consciousness
Headache with vomiting or syncope at the onset

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tions, intracranial infections, and sinus disease. History and physical examination findings may increase the yield of the diagnostic study discovering an intracranial space-occupying lesion in adults. Table 9.2 shows the scenarios that should warrant further diagnostic testing (limited evidence) [11, 13, 34]. The factors outlined in Table 9.2 increase the pretest probability of finding a secondary headache disorder.

What Neuroimaging Approach Is Most Appropriate in High-Risk Adults with New Onset of Headache?

Summary of Evidence CT examination studies have been the standard of care for the initial evaluation of acute onset headache because CT is faster, more readily available, less costly than MR imaging, and less invasive than lumbar puncture [13]. Although MR imaging, specifically fluid attenuation inversion recovery (FLAIR) sequence, has been reported in some articles to be more sensitive than CT for the detection of acute subarachnoid hemorrhage, CT is the preferred initial imaging study in the acute setting given its excellent sensitivity and its wide availability [35, 36]. The data reviewed demonstrate that 11% to 21% of patients presenting with new-onset headache have serious intracranial pathol-

ogy (moderate and limited evidence) [13, 37–39]. Unless further data becomes available that demonstrates higher sensitivity of MR imaging, CT study is recommended in the assessment of all patients who present with new-onset headache (limited evidence) [13]. Lumbar puncture is recommended in those patients in which the CT scan is normal or non-diagnostic and the clinical evaluation reveals abnormal neurologic findings or in those patients in whom subarachnoid hemorrhage (SAH) is strongly suspected (limited evidence) [13]. Figure 9.1 shows a suggested decision tree to evaluate adult patients with acute-onset headache.

Supporting Evidence A prospective study over a 5-year period evaluated 530 out of 3655 patients with the new presenting symptom of headache who had CT or MRI performed with imaging findings classified as normal, significant, or an

insignificant abnormality. Significant abnormalities were found in 2.1% of patients [40]. This percentage was higher among the subset of patients in whom a sinister pathology was suspected clinically (5.5%). Clinical features of patients who underwent imaging included signs of increased intracranial pressure, focal neurologic signs, epilepsy, recent onset headache, and change in headache pattern among others. Imaging findings in these patients included metastases, primary intracranial neoplasms, and malformations (e.g., Chiari). On the other hand, the percentage of significant abnormalities was lower in the subset of patients imaged that had a primary diagnosis of migraine (1.2%) and tension-type headache (0.9%). MRI showed more insignificant abnormalities (46%) than CT (28%). The data suggests that the use of neuroimaging should be selective for the small proportion of headache patients with sinister features either

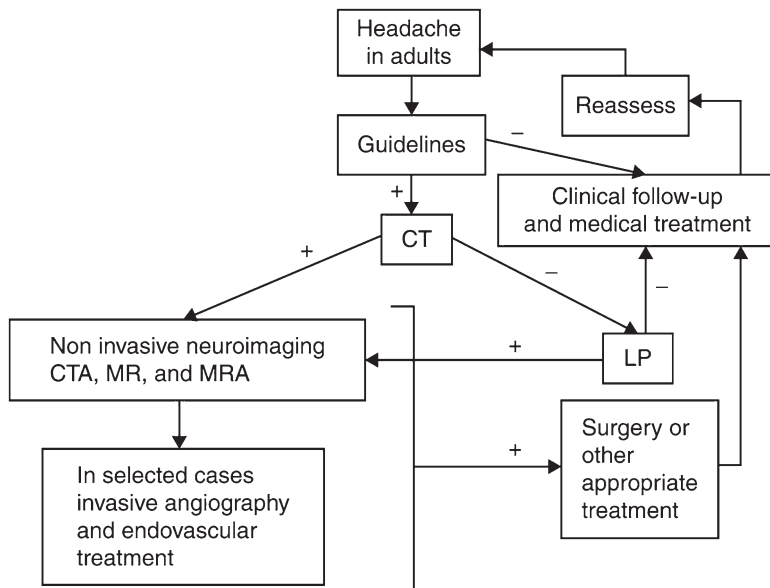


Fig. 9.1 Decision tree for use in adults with new-onset headache. For those patients who meet any of the guidelines in Table 9.2, CT is suggested. For patients who do not meet these criteria or those with negative workup, clinical observation with periodic reassessment is recommended. If CT is positive, further workup with CT angiography or MR imaging plus MR angiography is recommended. In selected cases, conventional angiography and endovascular treatment may be warranted. If CT is negative, lumbar puncture is advised. In patients with

suspected metastatic brain disease, contrast-enhanced MR imaging is recommended. In patients with suspected intracranial aneurysm, further assessment with CT angiography or MR angiography is warranted. Abbreviations: CTA CT angiography, LP lumbar puncture, MRA MR angiography, MRI MR imaging. (Reprinted with permission from Medina LS, D’Souza B, Vasconcellos E. Adults and children with headache: evidence-based diagnostic evaluation. *Neuroimaging Clin N Am*. 2003 May;13(2):225–35.)

in the history, physical exam, or in other investigations [40].

Duarte and colleagues studied 100 consecutive patients admitted to a neurology unit over a 1-year period with recent onset of headache, defined as persistent headache of less than 1 year's duration. All patients studied had an unenhanced and enhanced head CT with lumbar puncture, MR imaging, and MR angiogram performed in selected cases. Tumors were identified in 21% of patients, which comprised 16% of patients with a negative neurologic examination [37].

A smaller-scale prospective study examined the association of acute headache and SAH (limited evidence) [38]. All patients were examined using state-of-the-art CT scanner technology [38]. Patients had an average headache duration of approximately 72 h [38]. Of the 27 patients studied, 20 had a negative CT and 4 were diagnosed with SAH. Among the remaining three patients, one had a frontal meningioma, another had a hematoma associated with SAH, and the other had diffuse meningeal enhancement caused by bacterial meningitis. Lumbar puncture was performed in 19 of the patients with negative CT, yielding 5 additional cases of SAH. Hence, CT did not demonstrate SAH in five of nine patients.

A retrospective study of 1111 patients with acute headache who had CT evaluation revealed 120 (10.8%) abnormalities, including hemorrhage, infarct, or neoplasm (limited evidence) [39]. All imaging studies were done at two teaching institutions over a 3-year period. There were statistical differences in the percentage of intracranial lesions based on the setting in which the CT was ordered. The inpatient rate (21.2%) was twice that of emergency patients (11.7%) and three times more than for outpatients (6.9%; $P < 0.005$). Of 155 CT studies performed for headache as the sole presenting symptom (13.9%), 9 (5.8%) patients had acute intracranial abnormalities. One study in the outpatient setting that studied 1284 patients with new headaches found no serious intracranial disease (limited evidence) [10]. The difference in prevalence of disease between emergency patients, inpatients, and outpatients is probably related to patient selection bias.

Another study evaluated 623 outpatients retrospectively who had brain CT for the sole indication of headache (limited evidence). Of these, 2.1% of the scans showed findings potentially explaining the cause of headache, and only 0.2% showed an indeterminate finding that ultimately was a brain tumor. The study concludes that clinicians should avoid CT in patients only with headache when the likelihood of serious illness is low in order to avoid the potential risk of cancer from ionizing radiation exposure [41].

A study was conducted on 256 adult patients (median age 45 +/- 18 years, range 18–93) presenting to eight emergency departments of the Emilia-Romagna region in Italy for nontraumatic headache (NTH) as the chief complaint over a period of 30 days [42]. Non-contrast head CT was performed on all nonpregnant patients. An analysis comparing scenarios 1, 2, and 3 (malignant headaches) versus scenario 4 (benign headache) was performed based on 180 patients who completed the follow-up telephone interview at least 3 months after the ED visit. The authors concluded that a simple diagnostic algorithm can be used to distinguish malignant headaches from benign headaches, with the algorithm showing a sensitivity of 100% (95% CI, 81–100%) and a specificity of 64% (95% CI, 56–71%). The likelihood ratio for a positive test was 2.67 (95% CI, 2.15–3.31%), and the likelihood ratio for a negative test was 0.04 (95% CI, 0.003–0.64%). This algorithm could therefore be used by emergency department physicians as a risk stratification tool:

Scenario 1: Adult patients admitted to ED for severe headache (“worst headache”)

- With acute onset (thunderclap headache)
- With neurologic signs (or nonfocal as decreased level of consciousness)
- With vomiting or syncope at the onset of headache

Scenario 2: Adult patients admitted to ED for severe headache

- With fever and/or neck stiffness

Scenario 3: Adult patients admitted to ED for

- Headache of recent onset (days or weeks)
- Progressively worsening headache, or persistent headache

Scenario 4: Adult patients with a previous history of headache

- Complaining of a headache very similar to previous attacks in terms of intensity, duration, and associated symptoms [42]

What Is the Role of Neuroimaging in Adults with Migraine or Chronic Headaches?

Summary of Evidence Most of the available literature (moderate evidence) suggests that there is no need for neuroimaging in patients with migraine and normal neurologic examination. Neuroimaging is indicated in patients with non-acute headache and unexplained abnormal neurologic examination or in patients with atypical features or headache that does not fulfill the definition of migraine. Few studies have shown significant lesions in few patients (0.7–1.4%) with chronic headaches and normal neurologic exam (moderate evidence).

Supporting Evidence Evidence-based guidelines on the use of diagnostic imaging in patients presenting with migraine have been developed by a multispecialty group called the US Headache Consortium [43]. Data were examined from 28 studies (moderate and limited evidence): 6 non-blinded prospective and 22 retrospective studies. The specific recommendations from the US Headache Consortium are as follows: (1) Neuroimaging should be considered in patients with non-acute headache and unexplained abnormal findings on the neurologic examination. (2) Neuroimaging is not usually warranted in patients with migraine and normal findings on neurologic examination. (3) A lower threshold for CT or MRI may be applicable in patients with atypical features or with headache that does not fulfill the definition of migraine.

The study by Joseph and colleagues (limited evidence) [44] in 48 headache patients revealed 5 patients with neoplasms and 1 patient with an arteriovenous malformation. Of these patients, five had physical examination signs and one had headache on exertion. Weingarten and colleagues (limited evidence) [45] extrapolated data from 100,800 adult patients enrolled in a health maintenance organization and estimated that, in patients with chronic headache and a normal neurologic examination, the chance of finding abnormalities on CT requiring neurosurgical intervention was as low as 0.01% (1 in 10,000).

In 1994, the American Academy of Neurology provided a summary statement on the use of neuroimaging in patients with headache and a normal neurologic examination based on a review of the literature (moderate and limited evidence) [46]. They concluded that routine imaging “in adult patients with recurrent headaches that have been defined as migraine—including those with visual aura—with no recent change in pattern, no history of seizures, and no other focal neurologic signs of symptoms is not warranted” [13]. This statement was based on a 1994 literature review by Frishberg [47] of 17 articles published between 1974 and 1991 that were limited to studies with more than 17 subjects per study (moderate evidence). All patients had normal neurologic examinations. Of 897 CT or MR imaging studies performed in patients with migraine, only three tumors and one arteriovenous malformation were noted, resulting in a yield of 0.4% (4 in 1000). The summary statement mentions, however, that “patients with atypical headache patterns, a history of seizure, or focal neurological signs or symptoms, CT or MRI may be indicated” [13, 46].

In another study with 402 inpatients imaged (70 non-contrast CT, 292 contrast-enhanced CT, 40 both) for chronic headaches (defined as recurrent headache ranging from 6 months to several years), only 1.4% scans showed significant lesions such as osteomas, low-grade glioma, and aneurysm [48].

The medical records and MR images of 402 adult patients with chronic headache (duration of 3 months or more) who had been evaluated

by the neurology service and were found to have no other neurologic symptoms/findings were retrospectively reviewed and divided into negative or positive. The major abnormalities found in 15 (3.7%) patients were glioma, meningioma, metastases, subdural hematoma, arteriovenous malformation, hydrocephalus (three patients), and Chiari I malformation (two patients). These abnormalities were found in 0.6% of patients who had migraine, 1.4% of those who had tension headaches, 14.1% of those who had atypical headaches, and 3.8% of those who had other types of headaches [49]. A retrospective review was performed of the MR images of 306 patients (195 patients had contrast, 23 patients had repeated imaging) with chronic (duration of 1 month or more) or recurrent headaches without prior head surgery, head trauma, or seizure and normal neurologic findings. 55.2% had no abnormalities, 44.1% had minor abnormalities, and 0.7% (2) had clinically significant abnormalities (pituitary macroadenoma and subdural hemorrhage) [50]. Another study reviewed 1876 patients (>15 years old, mean age 38 years) referred to two neurology clinics in Spain with headache starting at least 4 weeks previously and 99.2% with normal neurologic exams. One-third of the headaches were new onset, and two-thirds were present for more than 1 year. Headaches included migraine (49%), tension (35.4%), cluster (1.1%), posttraumatic (3.7%), and indeterminate (10.8%). CT imaging was performed in 1432 patients, MRI in 580, and 136 patients had both. Twenty-two patients (1.2%, 95% CI 0.7, 1.8) had “significant abnormalities” on neuroimaging, and neurologic examination was normal in 17 of these patients. The findings in these 17 included pituitary adenoma (3), large arachnoid cyst (2), meningioma (2), hydrocephalus (2), Arnold-Chiari type I malformation (1), ischemic stroke (1), cavernous angioma (1), arteriovenous malformation (1), low-grade astrocytoma (1), brain stem glioma (1), colloid cyst (1), and posterior fossa papilloma (1). The rate of significant intracranial abnormalities in patients with headache and normal neurologic exam was 0.9% (95% CI 0.5, 1.4) [51].

What Is the Recommended Neuroimaging Examination in Adults with Headache and Known Primary Neoplasm Suspected of Having Brain Metastases?

Summary of Evidence In patients older than 40 years with known primary neoplasm, brain metastasis is a common cause of headache [52]. Most studies described in the literature suggest that contrast-enhanced MR imaging is superior to contrast-enhanced CT in the detection of brain metastatic disease, especially if the lesions are less than 2 cm (moderate evidence). In patients with suspected metastases to the central nervous system, enhanced brain MR imaging is recommended (moderate evidence).

Supporting Evidence Davis and colleagues (moderate evidence) [53] studied comparative imaging studies in 23 patients who had contrast-enhanced MR and double-dose-delayed CT. Contrast-enhanced MR imaging demonstrated more than 67 definite or typical brain metastases. The double-dose delayed CT revealed only 37 metastatic lesions. The authors concluded that MR imaging with enhancement is superior to double-dose delayed CT scan for detecting brain metastasis, anatomic localization, and number of lesions.

Golfieri and colleagues [54] reported similar findings (moderate evidence). They studied 44 patients with small cell carcinoma to detect cerebral metastases. All patients were studied with contrast-enhanced CT scan and gadolinium-enhanced MR imaging. Of all patients, 43% had cerebral metastases. Both contrast-enhanced CT and gadolinium-enhanced MR imaging detected lesions greater than 2 cm. For lesions less than 2 cm, 9% were detected only by gadolinium-enhanced T1-weighted images. The authors concluded that gadolinium-enhanced T1-weighted images remain the most accurate technique in the assessment of cerebral metastases. A study by Sze and colleagues [55] performed prospective and retrospective studies in 75 patients (moderate evidence). In 49 patients, MR imaging and contrast-enhanced CT were equivalent. In 26

patients, however, results were discordant, with neither CT nor MR imaging being consistently superior. MR imaging demonstrated more metastases in 9 of these 26 patients. Contrast-enhanced CT, however, better depicted lesions in 8 of 26 patients.

When Is Neuroimaging Appropriate in Children with Headache?

Summary of Evidence Determination of the appropriateness of imaging is made based on the frequency, pattern, family history, and associated seizure or neurologic findings (Table 9.3) (moderate evidence). These guidelines reinforce the primary importance of careful acquisition of the medical history and performance of a thorough examination, including a detailed neurologic examination [24]. Among children at risk for brain lesions based on these signs and symptoms, neuroimaging with either MR or CT is valuable in combination with close clinical follow-up (Fig. 9.2). Despite the existing evidence of equivalent diagnostic accuracy for CT and MRI (moderate evidence), a recent large retrospective study that included 15,836 patients demonstrated that the use of CT scans to evaluate pediatric headache

remains high despite existing guidelines, low diagnostic yield, and high potential risk [56].

Supporting Evidence In 2002, the American Academy of Neurology and Child Neurology Society published evidence-based neuroimaging recommendations for children [57]. Six studies (one prospective and five retrospective) met inclusion criteria (moderate evidence). Data on 605 of 1275 children with recurrent headache who underwent neuroimaging found only 14 (2.3%) with nervous system lesions that required surgical treatment. All 14 children had definite abnormalities on neurologic examination. The recommendations from this study were as follows: (1) Neuroimaging should be considered in children with an abnormal neurologic examination or other physical findings that suggest CNS disease. Variables that predicted the presence of a space-occupying lesion included (a) headache of less than 1-month duration, (b) absence of family history of migraine, (c) gait abnormalities, and (d) occurrence of seizures. (2) Neuroimaging is not indicated in children with recurrent headaches and a

Table 9.3 Suggested guidelines for neuroimaging in pediatric patients with headache

Persistent headaches of less than 6 months' duration
Headache associated with abnormal neurologic examination
Headache associated with seizures
Recent onset of severe headache or change in the type of headache
Persistent headache without family history of migraine
Headaches that persistently awaken a child from sleep or occur immediately on awakening
Family or medical history of disorders that may predispose one to CNS lesions and clinical or laboratory findings that suggest CNS involvement

Reprinted with permission from Medina LS, Pinter JD, Zurakowski D, Davis RG, Kuban K, Barnes PD. Children with headache: clinical predictors of surgical space-occupying lesions and the role of neuroimaging. *Radiology*. 1997 Mar;202(3):819–24

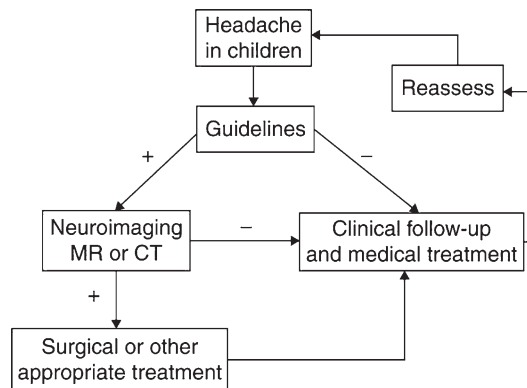


Fig. 9.2 Decision tree for use in children with headache disorder. Neuroimaging is suggested for patients who meet any of the signs or symptoms in the guidelines (Table 9.3). For patients who do not meet these criteria or those with negative findings from imaging studies, clinical observation with periodic reassessment is recommended. (Reprinted with permission from Medina LS, Pinter JD, Zurakowski D, Davis RG, Kuban K, Barnes PD. Children with headache: clinical predictors of surgical space-occupying lesions and the role of neuroimaging. *Radiology*. 1997 Mar;202(3):819–24.)

normal neurologic examination. (3) Neuroimaging should be considered in children with recent onset of severe headache, change in the type of headache, or if there are associated features suggestive of neurologic dysfunction.

A retrospective study that evaluated 1000 MR exams (400 of which included MR angiography) of the brain performed for headaches in pediatric patients found significant results (defined as finding requiring more diagnostic procedures or therapeutic interventions) in 5.6% including, in order of decreasing frequency, nonspecific T2 hyperintense lesions, post-ischemic scar, isolated internal hydrocephalus, hypoplasia of intra- or extracranial arteries, Chiari I malformation, brain tumor, aneurysm, cavernous hemangioma, and capillary hemangioma. They concluded that neuroimaging studies should not be routinely performed in pediatric patients with diagnosis of headache only due to the rarity of clinically relevant changes [58].

Regarding incidental nonspecific white matter lesions in children presenting with headache, a retrospective study with 527 patients had a rate of 4.4% (all supratentorial) and all the patients had normal neurological examination and psychomotor development. During a mean clinical follow-up period of 16.8 months, no patient showed neurological deterioration and no new lesions were seen in the reimaged patients (47.8%). The study concluded that nonspecific incidental white matter changes may be seen in children with headache and repeated imaging studies are not warranted if there is a normal clinical follow-up [59].

Medina and colleagues [24] performed a 4-year retrospective study of 315 children with no known underlying CNS disease who underwent brain imaging for a chief complaint of headache (moderate evidence). All patients underwent brain MR imaging; 69 patients also underwent brain CT. Clinical data were correlated with findings from MR imaging and CT, and the final diagnosis, using logistic regression. Thirteen (4%) patients had surgical space-occupying lesions, including nine malignant neoplasms, three hemorrhagic vascular malformations, and one arachnoid cyst.

In this study, they identified seven independent multivariate predictors of a surgical lesion, the strongest of which were sleep-related headache (odds ratio 5.4, 95% CI: 1.7–17.5) and no family history of migraine (odds ratio 15.4, 95% CI: 5.8–41.0). Other predictors included vomiting, absence of visual symptoms, headache of less than 6 months' duration, confusion, and abnormal neurologic examination findings. The risk of a surgical lesion increased with the increased number of these factors present ($P < 0.0001$). No difference between MR imaging and CT was noted in detection of surgical space-occupying lesions, and there were no false-positive or false-negative surgical lesions detected with either modality on clinical follow-up.

In a study by Schwedt and colleagues of 241 pediatric patients with headache who had MRI or CT, 23 patients (9.5%) had findings requiring a change in management [60] (limited to moderate evidence). These included five sinus disease, four tumors, four old infarcts, three Chiari I, two moyamoya, one intracranial vascular stenosis, one internal jugular vein occlusion, one arteriovenous malformation, one demyelinating disease, and one intracerebral hemorrhage. When sinus disease was excluded, three patients (1.2%) with normal neurologic symptoms and signs had imaging findings that resulted in a change in management (limited to moderate evidence).

A study that included 105 children under the age of 6 years aimed to retrospectively determine the frequency of headache subtypes, according to International Headache Society (IHS) criteria (limited evidence). Children with less than 15 days of daily headache or less than three headache attacks were excluded. The results demonstrated a difference in headache of preschool children (2.85%) compared to school-aged children (0.53%). The prevalence of potentially dangerous headaches in preschool children was higher than that in school-aged children, and causes included Chiari I malformation and brain tumors [61].

Another retrospective study in the United Kingdom compared the frequency of brain tumor signs and symptoms in children with and without

brain tumors. It included 195 patients with newly diagnosed brain tumors and 285 controls (limited evidence). Symptoms rarely or not observed among control children included head tilt, odd head movements, odd posture, back or neck stiffness, and unsteadiness without obvious cause. The study concluded that recognition of unusual symptoms or specific symptom patterns is key to identifying the one child among many who merits prompt investigation [62] and therefore could possibly benefit from neuroimaging.

What Is the Sensitivity and Specificity of CT and MR Imaging for Space-Occupying Lesions?

Summary of Evidence Sensitivity and specificity of MR imaging are greater than CT for intracranial lesions. For surgical intracranial space-occupying lesions, however, there is no difference between MR imaging and CT in diagnostic performance (moderate evidence). The use of intravenous contrast material after unenhanced CT of the brain in children does not frequently change the diagnosis (moderate evidence).

Supporting Evidence Sensitivity and specificity of CT and MR imaging for intracranial lesions are shown in Table 9.4. Medina and colleagues (moderate evidence) [24] showed that the overall sensitivity and specificity with MR imaging (92% and 99%, respectively) were higher than with CT (81% and 92%, respectively). Comparison of patients who underwent both MR imaging and

CT revealed no significant disagreement between the tests for surgical space-occupying lesions. The US Headache Consortium evidence-based guidelines from systematic review of the literature similarly concluded that MR imaging may be more sensitive than CT in identifying clinically insignificant abnormalities, but MRI imaging may be no more sensitive than CT in identifying clinically significant pathology [43].

A recent study performed by Branson et al. in 353 children with unenhanced and enhanced CT demonstrated that unenhanced CT of developing brains has high sensitivity and specificity in the diagnosis of pathologic findings [49]. Sensitivity, specificity, positive predictive value, and negative predictive value for unenhanced scans were 97%, 89%, 87%, and 97%, respectively [63]. The use of contrast material led to a change in the original normal or equivocal diagnosis to an abnormal diagnosis for only five (2.7%) of the 183 normal unenhanced scans. Therefore, the use of intravenous contrast material after unenhanced CT of the brain in children did not frequently change the diagnosis [63].

What Is the Sensitivity and Specificity of CT and MRI for Detecting an Intracranial Aneurysm in Patients with Headache and Subarachnoid Hemorrhage?

Summary of Evidence In North America, 80–90% of nontraumatic subarachnoid hemorrhage (SAH) in older children and adults is

Table 9.4 Diagnostic sensitivity and specificity of CT and MR imaging

Variable	Baseline %	Range %	Reference
Diagnostic tests			
MR imaging			
Sensitivity	92	82–100	[46, 84, 85]
Specificity	99	81–100	[46, 85]
CT			
Sensitivity	81	65–100	[46, 84, 85]
Specificity	92	72–100	[46, 84, 85]

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caused by the rupture of intracranial aneurysms [64]. CT angiography (CTA) and MR angiography (MRA) have sensitivities greater than 85% for aneurysms greater than 5 mm (moderate evidence). Most recent studies with newer generations of multi-detector CT report sensitivity and specificity greater than 90% for aneurysms greater than 4 mm (moderate evidence). Studies that have compared CTA and digital subtraction angiography (DSA) report similar sensitivities and specificities (moderate evidence). The sensitivity of CTA and MRA examinations drops significantly for aneurysms less than 5 mm. Thereby, DSA remains the current gold standard for evaluation of a ruptured intracranial aneurysm.

Supporting Evidence White et al. [65] searched the literature from 1988 through 1998 to find studies with ten or more subjects in which the conventional angiography results were compared with noninvasive imaging. They included 38 studies which scored more than 50% on evaluation criteria by using intrinsically weighted standardized assessment to determine suitability for inclusion (moderate evidence). The rates of aneurysm accuracy for CTA and MRA were 89% and 90%, respectively. The study showed greater sensitivity for aneurysms larger than 3 mm than for aneurysms smaller than 3 mm for CTA (96% vs. 61%) and for MRA (94% vs. 38%).

A recent retrospective study compared digital subtraction CT angiography with 3D DSA as reference standard in evaluating patients with suspected intracranial aneurysms. A total of 513 patients suspected of having or with known intracranial aneurysms and other cerebral vascular diseases underwent both digital subtraction CT angiography with a dual-source scanner and 3D DSA. Of these, 407 patients (79.3%) had 459 aneurysms at 3D DSA, 456 (99.3%) of which were correctly depicted with digital subtraction CT angiography. The sensitivity and specificity of digital subtraction CT angiography for depicting intracranial aneurysms were 97.8% and 88.7%, respectively, on a per-patient basis. On a per-aneurysm basis, the sensitivity and specificity were 96.5% and 87.8%, respectively. The technique was found to have higher sensitivity

for larger aneurysms (100% in those larger than 10 mm) than for smaller ones (91.3% in those less than 3 mm), as well as higher sensitivity for aneurysms in the posterior circulation (97.7%) than in the anterior circulation (95.8%). The inter- and intra-reader agreement was excellent on a per-patient and on a per-aneurysm basis [66].

White et al. [67] also performed a prospective blinded study in 142 patients who underwent DSA to detect aneurysms (moderate evidence). Results were compared with CTA and MRA. The accuracy rates per patient for the best observer were 87% and 85% for CTA and MRA, respectively. The accuracy rates for brain aneurysm for the best observer were 73% and 67% for CTA and MRA, respectively. The sensitivity for the detection of aneurysms 5 mm or larger was 94% for CTA and 86% for MRA. For aneurysms smaller than 5 mm, sensitivities for CTA and MRA were 57% and 35%, respectively.

More recent studies using CTA have shown even higher sensitivity and specificity, which may reflect technological improvements. Uysal and colleagues using spiral CT in 32 cases with aneurysm size from 3 to 13 mm [68] reported a sensitivity of 97% and specificity of 100% (limited evidence). Teksam and colleagues studied 100 consecutive patients with 113 aneurysms with multi-detector CT (MDCT) [69] and reported a sensitivity for detecting aneurysms of less than 4 mm, 4–10 mm, and greater than 10 mm on a per aneurysm basis of 84%, 97%, and 100%, respectively (moderate evidence). The overall specificity was 88%. Using CTA with three-dimensional techniques in 82 consecutive patients [70], Karamessini and colleagues demonstrated a sensitivity of 89% and specificity of 100% for CTA and sensitivity of 88% and specificity of 98% for DSA when compared with the reference standard of surgical findings (moderate evidence). Therefore, CTA was equivalent to DSA. Tipper and colleagues' study reported the results of 16-row MDCT in 57 patients with 53 aneurysms [71] and found a sensitivity and specificity of 96.2% and 100% for both CTA and DSA, respectively (moderate evidence). In this study, the mean diameter of the aneurysm was 6.3 mm

with a range of 1.9–28.1 mm [39]. A study published by Taschner and colleagues [72] in 2007 in 27 consecutive patients with 24 aneurysms using a 16-row multi-detector CTA reported an overall sensitivity and specificity of 100% and 83%, respectively (limited evidence). Papke and colleagues compared DSA with 16-row CTA in 87 patients [73] and reported a sensitivity and specificity of 98% and 100% for DSA and CTA, respectively (moderate evidence). Yoon and colleagues using 16-row multi-detector CTA in 85 patients [74] had overall sensitivity and specificity of 92.5% and 93.3%, respectively (moderate evidence). For aneurysms less than 3 mm, however, sensitivity decreased for reader 1 and reader 2 to 74.1% and 77.8%, respectively. A more recent study performed by Lubicz and colleagues [75] in 54 consecutive patients with 67 aneurysms using a 64-row multi-detector CTA reported an overall sensitivity and specificity of 94% and 90.2%, respectively (moderate evidence). For aneurysms less than 3 mm, CTA had a mean sensitivity of 70.4% [75]. Intertechnique and interobserver agreements were good for aneurysm detection with a mean kappa of 0.67 [75]. Agid and colleagues [76] studied 73 patients with 47 aneurysms using a 64-row multi-detector CTA and reported an overall sensitivity and specificity of 98% and 98%, respectively (moderate evidence).

What Is the Role of Advanced Imaging Techniques in Primary Headache Disorders?

Summary of Evidence Advanced MR imaging techniques such as hydrogen MR spectroscopy (H-MRS), diffusion tensor imaging (DTI), and functional MRI (fMRI) have shown fairly specific changes in patients with headache. Multiple publications with limited number of subjects have shown tendencies in patients with different types of headaches in particular areas of the central nervous system (limited evidence). The data available to date is still insufficient for complete characterization, but the future trend of advanced neuroimaging in headache evaluation is promis-

ing. High-resolution MR technique using transverse relaxation rates has demonstrated increased tissue iron levels in the brain stem (periaqueductal gray, red nuclei, and substantia nigra) in patients with headache disorders (limited evidence). Functional MRI has demonstrated activation of the red nuclei and substantia nigra in patients during spontaneous migraine episodes (limited evidence) [77, 78]. Patients with migraine disorders also have activation in the dorsolateral pons both on positron emission tomography (PET) and functional MRI (limited evidence) [79–83]. In cluster headache disorders, MR phosphorus spectroscopy (31P–MRS) has demonstrated brain mitochondrial dysfunction (limited evidence) [84, 85]. PET has demonstrated strong activation in the hypothalamic gray matter in acute cluster headache attacks (limited evidence) [86]. In contrast to migraine disorders, there is no brain stem activation during acute cluster headache episodes compared with the resting state [87]. These initial studies suggest that, although primary headaches such as migraine and cluster headache may share a common pain pathway—the trigeminovascular innervation—their underlying pathogenesis differs significantly [84].

Supporting Evidence The underlying pathophysiology of migraine disorders is not well understood [88]. Conventional CT and MRI studies are usually normal with no evidence of a structural lesion. Studies have shown involvement of the nociceptive pathways in chronic daily headaches and migraines [88]. A study performed by Raskin and colleagues [89] revealed migraine-like headaches in patients with electrodes implanted in the periaqueductal gray (PAG) matter. The ventral brain stem has also been identified to be involved in migraine disorders [89]. Reports of multiple sclerosis plaque [90] and cavernous malformation [91] involving the PAG and causing migraine-like disorders have been reported. Imaging studies have been performed to study the iron homeostasis in the midbrain. High-resolution MR techniques have been used to map the transverse relaxation rates R_2 ($1/T_2$), R_2^* ($1/T_2^*$), and

R2' (R2*-R2) in the PAG, red nuclei (RN), and substantia nigra (SN) [92]. A positive correlation ($r = 0.80$; $P < 0.006$) was identified between the duration of illness and the increase in R2' (increased tissue iron levels) for patients with episodic migraine disorders and chronic daily headaches [92, 93] (limited evidence). Another study that aimed to determine the H-MRS findings in episodic and chronic migraine patients showed that those with episodic migraine had the highest N-acetylaspartate to creatine (NAA/Cr) ratio at the dorsal pons in comparison with those of chronic migraine and controls. This suggests neuronal hypertrophy at the dorsal pons in patients with episodic migraine and a progressive dysfunction in chronic migraine, since the levels declined with increasing headache frequency and intensity (limited evidence) [94]. A recent meta-analysis regarding MR spectroscopy in migraine patients showed consistent findings among studies including lack of acidosis and a disturbed energy metabolism. The imbalance between ATP production and ATP use in migraine patients could be due to primary mitochondrial dysfunction or secondary to alterations in brain excitability (limited evidence) [95].

Another study by Kruit and colleagues [96] in patients studied in a 1.5 T MR scanner revealed higher iron concentrations in the RN and putamen in patients with migraines (limited to moderate evidence). Functional MR has demonstrated activation of the RN and SN in patients during spontaneous migraine episodes (limited evidence) [77, 78]. On the other hand, resting state functional MR has shown stronger connectivity between PAG and a subset of brain areas involved in nociceptive/somatosensory processing in migraine patients between episodes when compared to matched controls (limited evidence) [97].

A case-control study of 40 patients who suffered from migraine without aura used regional homogeneity analysis to identify the local features of spontaneous brain activity with functional MRI. A positive correlation was noted between disease duration and increased average regional homogeneity in the thalamus, brain

stem, and temporal pole in these patients. On the contrary, regional homogeneity values were negatively correlated with the duration of disease in the anterior/posterior cingulate cortex, insula, and superior occipital gyrus (limited evidence) [98]. Another study using diffusion tensor imaging (DTI) found statistically significant increased apparent diffusion coefficient (ADC) values in the red nuclei of migraineurs, further supporting the role of the brainstem in migraine episodes (limited evidence) [99].

In cluster headache, *in vivo* MR phosphorus spectroscopy (31P-MRS) has demonstrated brain mitochondrial dysfunction characterized by reduced phosphocreatine levels, an increased ADP concentration, and a reduced phosphorylation potential (limited evidence) [84, 85]. In a study of nine patients, PET demonstrated strong activation in the hypothalamic gray matter in acute cluster headache attacks (limited evidence) [86]. In contrast to migraine disorders, there is no brain stem activation during acute cluster headache episodes compared with the resting state [87]. Functional neuroimaging has shown altered regional homogeneity in the cingulate, prefrontal, and insular cortex (among other brain regions) in patients with spontaneous cluster headaches suggesting relation to pain processing and modulation (limited evidence) [100].

PET demonstrates activation in the rostral brainstem, *i.e.*, the dorsolateral pons, which lateralizes with the attack in both infrequent and frequent migraines. These changes persist after successful treatment of the attack but are not present interictally and are not seen in other primary headaches [79–83]. MR angiography has shown that blood flow changes do not cause migraine and cluster headaches; blood flow changes are a result of ophthalmic division pain. Functional neuroimaging performed on patients with typical migraine triggered by glyceryl trinitrate has shown that the changes in the dorsolateral pons lateralize with the migraine attack, suggesting that this portion of the brain is pivotal in the phenotypic expression of migraines. Again, these pontine changes persisted after resolution of the pain with a triptan and were not present interictally. When dull bilateral headache was

induced by glyceryl trinitrate in controls and migraineurs, the pontine change was not seen. Further study is needed, but these findings demonstrate that migraine is a disorder localized in the brain with pontine representation [79, 82, 101, 102].

What Is the Cost-Effectiveness of Neuroimaging in Patients with Headache?

Summary of Evidence No well-designed cost-effectiveness analysis (CEA) in adults could be found in the literature. A CEA study [103] assessed the clinical and economic consequences of three diagnostic strategies in the evaluation of children with headache suspected of having a brain tumor: MR imaging, CT followed by MR imaging for positive results (CT-MR imaging), and no neuroimaging with close clinical follow-up [103]. This model suggests that MR imaging maximizes quality-adjusted life years (QALY) gained at a reasonable cost-effectiveness ratio in patients at high risk of having a brain tumor (limited evidence). Conversely, the strategy of no imaging with close clinical follow-up is cost saving in low-risk children (limited evidence). Although the CT-MR imaging strategy maximizes QALY gained in the intermediate-risk patients, its additional cost per QALY gained is high. In children with headache, appropriate selection of patients and diagnostic imaging strategies may maximize quality-adjusted life expectancy and decrease costs of medical workup.

Supporting Evidence A CEA in children with headaches has been published in Pediatrics [103]. A decision-analytic Markov model and CEA were performed incorporating the risk group pretest probability, MR imaging and CT sensitivity and specificity, tumor survival, progression rates, and cost per strategy. Outcomes were based on QALY gained and incremental cost per QALY gained.

The results were as follows: For low-risk children with chronic non-migraine headaches

of more than 6 months' duration as the sole symptom (pretest probability of brain tumor was 0.01% [1 in 10,000]), close clinical observation without neuroimaging was less costly and more effective than the two neuroimaging strategies. For the intermediate-risk children with migraine headache and normal neurologic examination (pretest probability of brain tumor was 0.4% [4 in 1000]), CT-MR imaging was the most effective strategy but cost more than \$1 million per QALY gained compared with no neuroimaging. This cost is not typically justified by health policy makers. For high-risk children with headache of less than 6 months' duration and other clinical predictors of a brain tumor, such as an abnormal neurologic examination (pretest probability of brain tumor was 4% [4 in 100]), the most effective strategy was MR imaging, with a cost-effectiveness ratio of \$113,800 per QALY gained compared with no imaging.

The cost-effectiveness ratio in the high-risk children with headache is in the comparable range of annual mammography for women aged 55–64 years at \$110,000 per life year saved [104], colonoscopy for colorectal cancer screening for persons older than 40 years at \$90,000 per life year saved [104, 105], and annual cervical cancer screening for women beginning at age 20 years at \$220,000 per life year saved [104, 106]. Therefore, this CEA model supports the use of MR imaging in high-risk children.

The Centers for Medicare & Medicaid Services (CMS) developed an imaging efficiency measure for the use of brain CT in patients with atraumatic headache known as Outpatient Measure 15 (OP-15). A retrospective study was done with the objective of determining the reliability, validity, and accuracy of the OP-15. This study reviewed 748 patient emergency department visits labeled as including an inappropriate brain CT by CMS in 2009. The study concluded that this is not a reliable, valid, or accurate imaging efficiency measure. In fact, it may produce misleading information about emergency department performance. This was in part due to the limitations of administrative data [107]. In fact, this measure is no longer in use.

Take-Home Tables and Figures

Tables 9.1 and 9.2 present common causes of headaches and guidelines for neuroimaging for headaches in adults, respectively, while Table 9.3 covers guidelines for neuroimaging for headaches in pediatric patients. Table 9.4 summarizes the sensitivity and specificity of CT and MR imaging with regard to headaches. Figures 9.1 and 9.2 show algorithms for use in adults and children with headaches.

Imaging Case Studies

Case 1

Figure 9.3a, b presents a 14-year-old male with headaches and vomiting: colloid cyst.

Case 2

Figure 9.4a, b presents a 10-year-old female with headaches triggered by cough and exertion (Valsalva maneuver): Chiari I.

Case 3

Figure 9.5a, b presents a 7-year-old male with headaches: ataxia.

Suggested Protocols

1. CT imaging [108, 109]
 - (a) CT without contrast. Axial 5–10-mm non-spiral images should be used to assess for subarachnoid hemorrhage, tumor hemorrhage, or calcifications.

In infants and toddlers, axial 2.5–5-mm sections are recommended.
 - (b) CT with contrast. Axial 5–10-mm non-spiral enhanced images should be used in patients with suspected neoplasm, infection, or other focal intracranial lesion. If indicated, CT angiography can be performed as part of the enhanced CT. Contrast-enhanced CT angiography should ideally be done in a multi-detector CT scanner with multiplanar and 3D reconstructions.
2. MR imaging [108, 109]

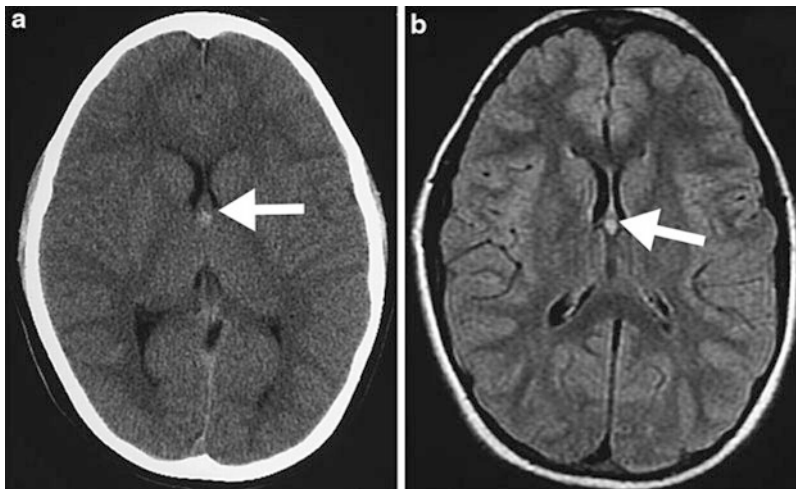


Fig. 9.3 A 14-year-old male presented with headaches for several months, increasing in frequency in the last 2 weeks and accompanied by vomiting. (a) Unenhanced CT shows a small focal lesion with increased density at the level of the foramen of Monro. (b) Axial FLAIR sequence reveals increased T2-weighted signal in the lesion. No hydrocephalus noted. Neuroimaging findings consistent

with colloid cyst. (Reprinted with kind permission of Springer Science + Business Media from Medina LS, Shah A, Vasconcellos E. Adults and children with headache: evidence-based role of neuroimaging. In Medina LS, Blackmore CC, editors. Evidence-based imaging: optimizing imaging in patient care. New York: Springer; 2006.)

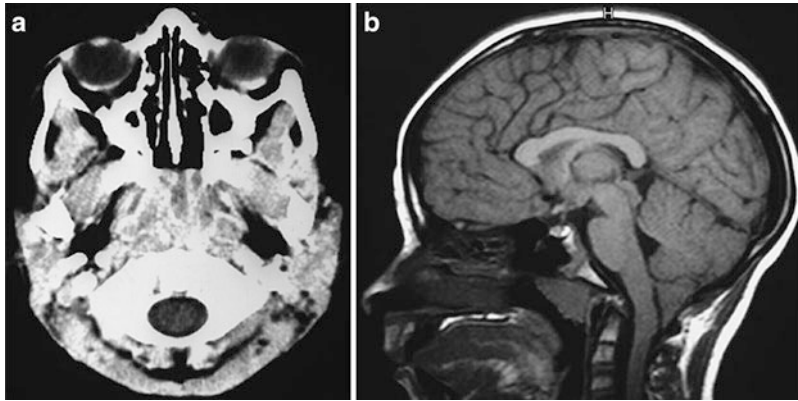


Fig. 9.4 A 10-year-old female presented with persistent headaches for the last 6 months triggered by cough and exertion (Valsalva maneuver), occasionally referred to the posterior aspect of the head. (a) Unenhanced CT at craniocervical junction was interpreted as unremarkable. (b) Sagittal MRI T1-weighted image reveals pointed cerebellar tonsils extending more than 5 mm below the foramen magnum consistent with Chiari I. No cervical cord hydro-

syrinx noted. (Reprinted with kind permission of Springer Science + Business Media from Medina LS, Shah A, Vasconcellos E. Adults and children with headache: evidence-based role of neuroimaging. In Medina LS, Blackmore CC, editors. Evidence-based imaging: optimizing imaging in patient care. New York: Springer; 2006.)

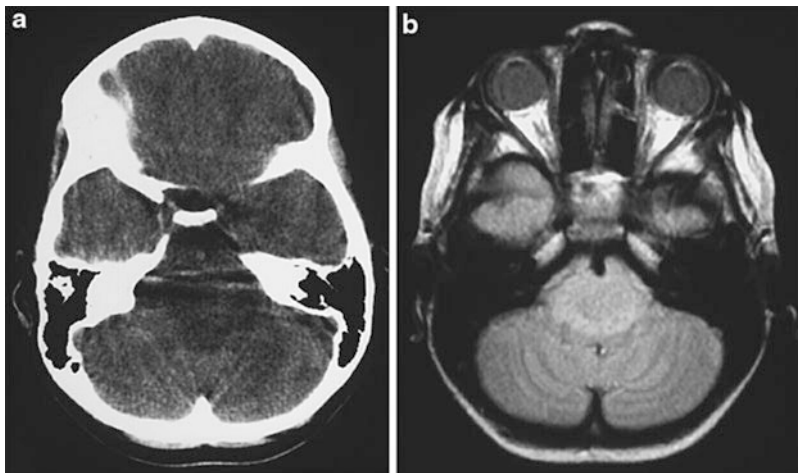


Fig. 9.5 A 7-year-old male presented with new-onset headache and ataxia. (a) Unenhanced CT through posterior fossa is limited by beam-hardening artifact. A hypodense lesion is seen in the pons. (b) Axial proton density MR image better depicts the anatomy and extent of the lesion without artifact. (Reprinted with kind per-

mission of Springer Science + Business Media from Medina LS, Shah A, Vasconcellos E. Adults and children with headache: evidence-based role of neuroimaging. In Medina LS, Blackmore CC, editors. Evidence-based imaging: optimizing imaging in patient care. New York: Springer; 2006.)

Basic brain MR protocol sequences include sagittal T1-weighted conventional spin-echo (repetition time, 600 ms; echo time 11 ms [600/11]), axial proton density-weighted conventional or fast spin-echo (2000/15), axial T2-weighted conventional or fast spin-echo (3200/85), axial FLAIR (fluid attenuation inversion recovery)

spin-echo (8800/152, inversion time [TI] 2200 ms), and coronal T2-weighted fast spin-echo (3200/85) images. In patients with suspected neoplasm, infection, or focal intracranial lesions, gadolinium-enhanced T1-weighted conventional spin-echo (600/11) images should be acquired in at least two planes. If MR angiogram is indicated,

then a 3D time-of-flight study of the circle of Willis should be performed. Consideration should be given to complementing the MRA with a multiphase dynamic contrast-enhanced study to reduce potential flow artifacts and to assess arterial, capillary, and venous phases.

Future Research

- Large-scale prospective studies to validate risk factors and prediction rules of significant intracranial lesions in children and adults with headache
- Large diagnostic performance studies comparing the sensitivity, specificity, and ROC curves of neuroimaging in adults and children with headache
- Cost-effectiveness analysis of neuroimaging in adults with headaches
- Role of advanced imaging in children and adults with primary headache

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Seizures in Adults and Children: Evidence-Based Emergency Imaging

10

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Key Points

- The objective of neuroimaging in the emergent setting is to exclude life-threatening pathology, such as neoplasm or intracranial space-occupying lesions.
- Noncontrast CT in emergency department is fast, inexpensive, and capable of excluding large intracranial masses or hemorrhage, which might require

immediate surgical intervention (strong evidence).

- CT imaging is indicated in sick or unstable patients (strong evidence).
- Magnetic resonance imaging (MRI) is indicated for patients with fever, altered mental status, abnormal neurologic examination, and/or associated psychiatric symptoms (strong evidence).
- Focal neurological deficit is an important predictor of an abnormality in the neuroimaging examination (moderate evidence).
- For simple febrile seizures (generalized convulsions, duration less than 15 min with no recurrence in 24 h in a febrile child), no neuroimaging is needed (limited evidence).
- Emergency imaging with CT or MR should be performed in cases of long-lasting postictal confusion or focal deficit, in first unprovoked or provoked seizure (limited to moderate evidence).
- Advanced imaging methods, such as positron emission tomography (PET) and subtraction ictal-interictal single photon emission computed tomography (SPECT), are not indicated in the acute setting (strong evidence).

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Definitions and Pathophysiology

Having seizures does not equate to having epilepsy. A seizure is referred to as a single event resulting from a burst of paroxysmal neuronal misfiring resulting in transient alteration of neurologic function secondary to abnormal excessive or (hyper)synchronous neuronal activity in the brain [1]. Epilepsy, in contrast, is a clinical condition of recurrent, unprovoked seizures. It is operationally characterized by at least two unprovoked seizures occurring greater than 24 h apart, by one unprovoked seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, or by the diagnosis of an epilepsy syndrome [1].

Two main types of seizures are recognized: focal (or partial) seizures, with electroencephalographic origin from a discrete location within a cerebral hemisphere, and generalized seizures, due to global brain electrical activity, which rapidly propagate through both hemispheres and do not have consistently localizing features.

Partial seizures are characterized by focal symptomatology or electroencephalographic (EEG) abnormalities with or without preservation of awareness. Focal seizures originate from a discrete location in the brain, typically from a focal gray matter area along the surface or deep within a hemisphere. Focal seizures are categorized according to clinical manifestations, depending on the subjective (auras) or objective (such as motor, sensory, autonomic) symptoms or cognitive disturbances and dyscognitive features and by the presence or absence of impairment of consciousness or awareness which further classifies partial seizures in complex (impaired awareness) and simple (no impaired awareness) partial seizures, although this is an older classification and this terminology is no longer recommended.

The main subtypes of generalized seizures are grand mal convulsions (tonic-clonic, atonic, tonic, and myoclonic) and/or petit mal or absence seizures, which are usually accompanied by a brief lack of awareness, except for some myoclonic seizures. Generalized seizures are not always convulsive, for example, in generalized petit mal seizures.

A particular seizure in children is the febrile seizure, occurring mostly between 6 months and 6 years of age [2]. Complex febrile seizures may present outside this age range and are characterized by focal symptoms (such as unilateral jerking), duration of more than 15 min or multiple episodes within 24 h. Some prolonged febrile seizures have been associated with the development of mesial temporal sclerosis and possibly to an increased risk of subsequent refractory epilepsy [2].

Seizures can also be classified according to etiology into unknown (cryptogenic), symptomatic (structural, immune, metabolic, infectious), and genetic (idiopathic) [3, 4]. Seizures have also been classified according to precipitating factors: the term symptomatic seizures indicating a known underlying cause such as fever, systemic metabolic derangement, or a focal brain lesion. Symptomatic seizures might be acute, in situations such as drug withdrawal, alcohol intoxication, hypoglycemia, or infection (e.g., viral encephalitis). Where a cause cannot be identified, these are labeled non-symptomatic or cryptogenic seizures. Some believe idiopathic seizures relate to unknown or presumed genetic factors. Unprovoked seizures refer to the absence of an identifiable precipitating factor, such as in the acute setting, where the cause of the seizure is being investigated.

Epilepsy syndrome refers to a group of clinical and electrographic characteristics that consistently occur together, including seizure type, electroencephalographic (EEG) manifestations, genetics, natural history, triggering factors, and prognosis. Status epilepticus is defined as a prolonged seizure (longer than 30 min) or multiple seizures with incomplete recovery to baseline mental status between episodes, resulting in risk of permanent neuronal injury [2]. Medically refractory epilepsy is the condition where seizures are not controlled by at least two appropriately chosen antiepileptic medications. The term seizure disorder is nonspecific and should be avoided.

Risk factors for seizures vary by age. Approximately 75% of epilepsy begins in childhood. In the pediatric population, fever (especially in neonates and infants), infections, malformations of cortical development, inborn

errors of metabolism, and tumors are important etiologic factors. In adults, structural brain lesions such as tumors, hemorrhage, and ischemia may present with seizures, as well as acquired metabolic abnormalities, toxic ingestion, and infection. Patients with traumatic brain injuries, dural venous sinus thrombosis, and vascular lesions such as cavernous and arteriovenous malformations may also present with seizures.

Epidemiology

Each year, approximately 2–5% of patients present to the emergency room with an unprovoked first seizure in the United States [2]. An estimated 10% of the population in the United States will have at least one seizure by age 80 [3]. Epilepsy is one of the most common neurologic conditions [5]. In the United States, the prevalence estimate in 2011 was 79 per 100,000 people, and about one third of patients suffer from refractory epilepsy [5]. The incidence of epilepsy varies with age, with peaks occurring in the extremes of life, and about 50% of cases affecting patients under 1 year of age or over age 60 [6]. The reported incidence of epilepsy is lower in high-income countries, whereas the prevalence appears to be lower in low-income countries. The discrepancy is attributed to the larger premature death rate in patients with epilepsy in resource-poor environments [7].

Population-based studies reveal that there are between 25,000 and 40,000 children per year in the United States who sustain a first-time, unprovoked seizure, 70% of which are idiopathic [8]. By 14 years of age, approximately 1% of children will experience an unprovoked seizure with the highest incidence being in children younger than 3 years. About 2% of children under 5 years of age will suffer a febrile seizure. The overall incidence of febrile seizures recurrence is 35% [9].

Overall Cost to Society

Murray et al. in 1994 calculated the cost of neuroimaging in the United States for adult refractory epilepsy. CT was performed in 60% of new

and in 5% of existing cases of epilepsy, whereas MRI was carried out in 90% of new and 12% of existing cases [10]. Costs were determined by multiplying the CT or MR utility rate by the number of new-onset seizures and the cost of the exams. The cost for an MRI of the brain in the United States is between \$1200 and \$2000 [11]. The economic impact of evaluating and treating patients with seizures is substantial, and neuroimaging contributes to the high costs. CT and MR imaging cost of evaluation of patients with new-onset seizures was estimated to range between \$28,000 and \$84,000 per 100,000 inhabitants in the United States in 1996 [12].

In a single center study of a pediatric population, the average cost per workup for seizure episode in the emergency department was \$17,126, with imaging costs estimated at \$359 [total \$32,315 for all 90 patients] [13].

Goals of Imaging

Evaluating patients with new-onset seizures requires immediate stabilization of vital signs and oxygenation. A careful history and physical exam is needed to guide subsequent testing. The clinical history will help to characterize and identify potential triggers of the patient's seizure. A history of trauma or symptoms of infection are potential clues. Medication and potential drug and/or alcohol use are essential to revealing a cause. Clinical features of the seizures including the level of consciousness, auras, and sensory and motor and autonomic manifestations are important. Patients who present with new-onset seizures require diagnostic testing which may include laboratory studies, lumbar puncture, electroencephalography, and neuroimaging.

The primary objective of emergent neuroimaging in a patient with seizures is to identify potentially treatable structural lesions or reversible causes that require immediate treatment. Focal neurologic findings on examination mandate emergent neuroimaging.

Methodology

PubMed search strategies were adopted as below:

1. Seizure [Title/Abstract] OR epilepsy [Title/Abstract] AND acute [Title/Abstract] or emergent [Title/Abstract] AND neuroimaging [Title/Abstract]. Limits: Publication date from January 1995 to June 2015; only articles in English; and in humans.

Titles and abstracts were reviewed to determine appropriateness of content. Articles were excluded if they had less than 20 patients, lacked pathological verification, had no standard of reference, or had no significant influence on clinical decision-making. The specificity, sensitivity, likelihood ratios, probability, predictors, and techniques were summarized for each procedure. Adult and childhood seizures were addressed as well as febrile seizures due to their clinical and radiological importance. Each of the selected articles was reviewed, abstracted, and classified by one reviewer. Of a total of 250 abstracts, 50 articles met inclusion criteria and the full text was reviewed in detail.

Discussion of Issues

Should Children with New-Onset Febrile Seizures Undergo Emergent Neuroimaging?

Summary of Evidence Neuroimaging is not recommended for a simple febrile seizure (limited evidence).

There is insufficient data to recommend or not recommend neuroimaging in complex febrile seizures (limited or no evidence).

Supporting Evidence No articles with strong or moderate evidence were found.

Febrile seizures affect up to 5% of children, and approximately one in three will have at least one recurrent seizure. Simple febrile seizures, lasting fewer than 15 min, do not need emergent neuroimaging.

In an evidence-based review of the literature (limited evidence), Offringa et al. concluded that neuroimaging is not needed for simple febrile seizures [14]. Combining the yield of CT and MRI scans, only 1.2% of 2100 cases of seizures associated with fever had significant findings (e.g., tumor, malformations, and atrophy). The American Academy of Pediatrics also suggested that CT or MRI has no role in simple febrile seizures [15].

Special Case: Complex Febrile Seizures in Children

CT or MRI may be indicated to evaluate for acute intracranial processes in children with complex febrile seizures (limited evidence).

Unlike the case for simple febrile seizures, no society guidelines or recommendations exist for children with complex febrile seizures (CFS). Complex febrile seizures are prolonged (duration greater than 15 min), associated with focal symptoms during the ictus phase (such as focal jerking), and may recur multiple times within a 24-h time interval and may have prognostic implications.

Teng et al. reported neuroimaging findings in a retrospective study (limited evidence) of 71 children presenting to the ER following their first complex febrile seizure (diagnosed and classified by two epileptologists) [16]. Fifty-one children (72%) had one of three features (multiple, prolonged, or focal features) that characterize a complex febrile seizure, while 20 children (28%) had multiple complex features (long duration, involvement of only one side of the body, and long postictal state). However, none of the 71 patients had intracranial findings on neuroimaging that required emergency intervention. The authors in these studies suggested that routine emergency neuroimaging was unnecessary.

A more recent retrospective study (limited evidence) of 526 children with complex febrile seizures evaluated in a single pediatric emergency department, in whom 50% had emergency CT imaging, revealed clinically significant pathology in 1.5% [17]. These authors concluded that emergent neuroimaging was not indicated in well-appearing children presenting with their

first complex febrile seizures. Whether to perform urgent neuroimaging should be based on clinical suspicion and additional signs and symptoms suggestive of a bleed or mass effect. In the same study, the authors identified the subgroup with recurrent febrile seizures within 24 h as being at particularly low risk.

Along the spectrum of complex febrile seizures, the extreme is represented by febrile status epilepticus (FSE), with seizures lasting more than 30 min and not associated with central nervous system infections in children aged between 6 months and 6 years. Two studies suggested that prolonged seizures with hippocampal edema evolved to the development of mesial temporal sclerosis later on in a small number (7%) of children (limited evidence) [18, 19]. However, none of them have developed temporal lobe epilepsy. Studies have demonstrated that hippocampal volumes reduced over a year in 20% of children with FSE and suggested that these patients would require follow-up. Finally, studies have shown that acute ictal findings on MRI, such as restricted diffusion in one or both hippocampi, do not alter emergent clinical management.

Boyle et al. looked at factors that were associated with diagnostic workup including neuroimaging in a retrospective study (limited evidence) of 190 pediatric patients who presented to a tertiary care pediatric emergency department with complex febrile seizures [20]. In their review of 53 patients who underwent CT, the imaging findings did not guide therapy in any patients. They noted that patients with focal signs were more likely to have neuroimaging performed.

What Is the Role of Neuroimaging in the Acute Setting in Patients with First Unprovoked Seizure?

Summary of Evidence Emergent neuroimaging should be performed in patients with persistent decreased mental status (in the postictal state) or a new focal neurologic abnormality (strong evidence).

In the emergency setting, CT is valuable to detect intracranial hemorrhage, tumors, or large

territory ischemia that may warrant urgent intervention (strong evidence).

Neuroimaging with CT or MRI is advised in those with significant unexplained cognitive or motor impairment or long-lasting postictal confusion or focal deficit (strong evidence).

In children less than 1 year of age with significant and unexplained cognitive impairment, focal neurological examination or focal symptoms during the seizures (partial seizures), or EEG with focal abnormalities during the ictal/interictal state, MRI should be considered (limited evidence).

For the workup of first unprovoked seizures, MRI is the neuroimaging study of choice (strong evidence).

Neuroimaging may be scheduled on an outpatient basis for patients with stable vital signs who are awake and have returned to neurologic baseline (moderate evidence).

Supporting Evidence No level I studies in either adults or children were found. No level II studies for adults were found.

Neuroimaging is positive in 3–41% of cases in studies (adults and children). The probability is higher (up to 82%) in patients with partial seizures and focal neurological deficits. Significant neuroimaging findings impacting medical care were found in up to 17% of adults and in 15% of children.

In a cohort study by Shinnar et al. (moderate evidence), 21% of neuroimaging studies (159 CT and 59 MR) performed in 218 of 411 children presenting with first seizures revealed abnormalities [21]. The cohort was followed for an average of 10 years (used as reference standard), and no patients had evidence for neoplasm. The most common diagnoses were encephalomalacia (in 16 cases) and cerebral dysgenesis (in 11 cases). Six children had gray matter migration disorders, which were only seen by MRI. In this study, a higher number of MRIs (34%) than CTs (22%) were abnormal. In four cases (1.8%), imaging findings altered both the diagnosis and the acute management of patients. Children in this study who had a neurological deficit (56% vs. 12%, $P < 0.001$) or abnormal EEG and partial seizures

($P < 0.05$) were more likely to have abnormal imaging.

In a more recent multicenter prospective study (level II, moderate evidence) of 475 children presenting after their first unprovoked seizure, neuroimaging performed with MRI or CT within a 4-month interval revealed clinically relevant intracranial abnormalities in 11%, of which only 0.8% were emergent [22]. The authors concluded that in most cases children with first unprovoked seizures do not need emergent imaging. All three children with emergent/urgent neuroimaging findings had focal seizures. By logistic regression, certain findings on patient history (such as a history of a brain tumor, other neoplasm, stroke, coagulopathy, sickle cell disease, anatomic cardiac defect, or presence of an intracranial ventricular shunt) or characteristics of the seizures (such as focal or prolonged, or repeat or speech change) were independently associated with clinically relevant abnormalities and might indicate the need for nonurgent neuroimaging.

Berg et al. conducted a prospective cohort study (moderate evidence) in children with newly diagnosed epilepsy. In this study, 488 of 613 children were imaged with MRI (388, 63.3%), CT (197, 32.1%), or both (97, 15.8%). Abnormal findings were found in 62 (12.7%); this increased to 15.4% if only partial seizures were computed [23]. Similar results were described by Khodapanahandeh et al. in a retrospective study (limited evidence) of 125 children with new-onset seizure where neuroimaging (CT or MRI) found abnormalities in 12 of 119 (10%) children. They suggested the use of neuroimaging studies for children who present with focal seizures and abnormal neurological findings or who are younger than 2 years of age [24].

In a more recent prospective cohort study (moderate evidence), Byars et al. explored the yield of MRI in 249 children following their first seizure. Thirty-four children (13.7%) had structural brain abnormalities that possibly were related to their seizures [25]. They did not differentiate between provoked and unprovoked seizures, in this study, so this result should be considered as a global yield of MRI in all cases of first seizure.

King et al. reported a level III (limited evidence) study of 300 adults and children with an unexplained first seizure, and 92% percent of these patients had neuroimaging (263 only MRI and 14 only CT) [26]. Epileptogenic lesions were found in 38 patients (13%). Of these, 17 had neoplasm, which changed medical care. MRI detected abnormalities in 17% of 154 patients with partial epilepsy. CT was performed in 28 of the 38 cases with lesions on MRI being concordant with MRI in only 12 cases. CT missed a cavernous angioma and eight tumors. In 49 patients that had generalized epilepsy as supported by generalized epileptiform abnormalities on EEG, none of the 49 had lesions on MRI [26].

In a level III (limited evidence) study by Hopkins et al., of 408 adults (age 16 and up) with their initial seizure, CT scanning revealed tumors in 3% of patients. These patients were more likely to have recurrent seizures [27]. Another study by Schoenenberger et al. demonstrated a higher percentage of positive imaging results in this population [28]. A total of 119 adult patients with new-onset seizure underwent CT of the brain. Focal structural brain lesions were found in 40 patients (34%; 95% confidence interval, 25–42%). In 50% of these patients, imaging findings prompt an important change in therapeutic management. The major predictor for finding a focal lesion on CT was the presence of a focal neurological deficit (sensitivity of 50%, specificity of 89%) [28].

Henneman et al. conducted a retrospective study (limited evidence) on 333 patients with new-onset seizures, not associated with acute head trauma, hypoglycemia from diabetic therapy, or alcohol or recreational drugs. Of the 325 patients studied with CT scans, 134 (41%) had clinically significant results [29]. The role of CT in evaluating children with new-onset unprovoked seizure was analyzed in a retrospective study (limited evidence) by Maytal et al. [30]. Of 66 patients, 21.2% had abnormal CT results. The seizure etiology was clinically determined to be cryptogenic in 33 patients. Two children (6%) had abnormal nonspecific CT findings that did not require intervention. No abnormal CT results were seen in 13 cases with complex febrile seizures [30].

The role of CT in the evaluation of children with and without risk factors, following their first seizure (including febrile seizures) has been studied by Garvey et al. [31]. In this retrospective analysis (level III, limited evidence), 19 (18%) out of 107 children presenting to the emergency room with unprovoked seizures had brain abnormalities, 7 (6.5%) of whom required further investigation or intervention. Two risk factors for significant CT abnormality were identified: first unprovoked seizure ($p < 0.01$) and focal seizures or focal postictal clinical abnormality ($p < 0.04$).

In a retrospective review (limited evidence) of 50 children without risk factors, following their first seizure, 16 (32%) had abnormal neuroimaging, with only 1 (2%) showing a significant abnormality (Moyamoya disease) [32]. The authors suggested that the routine use of neuroimaging in pediatric patients with first seizure was not useful.

In a retrospective cohort study (limited evidence) of previously well children admitted to a pediatric ICU, Bautovich et al. clinically found significant findings on CT in 19% that changed acute clinical management in 7% of cases [33]. In a retrospective cohort study (limited evidence) of adults with first seizure admitted in the emergency department, brain abnormalities were detected on CT 154/439 (35%), out of which 14.7% were considered clinically significant. Abnormal imaging predicted higher rate of recurrence within 6 months [34].

In a cross-sectional series (limited evidence) of 96 children in multiple centers presenting with seizures without fever or known systemic illness, 27% demonstrated abnormal findings on imaging [35]. In a similar group of adult patients with new-onset seizures, 177/764 (23%) demonstrated potentially epileptogenic lesions on MRI [36]. The frequency of abnormal imaging findings was higher in patients with focal seizures (53%). The most common lesions were gliosis/encephalomalacia, tumors, cavernous malformations, and mesial temporal sclerosis.

In developing countries, neurocysticercosis is one of the major causes of symptomatic seizures and epilepsy. A prospective study of 61 children with afebrile seizures showed that 23 children

(38%) had positive IgG for anti-cysticercus antibody, suggesting a potential etiology [37]. It should be borne in mind that the prevalence of IgG antibodies to cysticercus may be relatively high (15%) in endemic areas, but neurocysticercosis should be a consideration in exposed patients presenting with seizures [38].

Immediate noncontrast CT is useful for emergency patients presenting with seizure to guide appropriate acute management especially if there is an abnormal neurologic examination, predisposing history, or focal seizure onset according to a 1996 society guideline [39].

The Quality Standards Subcommittee of the American Academy of Neurology, the Child Neurology Society, and the American Epilepsy Society (2009) evidence-based practice guidelines (limited evidence) for the evaluation of first nonfebrile (unprovoked) seizures in children show similar diagnostic performance to the adult literature [40]. Results show that 0–7% of children had lesions on CT, which changed management (i.e., tumors, hydrocephalus, arachnoid or porencephalic cysts, and cysticercosis). Overall MRI found more lesions than CT but did not always change medical management (i.e., atrophy, mesial temporal sclerosis, and brain dysgenesis). This report concluded that there is insufficient evidence to support the recommendation for routine neuroimaging after the first unprovoked seizure. The authors recommended emergent neuroimaging for children with persistent postictal neurologic deficit and children that are not back to baseline neurologic status within a few hours. According to these guidelines, children with focal manifestations and age <1 year are candidates for non-emergent MR neuroimaging, and neuroimaging may be indicated in cases of focal seizures associated with positive neurological clinical findings. If a neuroimaging study is required, MR is the preferred modality [40]. However, the overall effect of neuroimaging on medical management was less in children than adults.

In a structured evidence-based literature review on the role of neuroimaging after first seizure, the Therapeutics and Technology Assessment Subcommittee of the American

Academy of Neurology concluded that, in adults, cranial CT imaging could change the clinical course in 9–17%, while in children, acute management was altered in 3–6%. In children <6 months up to 50% had imaging abnormalities [41]. Abnormal neurologic examination, predisposing history, or focal seizure onset were probably predictive of an abnormal CT study.

In the United Kingdom, the UK Guidelines for Emergency Medicine Network (a group of emergency physicians) carried out an evidence-based literature review in 2009 and found abnormal head CT scan results in 12–41% of all patients with a first seizure [42]. This figure rises to 59–82% if there are focal abnormalities on examination. Even if there are no focal neurological signs on examination, abnormalities are still found on 6–22% of CT scans. These authors concluded that neuroimaging should be performed immediately whenever an intracranial lesion is suspected and specifically in patients with new focal deficit or persistent altered mental state, fever, persistent headache, focal or partial onset before generalization, or a history of acute head trauma, malignancy, immunocompromise, human immunodeficiency virus (HIV) infection, alcoholism, anticoagulation, or bleeding diathesis. Deferred early outpatient neuroimaging may be used when reliable follow-up is available. Otherwise, they recommended neuroimaging in the ED should be performed on all patients presenting with seizures.

According to the same guidelines, MRI (magnetic resonance imaging) is preferable to CT (computed tomography), if readily available within an acceptable time period, in a patient who has fully recovered. CT should be used if MRI is not readily available or in an individual who has not fully recovered. In acutely ill patients, CT is the modality of choice [42].

In 2009, the International League Against Epilepsy (ILAE) published imaging guidelines for infants and children with new-onset epilepsy, offering a five-point scale classification of neuroimaging findings. While not aimed at first-time seizure per se, this neuroimaging classification is relevant to assessing the results of emergent imaging [43]. In this review of multiple prospective and retro-

spective studies, nearly 50% of children with localization onset seizures had abnormalities, with 15–20% of studies providing useful information on etiology, and 2–4% revealed significant abnormalities requiring urgent intervention [43]. The authors also recommended MRI over CT for its superior resolution, versatility, and lack of radiation.

Special Case: Small Children (<36 Months) and Infants

Young children appear more likely to have findings on emergent neuroimaging that will alter the acute medical or surgical management, with one study reporting a prevalence of 29% among children younger than 33 months compared to an estimated 2–4% overall [44, 45].

Sharma et al. found in a well-described retrospective study (moderate evidence) clinically significant abnormal neuroimaging in 8% of 475 children with “new-onset afebrile seizures” (95% CI: 6.4–11.8). Two risk factors were associated with a higher risk of significant abnormal neuroimaging: the presence of a predisposing condition (such as sickle cell disease, bleeding disorders, cerebrovascular disease or malignancy, human immunodeficiency virus or Acquired Immune Deficiency Syndrome (AIDS), hemihypertrophy or hydrocephalus, exposure to cysticercosis, and closed-head injury) and focal seizures in children younger than 33 months of age. In these high-risk groups, 24% and 29% yielded abnormal neuroimaging, respectively [44].

In a more recent prospective study (moderate evidence) of 317 infants with new-onset seizures presenting to an emergency department, 94% had head CT and 57% had MRI performed. One third of CTs were abnormal and 9% had a significant abnormality requiring urgent intervention [45]. Over half of the MRIs were abnormal with cerebral dysgenesis being the most common finding. The authors concluded that due to the higher rate of localization-related seizures in children under 2 years, the higher rate of abnormalities in infants compared with older children, the prognostic implications, and the superior yield of MRI compared to CT in identifying and defining abnormalities, MRI should be obtained in all infants presenting with a new-onset afebrile seizure

(moderate evidence). They recommended in cases in which urgent neuroimaging is not indicated and in which the infant could be observed, to avoid CT, and thus unnecessary radiation, and to organize a brain MRI instead [45].

Special Case: Neonates

Seizures are the most common sign of neurological dysfunction in full-term neonates, with an incidence estimated at 1–1/1000 live births [46, 47]. The accurate diagnosis and management of seizures in neonates is difficult, since they are difficult to differentiate from other abnormal movements, which can often be attributed to seizures. Seizures are rare in preterm and term neonates and are most commonly caused by hypoxic ischemic brain injury, followed by ischemic stroke and intracranial hemorrhage [47]. Computed tomography (CT) is now less commonly used and should only be performed in an infant who may acutely need neurosurgical intervention. Magnetic resonance imaging (MRI) is increasingly used and recognized as the best imaging modality. Ultrasound (US) is portable and inexpensive and can be used as a screening tool and is sensitive for detection of intraventricular hemorrhage and secondary hydrocephalus. Cranial US should be used in the acute phase and may show severe and centrally located lesions, as well as calcification, which might not be detected by MRI. However, the sensitivity of ultrasound for detection of hypoxic ischemic injury is limited, and for this indication, MRI is the modality of choice.

Special Case: Seizures of Temporal Lobe Origin

MRI is more sensitive as CT in detecting temporal lobe pathology (limited evidence) [48–50].

The sensitivity of MRI and CT in detecting structural lesions in pediatric temporal lobe epilepsy (TLE) (new onset and chronic) was assessed by Sinclair et al. [48]. In their retrospective study of 42 children (limited evidence) comparing neuroimaging with pathology, MRI had a sensitivity of 64% (27/42 children), while CT had a sensitivity of 31% (12/39 children). If the first seizure is of temporal lobe type (e.g., complex partial seizure), the yield of MRI is higher ranging between 38 and 64% [48, 49].

Harvey et al. in a prospective cohort study (moderate evidence) found structural abnormalities in 24 of 63 (38%) children with new onset of TLE, of whom 8 (13%) showed findings requiring medical intervention [49]. They classified patients with new-onset TLE into three categories based upon neuroimaging findings including developmental abnormalities (slow growing tumors and malformations), hippocampal sclerosis with antecedents (previous infection or significant illness), and cryptogenic (no past history and normal neuroimaging findings) and concluded that structural abnormalities correlated with greater risk of developmental delay and further seizures.

In a community-based prospective study (moderate evidence) by Sztrihai et al. of 30 children with first-time seizures of temporal origin, 50% of MRIs performed showed structural abnormalities. Using the classification described by Harvey et al., they also found that in patients without structural lesions with TLE (cryptogenic group), the incidence of developmental delay and seizures was less than for children with structural lesions by neuroimaging [51]. More recently, in a prospective cohort (moderate evidence) study by Spooner et al. of 77 children with new-onset epilepsy, 64 of whom had temporal lobe epilepsy (TLE) and temporal lesions were found in 28 patients (44%) (hippocampal sclerosis in 10, tumor in 8, and cortical dysplasia in 7). The yield increased to 48% if only the MRI cases were taken into account. All children with newly diagnosed temporal lobe seizures and lesions on MRI were not seizure free on more than 10-year follow-up [52].

What Neuroimaging Examinations Are Indicated in Patients Presenting with New-Onset Seizures with Clinical Signs or Features Suggesting a Structural Lesion?

For clarity, this includes seizures occurring in patients having neurological symptoms or findings pointing to an underlying abnormality. It excludes meningitis, encephalitis, abscess, and empyema.

Summary of Evidence Emergency neuroimaging should be considered in all patients with a first seizure, particularly when risk factors (such as an underlying cause and focal signs) are present (moderate evidence).

CT scan is the best imaging study in the evaluation of patients with acute symptomatology as it is sensitive for finding abnormalities such as acute intracranial hemorrhage, which may require immediate medical or surgical treatment (moderate evidence).

While it may not be necessary in the emergent setting, MRI is more sensitive in detecting a structural lesion (moderate evidence) and can be performed later. For those with refractory epilepsy, a high-resolution epilepsy-focused protocol may be indicated.

Supporting Evidence No articles meeting the criteria for strong or moderate evidence were found.

Neuroimaging is positive in up to 82% of cases of adults and children with focal neurological deficits on examination. Significant neuroimaging findings impacting medical care were found in up to 44% of patients (up to 25% in adult studies and in 4% of studies in children).

In a prospective cohort study (moderate evidence) of 163 patients, who presented to the emergency room with first seizure, all patients older than 6 years of age who had recent head trauma, focal neurologic deficit, or focal seizure activity underwent head CT [53]. The authors, Eisner et al., reported CT abnormalities in 5 (25%) of 19 patients, including one subdural hematoma, resulting in a change of medical care. CT resulted in a change of diagnosis in 44% of patients and a change in disposition in 26% of patients in whom it was used.

In a prospective study, Earnest and colleagues found CT abnormalities in 6.2% of 259 patients with alcohol withdrawal seizures (moderate evidence). Medical management was altered in 3.9% of these patients [54].

Feussner et al. retrospectively reviewed (limited evidence) a population of patients with alcohol withdrawal seizures found CT abnormality in 51% with 34.4% demonstrating dif-

fuse atrophy and 15% having focal structural lesions. Of the focal lesions, 11 were old strokes and another 11 were considered potentially reversible abnormalities (7 subdural hematomas, 2 hygromas, 2 intracranial hemorrhages) of which 6 went to surgery. Thirty percent of patients with focal deficits had abnormal CTs, whereas abnormalities on CT were found in only 6% of patients without focal deficits [55]. Of patients treated surgically, 9% had focal neurologic deficits and 1% did not. Interestingly, a cohort of alcoholics without seizures yielded similar CT results.

Reinus et al. retrospectively evaluated (limited evidence) the medical records of 115 consecutive adult patients presenting to a trauma center following seizures who underwent a noncontrast cranial CT. Of the 38 patients with new-onset seizure, 7 (18%) had an abnormal CT [56]. An abnormal neurologic examination predicted 95% (19 of 20) positive CT scans. There was also an association between known malignancy and positive findings by neuroimaging. The authors suggested that patients with abnormal neurological examination or prior malignancy would most benefit from neuroimaging.

In a retrospective review (limited evidence), Pesola et al. reported that 6 out of 26 HIV-positive patients with new onset of generalized seizures presenting to the emergency department had an acute lesion found on CT, 2 of which were not suspected on physical examination [57]. They recommended that the workup of all new-onset seizures in HIV-infected patients include neuroimaging on initial seizure presentation, with a lumbar puncture if the imaging study is nondiagnostic, which is in line with the 1996, 1997, and 2007 society guidelines [39, 41, 58].

In a cross-sectional retrospective single center study (limited evidence), of 319 children with first seizure and focal manifestations, 4% had clinically relevant intracranial imaging findings (by CT and MRI), important to initial management [infarction, hemorrhage, and thrombosis] [59]. Patient characteristics associated with higher risk of clinically urgent intracranial abnormality included those with Todd's paralysis and those under 15 months of age.

Bradford et al. performed an evidence-based review (limited evidence) of diagnostic tests in patients with new onset of seizures [60]. The authors reported a diagnostic yield of 87% for CT. Predictors of abnormal CT scan in patients with new onset of seizures were head trauma, abnormal neurological findings, focal or multiple seizures (within a 24-h period), previous central nervous system CNS disorders, and history of malignancy. The authors concluded that there is supportive data to perform CT scanning in the evaluation of all first-time acute seizures of unknown etiology.

The American Academy of Neurology recommends considering emergent head CT for all patients with a first seizure, particularly those who have risk factors for abnormal neuroimaging [including alcohol abuse, bleeding disorders, anti-coagulation therapy, risk of cysticercosis, stroke or malignancy, HIV or AIDS, neurocutaneous disorders, recent head trauma, sickle cell disease, hydrocephalus or recent shunt surgery, persistent altered mental status, and age <6 months or >65 years] [61].

The UK Guidelines for Emergency Medicine Network (a group of emergency physicians), in their 2009 evidence-based literature review, reported abnormal head CT scan results in 12–41% of all patients with first seizures, with the figure rising to 59–82% if there are focal abnormalities on examination [42]. They concluded that neuroimaging should be performed immediately whenever an intracranial lesion is suspected and specifically in patients with new focal deficit or persistent altered mental state, fever, persistent headache, focal or partial onset before generalization, or a history of acute head trauma, malignancy, immunocompromise, HIV infection, alcoholism, anticoagulation, or bleeding diathesis. In the same review, patients over 40 years old had a significant increase in the likelihood of having an abnormal CT, the frequency of abnormal scans nearing 60% in the over 50s. This increased yield from scanning is most often related to cerebrovascular events and tumors, with an increase in tumor prevalence beginning at age 40 and stroke in the over 60-year age group. Because of this, some physicians operate an age-

dependent policy with regard to neuroimaging [42].

The Scottish Intercollegiate Network (SIGN) and the National Institute for Clinical Effectiveness (NICE) guidelines also recommend MRI over CT where resources permit.

However, both institutes suggest that in an acute situation, CT may be used instead of MRI for emergency neuroimaging [62, 63]. The American College of Emergency Physicians (ACEP) guidelines discuss only the indications for CT scanning in the ED and do not compare CT with MRI [58]. The ILAE guidelines for neuroimaging studies suggest that a CT may be used if an MRI is not available although MRI is the imaging procedure of choice in patients with suspected focal epilepsy [43].

Can Findings on Emergency Neuroimaging Predict the Likelihood of Future Seizures?

A concern for any patient presenting with their first seizure is whether they will recur or subsequently develop an epilepsy syndrome. The implications for driving, working, and everyday activities can be significant in patients with breakthrough recurrent seizures. Their caregivers will want to know their risks of developing further seizures or epilepsy, and imaging findings play a role in risk stratification and prognosis. Patients and caregivers will also require appropriate advice and recommendations/guidance, because some will need further investigations or follow-up and management. Therefore, knowing the diagnostic accuracy (sensitivity) of emergent neuroimaging for structural lesions that may cause recurrent seizures or epilepsy is essential.

Summary of Evidence The risk of recurrence following a seizure is highest immediately following the seizure (moderate evidence). The rate for first recurrences drops off with increasing time since the first seizure, with 80–90% of individuals who recur doing so within 2 years of the initial seizure.

Patients with significant brain-imaging abnormalities on imaging (particularly tumors) have increased risk for recurrence (moderate evidence).

The risk of recurrence of seizures (34%) was higher in elderly patients presenting with their first seizure (limited evidence).

Structural causes (stroke in the elderly), symptomatic or nocturnal seizures, and EEG abnormality (epileptiform or nonspecific abnormality) are significantly associated with increased risk of seizure recurrence (moderate evidence).

Focal lesions found by MRI are predictors of intractable seizures in children with new-onset TLE (moderate evidence).

In neonates, the neuroimaging findings of diffuse or multifocal cortical or subcortical gray matter lesions, cerebral dysplasia, or changes related to global hypoxia-ischemia are associated with greater seizure recurrence and worse outcomes (limited evidence).

Supporting Evidence Two large-scale randomized trials provided definitive estimates of the risk of recurrence after an untreated first unprovoked seizure. These are the multicenter study from Italy, the first seizure trial (FIR.S.T) group and the European-wide Multicenter Epilepsy and Single Seizure (MESS) study, which included both first seizures and newly recognized epilepsy [64, 65]. Both of the randomized trials, especially the second, demonstrate a pattern seen in virtually all of the long-term observational studies of first seizures. Specifically, the risk of a recurrence is highest during the period immediately after the initial seizure. The rate, at which first recurrences occur, drops off with increasing time since the first seizure. Across a number of studies with prolonged follow-up periods, 80–90% of individuals who recur do so within 2 years of the initial seizure [66].

Studies have tried to evaluate risk factors or features that predict future seizures. A past history of seizures, developmental delay, learning disabilities, neurological deficit, and abnormal EEG were found to be potential risk factors, in a

population of patients who subsequently developed epilepsy [66]. Many studies have found a greater risk of seizure recurrence in patients with remote symptomatic seizures than in those with idiopathic seizures [66, 67]. In a prospective study of 408 adults (moderate evidence), Hopkins et al. found no features on head CT that predicted future occurrence of seizures other than brain tumors [27]. In a retrospective study (limited evidence) by Phabphal et al. of an elderly population with new-onset seizure (mostly focal), recurrence occurred in 34% of survivors after 2 years of follow-up. In a multivariate regression analysis, a structural cause (stroke in the elderly) of the seizure and EEG abnormality (epileptiform or nonspecific abnormality) were significantly associated with increased risk of seizure recurrence [68]. Patients with significant brain-imaging abnormalities have increased risk for recurrence. MRI is the modality of choice to screen for structural abnormalities and should be performed with a dedicated epilepsy protocol [2].

In a retrospective review of a population of children with newly diagnosed epilepsy, focal lesions identified with MRI conferred a higher risk of refractory seizures (limited evidence) according to Dhamija et al. [69]. Among the structural lesions, identified with MRI, encephalomalacia was much less likely to be associated with refractory epilepsy compared to mesial temporal sclerosis, malformations of cortical development, or vascular malformations.

Tekgul et al. studied MRI predictors of neurodevelopmental outcome in a retrospective study (limited evidence) of 89 term infants with neonatal seizures [70]. Cortical dysplasia and global hypoxia-ischemia were associated with poor developmental outcome. Thirty-six infants (40%) had severe cognitive impairment, and 31% had persistence of seizures after intensive care unit discharge. Overall outcome was judged poor in 50% of children with diffuse lesions. In contrast, only 1/18 (6%) in the group with normal neuroimaging were graded as having a poor outcome.

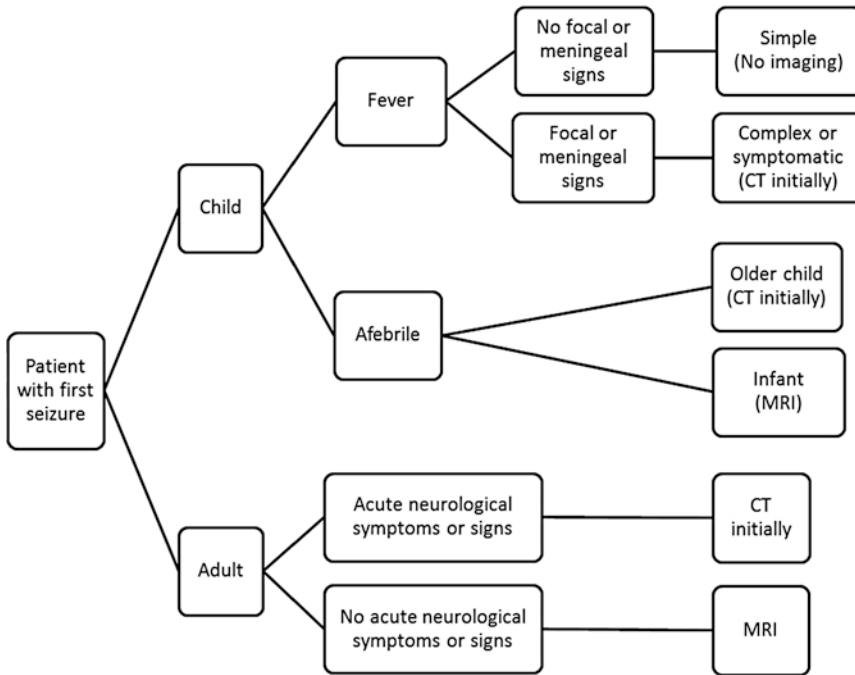


Fig. 10.1 Algorithm for decision-making in patients presenting to the emergency department with their first seizure. An infant is a child aged less than a year. *CT*

computed tomography, *MRI* magnetic resonance imaging. Many patients who have CT in the acute setting would benefit from MRI imaging at a later stage

Take-Home Figure

In Fig. 10.1, an algorithm for decision-making for ER patients with first seizures is presented.

Imaging Case Studies

Case 1

In Fig. 10.2, we have presented a 39-year-old man with seizures originating in the temporal lobe.

Case 2

Figure 10.3a–d presents a 4-year-old boy with focal seizures with a cerebral pyogenic abscess.

Case 3

A 59-year-old woman with mental status changes, headache, fever, and seizure is presented in Fig. 10.4a–d.

Case 4

In Fig. 10.5a, b, we have presented a 5-week-old infant female with lethargy, poor feeding, and seizures.

Case 5

Figure 10.6a, b presents a 62-year-old woman with a seizure indicative of temporal lobe origin.

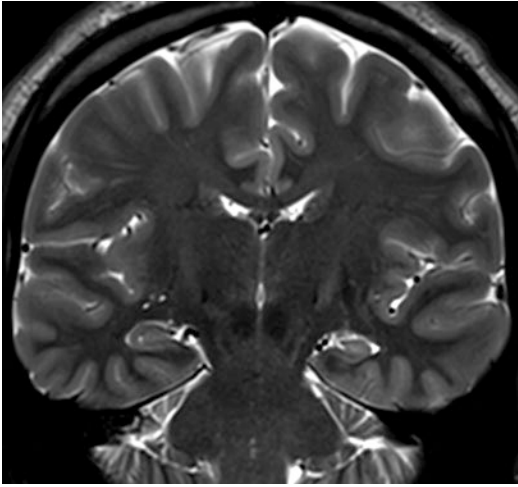


Fig. 10.2 A 39-year-old man with seizures of temporal lobe origin. Coronal T2-weighted image shows decreased volume and increased signal intensity in the left hippocampus consistent with mesial temporal sclerosis

Suggested Imaging Protocols

Noncontrast Brain CT Protocol

In the acute or emergent setting, we recommend non-enhanced axial contiguous 5 mm sections through the entire brain. Radiation doses should follow the as low as reasonably achievable (ALARA) recommendation.

MRI Imaging

MRI of the brain for the workup of epilepsy and nonfebrile seizures should include a high-resolution dedicated epilepsy protocol which includes sequences that optimize contrast resolution and signal abnormalities.

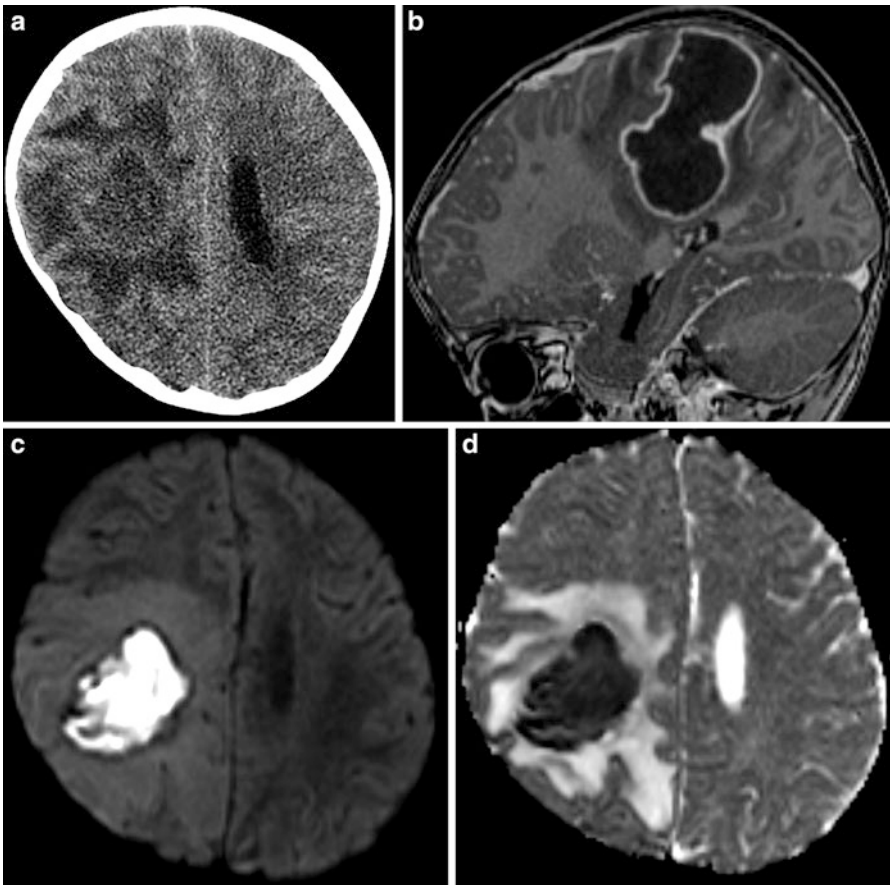


Fig. 10.3 A 4-year-old boy with focal seizures with a cerebral pyogenic abscess on neuroimaging. Axial non-contrast head CT image (a) shows large right hemispheric mass lesion with surrounding hypodensity suggestive of vasogenic edema. Sagittal contrast-enhanced T1-weighted

MR image (b) shows large rim-enhancing mass lesion. Diffusion-weighted image (c) shows high signal intensity of the lesion contents, with corresponding hypointense signal on ADC map (d), indicating restricted diffusion from purulent content

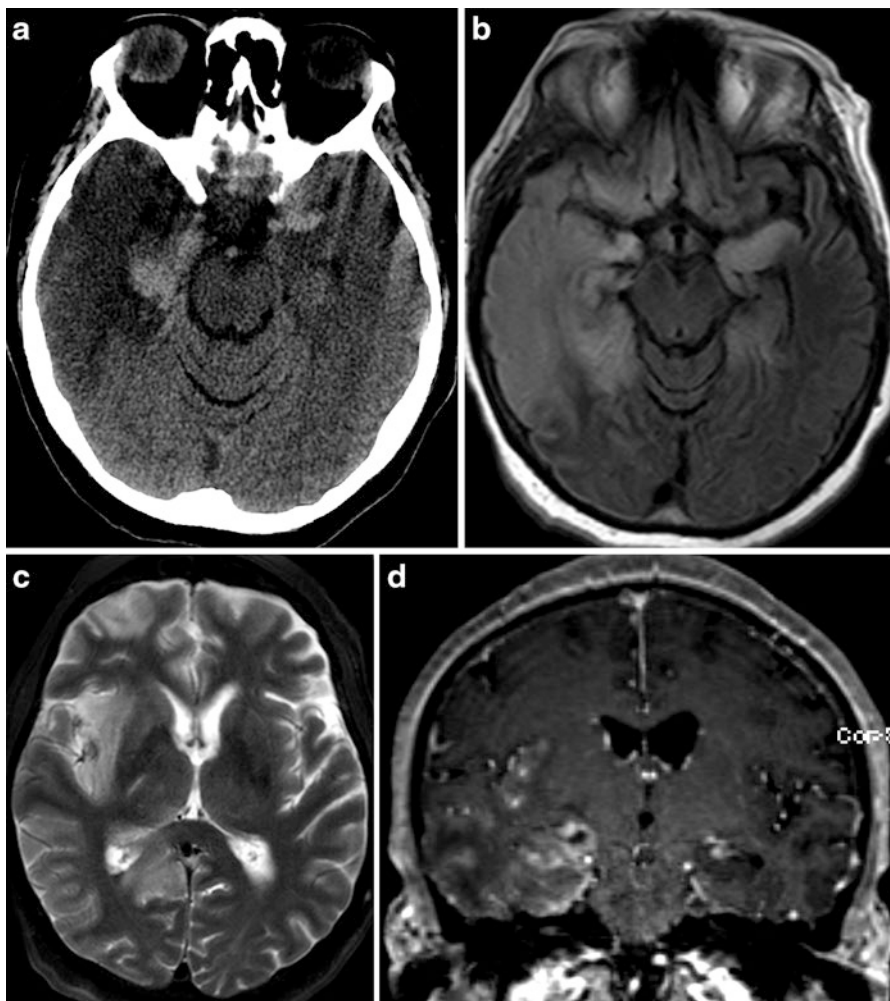


Fig. 10.4 A 59-year-old woman with mental status changes, headache, fever, and a seizure. Imaging suggested herpes (HSV1) encephalitis. Axial noncontrast head CT (**a**) shows marked hypodensity of the right temporal lobe and bilateral areas of high density consistent with acute hemorrhage in the bilateral mesial temporal lobes. Axial T2-FLAIR MR image (**b**) shows bilateral

asymmetric high signal intensity within the temporal lobes. Axial T2-weighted MR image (**c**) shows additional involvement of the right insula and posterior cingulate gyrus as areas of high signal intensity. Coronal contrast-enhanced T1-weighted image (**d**) shows leptomeningeal and cortical enhancement in the right temporal lobe and insula

The suggested MRI protocol includes the following sequences: T1-weighted, coronal 3D volume 1 mm section thickness (ST) no gap, axial and coronal oblique fluid-attenuated inversion recovery, axial dual echo (gradient and spin echo), diffusion-weighted axial, and T2-weighted coronal fast spin-echo images through the entire brain. At least one post-contrast sequence should be obtained to exclude enhancing lesions.

Neonatal MRI Protocol (48)

A standard neonatal MRI protocol should include sagittal T1-weighted images (T1WI), axial or coronal T2-weighted images (T2WI), and T1WI or inversion recovery-weighted images and diffusion-weighted images (DWI), including diffusion coefficient (ADC) mapping. Magnetic resonance venography (MRV), MR angiography

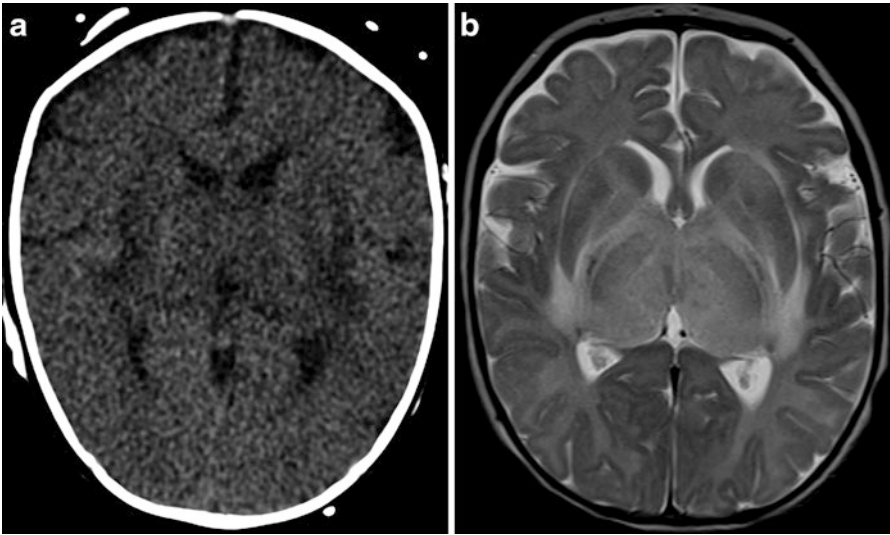


Fig. 10.5 A 5-week-old girl with lethargy, poor feeding, and seizures. Imaging revealed acute necrotizing encephalitis. Axial noncontrast head CT image (a) shows abnormal patchy hypodensity involving the bilateral deep gray

nuclei. Axial T2-weighted MR image (b) shows abnormal swelling and hyperintense signal of the thalami, basal ganglia, and adjacent white matter tracts

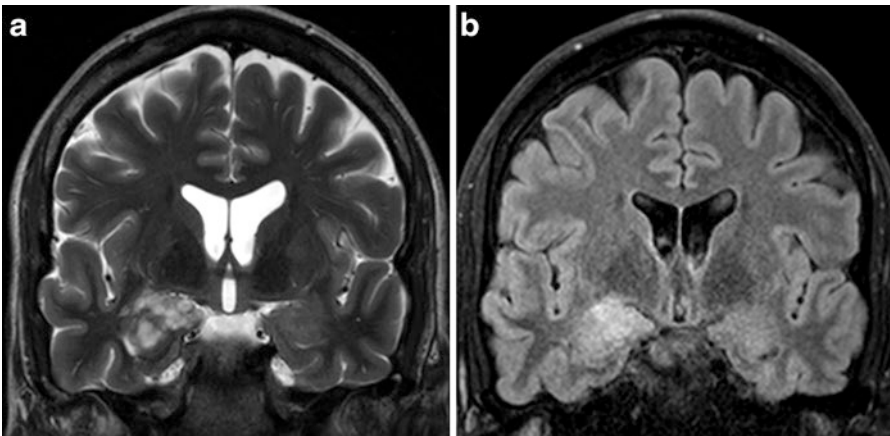


Fig. 10.6 A 62-year-old woman presented with a seizure indicating temporal lobe origin. Imaging revealed a neuroglial tumor. Coronal (a) T2-weighted MR image shows

a multicystic mass lesion centered in the right amygdala, with corresponding high T2 signal intensity on the coronal T2-FLAIR image (b)

(MRA), 1H-magnetic resonance spectroscopy (MRS), and susceptibility-weighted images (SWI) should preferably be available as well.

DWI is especially important in hypoxic-ischemic encephalopathy HIE and perinatal arterial ischemic stroke (PAIS) and is also useful in central nervous system (CNS) infections. MRV should be

added when a cerebral sinus venous thrombosis (CSVT) is suspected. MRA can be useful in (PAIS) and in diagnosing arteriovenous malformations. 1H-MRS can provide additional information in suspected metabolic disorders, and HIE and SWI are useful in diagnosing (small) hemorrhages. Section thickness should be 2 mm or less.

Future Research

- To define better the different first seizure risk groups so neuroimaging can be tailored appropriately.
- To perform formal cost-effectiveness analysis of the role of imaging in patients of different age groups presenting with their first seizure.
- More research is needed in evaluating the role of neuroimaging in first complex febrile seizures.
- To determine the role, advantages, limitations, indications, and pitfalls of new imaging studies such as diffusion tensor-/diffusion-weighted imaging in evaluation of first unprovoked seizures.
- To determine if MRI or DTI/DWI findings in first unprovoked seizure can predict future risk of recurrent seizures.

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Acute Spine Trauma in Adults and Children: Evidence-Based Emergency Imaging

11

C. Craig Blackmore

Key Points

- The NEXUS and Canadian cervical spine rules are validated clinical prediction rules that can identify subjects at risk for cervical spine fracture, in whom imaging is appropriate (strong evidence).
- Cervical spine CT is the best imaging modality in high- and intermediate-risk patients (moderate evidence).
- In low-risk trauma victims not undergoing head CT, radiography is an acceptable cervical spine imaging approach (limited evidence).
- Selection of subjects for thoracolumbar spine imaging can be made based on clinical criteria (moderate evidence).
- CT, including reformations from CT scans performed of the chest, abdomen, and pelvis, is more accurate than radiographs in the thoracic and lumbar spine, but radiography may still be appropriate in low-risk subjects (limited evidence).

Definition and Pathophysiology

Spinal trauma can lead to permanent neurologic damage. In addition to the neurological deficit, spinal cord injury has additional important ramifications. This includes a precipitous decline in probability of employment, educational achievement, and intact marriage [1]. Therefore, although spinal cord injury is relatively uncommon, spine imaging is frequently performed to exclude suspected and occult fractures. As a result of wide spread utilization, the positive yield of spine imaging is estimated to be only 2.4% in the cervical spine when all patient populations are included [2]. Using the best available evidence, this chapter addresses diagnostic imaging of the spine in trauma including clinical prediction rules and cost-effectiveness.

Spinal fractures are estimated to account for 3–6% of all skeletal injuries in the USA. A Canadian study in 2006 estimated that 56% of spinal fractures are associated with spinal cord injuries and there is a general mortality rate of 8% [3]. Although no recent epidemiologic studies were identified, the annual incidence of cervical spine fracture was estimated at 10,000 per year in the USA in 1992 [4]. Better statistics are maintained for spinal cord injury of all causes and available from the National Spinal Cord Injury Statistical Center, Birmingham, Alabama. From this database the annual incidence of spinal cord

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injury is estimated at 40 cases per million per year in the USA or 12,000–20,000 per year when on scene fatalities are excluded [1]. The incidence of cervical spine fracture was recently estimated at 118 per million per year in Norway [5].

Spinal cord injury is predominantly a disease of young (average age 33.7 years) males (80.8%). The most common causes are traffic accidents, falls, and violence in decreasing frequency [1]. The hospital mortality for acute spinal injuries is high, up to 17%, reflecting the presence of other severe injuries.

The cervical spine is both the most commonly fractured region in spinal trauma and the area where risk of cord injury is greatest compared to that of thoracic, lumbar, or sacral fractures [6]. Though generally symptomatic, spine fractures may be clinically occult in trauma victims with other distracting injuries or who are unexaminable from obtundation, medication, or intoxication. In patients suffering from blunt trauma resulting in trauma team activation, the prevalence of cervical fracture is greater, 3.7%, and up to 7.7% in unexaminable patients. Once detected, between 42% and 57% of all cervical spine injuries are potentially unstable [7, 8].

Elderly patients have approximately doubled risk of significant injury, which may result from relatively low-energy mechanisms of injury [9]. The elderly spine has altered biomechanics, including decreased range of motion, lower muscular strength, and increased rigidity from degenerative changes, including ankylosis. In addition, degenerative changes may contribute to narrowing of the spinal canal with associated increased risk of cord injury [9].

Overall Cost to Society

Cervical spine injuries cause an estimated 6000 deaths and 5000 new cases of quadriplegia each year [1]. The total number of people with spinal cord injuries in the USA is estimated to be 265,000 persons, with a range of 232,000 to 316,000 persons [1]. The cost of care is dependent on severity

of injury and is highest during the first year following injury. In 2010 dollars the average annual expense for cervical spine injury resulting in incomplete motor function at any level was \$321,720 in the first year and \$39,077 for each subsequent year of life. In cases of high tetraplegia (C1–4), the first year cost of care averages \$985,774 and \$171,183 for each subsequent year of life [1]. The most recent comprehensive analysis of spinal cord injuries performed in 1996 concluded that the estimated total annual cost of all cervical spinal cord injuries was \$9.7 billion per year [10].

Goals of Imaging

The primary goals of imaging are to (1) detect potentially unstable injuries to enable immobilization or stabilization and prevent development or progression of neurologic injury and (2) inform prognosis and guide surgical intervention for unstable fractures.

Methodology

A PubMed (National Library of Medicine, Bethesda, Maryland) search for original research publications discussing diagnostic performance and clinical predictors of cervical and thoracic spine injury was performed. This includes publications from 1966 to May 6, 2015. The search strategy employed different combinations of the following terms: (1) spine, (2) radiography or imaging or computed tomography or magnetic resonance imaging, and (3) fracture or injury. MeSH headings included (1) spine and diagnosis, (2) imaging and spine, and (3) magnetic resonance imaging. Bibliographies of identified articles were reviewed for further papers. The articles were limited to human studies published in the English language. An initial review of the titles and abstracts of identified articles was followed by review of the full text of articles that were relevant.

Discussion of Issues

Who Should Undergo Cervical Spine Imaging After Blunt Trauma?

Summary of Evidence The NEXUS [2] and Canadian C-spine [11] rules are two clinical prediction rules that have undergone multicenter validation, with the intent of determining which patients should undergo cervical spine imaging in blunt trauma. Both clinical prediction rules report sensitivity greater than 99%, with specificity of 42.5% for the Canadian C-spine rule and 12.9% for NEXUS (Table 11.1). A single randomized trial was implemented applying the Canadian C-spine rule which found that adherence to the decision rule demonstrated efficacy at

reducing imaging of the cervical spine (strong evidence).

Supporting Evidence

Nexus Prediction Rule

The National Emergency X-Radiography Utilization Study (NEXUS) was a multicenter observational study involving 23 diverse emergency departments throughout the USA in the 1990s. Based on identified best practices at the time, the NEXUS study was designed to assess the validity of four predetermined clinical criteria for prediction of cervical spine injury. The presence of any of the four criteria would indicate that imaging should be performed in case of (1) altered neurologic status, (2) intoxication, (3) midline posterior bony cervical spine tenderness,

Table 11.1 Diagnostic performance of the clinical prediction rules and diagnostic imaging modalities in suspected blunt spine trauma

	Sensitivity%	Specificity%	Potential decrease in radiography%
<i>C-spine prediction rules</i>			
NEXUS ^a	99.6	12.9	12.6
Canadian C-spine rule ^b	100	42.5	41.8
<i>TL-spine prediction rules</i>			
Hsu et al. ^c	100	11.3	Not reported
Holmes et al. ^d	100	3.9	3.7
Inaba et al. ^e	98.9	29.0	26.6
<i>C-spine radiography^f</i>			
	Overall	89–94	95.3
	Low risk		96.4
	High risk		78.1–89.3
CT ^g	Overall	99.0	93.1
<i>TL-spine radiography^h</i>			
	Conventional imaging	63.0	94.6
	CT	97.8	99.6

^aFrom reference [2]

^bFrom reference [11]

^cFrom reference [78]. Has not been validated

^dFrom reference [79]. Has not been validated

^eFrom reference [69]. Has not been validated

^fOlder references with clinical reference standard. It is unclear if these results are still valid. Adapted from references [17–19]

^gAdapted from references [19–22, 38–42]

^hPooled from references [72, 81–87]

N/A: not applicable

Adapted from Springer Science + Business Media from Blackmore CC, Avey GD. Imaging of the Spine in Victims of Trauma. In Medina LS, Blackmore CC (eds): Evidence-Based Imaging: Optimizing Imaging in Patient Care. New York: Springer Science + Business Media, 2006

or (4) distracting injury (meaning an injury of sufficient pain to potentially distract the patient from noticing a cervical spine injury). In the NEXUS prospective validation study, 34,069 patients underwent radiography of the cervical spine following blunt trauma. The NEXUS criteria had a sensitivity of 99.6% and specificity of 12.9% for clinically significant injury [2]. In the participant population, 818 (2.4% of total) had a cervical spine injury. It was estimated that adherence to the NEXUS criteria would reduce utilization of radiographs by 12.6% (strong evidence).

Though validated in multiple different emergency departments, the NEXUS has been questioned in high-energy trauma patients in whom the trauma team is activated. There is limited evidence that the NEXUS criteria determined on patients with a normal Glasgow Coma Scale (GCS) cannot be used to exclude cervical spine fracture in victims of major trauma. In a 2007 study of major trauma victims, Duane et al. prospectively evaluated 534 patients imaged by cervical spine CT, and the performance of clinical exam was compared to that of CT [12]. In evaluable patients with GCS of 15 or greater who were not intoxicated and did not have a distracting injury, 17 patients had cervical spine fractures, 7 of which had a negative clinical exam. Of the seven fractures undetected clinically, three were transverse process fractures requiring no further intervention (and of uncertain clinical importance), and four required treatment with extended use of a rigid cervical collar. In follow-up studies in 2011 and 2013, by Duane et al., both the NEXUS and Canadian C-spine criteria were determined to be insufficient to exclude fracture in trauma team activation patients [13, 14].

There are no implementation studies documenting the efficacy of NEXUS for reducing overall utilization of imaging.

Canadian Cervical Spine Prediction Rule

The Canadian C-spine rule is similar to the NEXUS study in attempting to identify valid clinical predictors of patients who do not need imaging. The Canadian C-spine study, published subsequent to NEXUS, was a prospective cohort study of 8924 subjects from 10 community and

Table 11.2 NEXUS criteria. Imaging of the cervical spine is not necessary if all five of the NEXUS criteria are met

1. Absence of posterior midline tenderness
2. Absence of focal neurological deficit
3. Normal level of alertness
4. No evidence of intoxication
5. Absence of painful injury distracting attention from the spine

Data from Hoffman JR, Mower WR, Wolfson AB, Todd KH, Zucker MI. Validity of a set of clinical criteria to rule out injury to the cervical spine in patients with blunt trauma. National Emergency X-Radiography Utilization Study Group. *N Engl J Med.* 2000 Jul 13;343(2):94–9 Reprinted with kind permission of Springer Science + Business Media from Blackmore CC, Avey GD. Imaging of the spine in victims of trauma. In: Medina LS, Blackmore CC, editors. Evidence-based imaging: optimizing imaging in patient care. New York: Springer Science; 2006

university hospitals across Canada. The Canadian C-spine study was derived from an initial observational study which evaluated 20 potential predictive factors. According to the Canadian C-spine rule (Table 11.3), imaging is not indicated if all of the following three determinations are made: (1) absence of high-risk factor (age >65, dangerous mechanism, paresthesia's in extremities), (2) presence of a low-risk factor (simple rear end motor vehicle collision, sitting position in ED, ambulatory at any time since injury, delayed onset of neck pain, or absence of midline cervical C-spine tenderness), or (3) patient who is able to actively rotate neck 45 degrees to left and right. The Canadian C-spine rule has reported sensitivity of 100% and specificity of 42.5% with the rate of requested radiography estimated to be reduced by 58.2% (strong evidence) [11].

The implementation of the Canadian C-spine rule has also been investigated through a cluster randomized trial involving 12 Canadian emergency departments. A total of 11,824 alert and stable adults were included. The intervention group showed a relative reduction in cervical spine imaging of 12.8% and the control group a relative increase of 12.5% of cervical spine imaging [15].

There is no head-to-head trial supporting the adoption of either cervical spine prediction rule over the other, and a strong recommendation cannot be made of one clinical prediction rule over

Table 11.3 The Canadian C-spine rule

If the following three determinations are made, then imaging is not indicated	
1. No high-risk factor, including:	
	Age > 64 years
	Dangerous mechanism, including:
	Fall from >3 m/5 stairs
	Axial load to head (diving)
	High-speed vehicular crash (60 MPH, rollover, ejection)
	Bicycle collision
	Motorized recreational vehicle
	Paresthesia in extremities
2. Low-risk factor is present	
	Simple rear end vehicular crash, excluding:
	Pushed into oncoming traffic
	Hit by bus/large truck
	Rollover
	Hit by high-speed vehicle
	Sitting position in emergency department
	Ambulatory at any time
	Delayed onset of neck pain
	Absence of midline cervical tenderness
3. Able to actively rotate neck (45 degrees left and right)	

Adapted with permission from Bandiera G, Stiell IG, Wells GA, et al. The Canadian C-spine rule performs better than unstructured physician judgment. *Ann Emerg Med.* 2003 Sep;42(3):395–402

the other. A retrospective analysis comparing Canadian C-spine and NEXUS prediction rules was attempted. However, for this analysis, altered level of consciousness was not used as a criterion [16, 17], potentially biasing against the NEXUS rule, as this was a NEXUS criterion. In addition, the Canadian C-spine rule requires the active evaluation of cervical spine rotational range of motion, an approach which may not be acceptable in many US emergency departments.

What Imaging Modality Should Be Used for the Cervical Spine in Blunt Trauma?

Summary of Evidence Cervical spine CT is both more sensitive and specific than radiography for identifying cervical spine fractures (Table 11.1).

In addition, cost-effectiveness analysis supports the use of CT as the initial modality in patient populations at high and moderate risk of cervical fracture. Use of CT has been shown to reduce repeat imaging and identify the rare fractures which may have been missed from radiography with the potential to lead to severe neurological deficit (moderate evidence). In patient populations with low probability for cervical fracture, properly performed cervical spine radiography remains a reasonable imaging choice (limited evidence). MRI is not recommended in the acute setting as the initial evaluation of the cervical spine (moderate evidence).

Supporting Evidence

Accuracy of Imaging

Historically, the sensitivity of cervical spine radiography has been reported in the 89–94% range, when adequate three view radiographs were obtained on all patients [2, 18–20]. Weighted pooling of the larger studies using a clinical gold standard suggests that radiography is relatively accurate with a sensitivity of 94% and a specificity of 95% when all trauma patients are included (Table 11.1) [20]. Distressingly, however, more recently performed observational studies have reported much lower sensitivity for cervical spine radiography. The discrepancy seems related at least in part to choice of reference standard and adequacy of cervical spine radiographs. A representative in 2003 study performed by Griffen et al. in a level I trauma center concluded that the sensitivity of radiography was 65%, using CT follow-up as the reference standard [21]. In a 2014 systematic review, the sensitivity of cervical spine radiography for fractures was estimated to be between 36 and 65% using CT as the reference standard [22]. As with all diagnostic accuracy studies, using one modality as the reference standard biases strongly in favor of that modality, in this case with strong bias in favor of CT and against radiography. Accordingly, studies using fractures that become apparent clinically as the reference standard are probably more relevant for clinical practice. In addition, many recent studies are biased by comparing CT to inadequate

radiography examinations that did not include all necessary views or did not visualize the entire cervical spine. Furthermore, inadequate visualization is often seen as rationale for proceeding to CT imaging increasing bias against radiography. In a 2009 study, Bailitz et al. included 1583 consecutive major trauma patients that were evaluated with both cervical spine CT and 3-view cervical radiography [23]. In this particular study, the final diagnosis in the medical record at discharge was used as the gold standard for cervical spine injury, and a clinically significant injury was one defined as requiring either an operative procedure, halo application, or rigid cervical collar application. Of the 78 patients with radiographic evidence of fracture, 50 (3.3%) were determined to have clinically significant injuries, and 42% of the 50 required operative intervention or halo application. Using the risk stratification criteria defined by Blackmore et al. [24], 16 clinically significant cervical fractures were present in the low-risk patients of which only 4 were identified by cervical spine radiography (25% sensitivity). It should be noted however that of the 32 clinically significant injuries “missed” by cervical spine radiography, only 6 had adequate radiography.

The disconnect between historical estimates of radiography sensitivity of 89–94% and current estimates of 36–65% confounds determination of appropriate imaging. It is likely that the methodological limitations in the more recent literature, including consideration of inadequate radiographs as normal, use of an imaging rather than a clinical reference standard, and inclusion of only high-risk trauma patients, explain much of this difference. Historical data indicating that missed cervical spine injuries were in fact rare prior to widespread use of CT also calls into question recent low estimates of radiograph sensitivity. However, with decreased utilization of cervical spine radiographs comes decreased proficiency at performance and interpretation, and sensitivity today may actually be lower as a consequence.

High- and Moderate-Risk Patients

Cervical spine radiography is less accurate in patients at moderate and high risk of cervical

fracture (probability >4%) [20]. These patients are commonly immobilized on backboards, have multiple injuries, and are unable to cooperate. These factors result in lower specificity, more inadequate radiographs and repeat imaging, greater utilization of hospital resources, and ultimately higher cost [25]. Additionally, CT evaluation has been shown to be more time efficient when compared to radiography, allowing for faster disposition of patients from the emergency department [26, 27]. This is particularly true when evaluation of the cervical spine follows CT scan of the head [28]. The decreased sensitivity of radiography in the major trauma population, time efficiency, and increased prevalence of cervical fracture support initial evaluation of the cervical spine utilizing CT in moderate- and high-risk patients. Cost-effectiveness analysis supports use of CT in this population. In a 1999 study, Blackmore performed a cost-effectiveness analysis from the societal perspective comparing cervical radiography to that of CT and found that CT was cost-effective in high and moderate risk [18]. This was confirmed by Grogan et al. in 2005 (moderate evidence) [29].

Low-Risk Patients

There is neither strong evidence nor consensus on the appropriate approach to cervical spine imaging in trauma victims who require imaging under the NEXUS or the Canadian C-spine rule but who are at low risk of injury. The standard has been radiography, but more recently, CT has been promoted as an initial imaging strategy, even in low-risk individuals. Recent societal consensus guidelines in the USA, including the ACR Appropriateness Criteria [30] and Eastern Association for the Surgery of Trauma [31], have advocated for use of CT for all patients who undergo cervical spine imaging in trauma. However, guidelines supporting the use of CT in low-risk patients generally rely on recent estimates of accuracy, despite the methodological limitations discussed above. In addition, such guidelines do not consider the fact that use of CT carries much greater radiation risk and societal cost.

Radiography may be most appropriate in the evaluation of patients who cannot be cleared clinically but have low-risk factors for significant cervical trauma such as young age, low-impact trauma, and no distracting injuries [20, 24, 32]. Inability to obtain technically adequate radiographs due to incomplete visualization or suboptimal quality (low specificity) is the single biggest limitation of radiography (Table 11.1) [22]. In the very low-risk patient population, adequate images are more easily obtained. CT is indicated when adequate radiographs cannot be obtained.

Radiation risks are difficult to estimate with any precision due to the need for extrapolation of radiation effects from higher administered doses to the very low doses found in diagnostic imaging. However, the use of CT rather than radiography for evaluation of the cervical spine comes with an estimated 14-fold greater patient exposure to ionizing radiation (26 mGy compared to 1.8 mGy) [33], resulting in increased risk of radiation-induced malignancy [34]. Thyroid doses in particular from cervical CT are high, ranging from 4.4 to 66.5 mGy [35].

Reconciliation of the higher sensitivity of CT versus the lower cost and radiation dose of radiography is challenging. From 2002 to 2007, there was a significant increase in the use of CT and plain radiographs in the management of trauma patients, leading to significantly higher radiation exposure with no demonstrable improvements in the diagnosis of missed injuries, mortality, or length of stay [36].

Table 11.4 makes the trade-offs explicit through a crude estimation of the number needed to treat and the number needed to harm when substituting CT for radiography in low-risk patients. There is substantial uncertainty in the estimates of both benefits and harms from CT. However, it is likely that the rate of cancer mortality is at least an order of magnitude greater than the probability of preventing paralysis through use of CT in low-risk trauma patients. Accordingly, radiography, when adequately performed, should be considered as the initial imaging approach in patients at low risk (limited evidence).

Table 11.4 Number needed to treat and harm for cervical spine imaging in low-risk patients

Variable	Estimate	Range	Source (references)
Risk of fracture	0.005	0.002–0.02	[2, 11, 37]
Chance of missing fracture (1-sensitivity)	0.1	0.06–0.20	[2, 18–20, 23]
Chance of paralysis (from missed fracture)	0.05	0.01–0.15	[20, 34]
Number needed to treat ^a (to prevent one case of paralysis)	40,000	10,000–200,000	
Number needed to harm ^b (to cause one case of fatal cancer)	2000	1000–20,000	[33, 34, 35]

Notes: ^aNumber needed to treat is number of patients who have to undergo CT instead of radiography to prevent one case of paralysis in this population (equal to risk of fracture × chance of missing fracture × chance of paralysis)

^bNumber needed to harm is the number of patients who would have to undergo CT instead of radiography to cause one case of fatal cancer in the course of their lifetime

Used with permission from Blackmore CC, Smith JB: Spine Trauma: Evidence-Based Neuroimaging. Medina LS et al. (eds): Evidence-Based Neuroimaging Diagnosis and Treatment. New York: Springer Science + Business Media, 2013

Cost-effectiveness analysis also supports radiography as initial imaging strategy in low-risk patients. The threshold for when CT becomes cost-effective is somewhat uncertain. In the original cost-effectiveness analysis, Blackmore found a risk threshold of 4% to be the criterion for use of CT. However, subsequent investigators have proposed lower thresholds. Grogan suggested 0.9%, though this was based on extremely low estimates of radiograph sensitivity (64%) found in severely injured patients. Likely, however, the appropriate threshold is lower than the original 4% estimate, due to lower current estimates of performance of radiography detailed above.

Determination of appropriate imaging therefore requires stratification of patients into low- and

Table 11.5 Harborview high-risk cervical spine criteria

1. High-energy injury mechanism
High-speed (>35mph) motor vehicle or motorcycle crash
Motor vehicle crash with death at scene
Fall from height greater than 10 feet
2. High-risk clinical parameter
Significant head injury, including intracranial hemorrhage or unconscious in Emergency Department
Neurological signs or symptoms referable to the cervical spine
Pelvic or multiple extremity fractures

Presence of any of the following criteria indicates a subject at sufficiently high risk to warrant initial use of CT to evaluate the cervical spine

Adapted with permission from Hanson JA, Blackmore CC, Mann FA, Wilson AJ. Cervical spine screening: A decision rule can identify high-risk patients to undergo screening helical CT of the cervical spine. *AJR*. 2000;174:713–8

higher-risk cohorts. Blackmore [24] and Hanson [37] developed and validated a clinical prediction rule to identify subjects at high risk (Table 11.5). In the validation cohort, subjects lacking any of the high-risk factors had a risk of cervical spine fracture of only 0.2%, indicating that radiography was the preferred imaging approach. In the NEXUS study, the probability of fracture was 2.4% overall but 0.4% in the low-risk patients [2], again confirming that a group can be identified where adequate cervical spine radiography is appropriate as the initial screening tool.

Special Cases

Obtunded Patients

Summary of Evidence A normal cervical CT in obtunded patients with blunt trauma essentially excludes unstable cervical spine injuries. MRI is unlikely to change management when there is no neurological deficit or abnormality by cervical spine CT and is therefore not routinely recommended given risks and benefits (limited evidence).

Supporting Evidence There are several valid cohort studies of the accuracy of cervical spine CT in excluding unstable injuries in obtunded or

clinically unexaminable patients. Hennessy in 2010 reported a prospective cohort study of 402 intubated, unexaminable blunt trauma patients with normal CT. Using flexion-extension radiography and clinical follow-up as a reference standard, one patient was found to have an unstable injury missed by the CT (negative predictive value 99.7%) [38]. Hogan et al. retrospectively examined 366 patients with negative CT, using MR and clinical follow-up as the reference standard. The authors concluded that the negative predictive value of CT for ligamentous injury was 98.9% and 100% for unstable cervical spine (CS) injury [39]. Harris and colleagues evaluated a retrospective cohort of 367 obtunded patients using a clinical and radiographic reference standard. A normal multi-detector row CT scan of the cervical spine in obtunded patients with blunt trauma had a negative predictive value of 99.7% [40]. Brohi and colleagues prospectively evaluated 442 consecutive unconscious trauma patients and defined the sensitivity of CT at 98.1% (51/52), with a negative predictive value of 99.7% [41]. In addition, a 2005 retrospective cohort study by Schuster et al. included 93 patients with a normal motor examination and a negative cervical spine CT with MR as the reference standard. In this study all patients had negative MRI examinations unless there was a neurological deficit or a positive CT [42]. Como evaluated 197 patients who were obtunded by moving all four extremities and reported no missed injuries on CT, with clinical or MRI follow-up [43]. The recent recommendations of the Eastern Association for the Surgery of Trauma based on evidence review also now recommend CT alone in obtunded patients (moderate evidence) [44].

However, it is also clear that CT is imperfect. As an example, Schoenfeld and colleagues culled from the medical literature multiple cases (particularly of ligamentous injuries) missed at CT but discovered on subsequent MRI [45]. However, in a common failing of the literature on this topic, the authors omitted to mention the number of true-negative CT scans, instead only reporting the number of false-negative CT scans among the group who went on to MRI. This verification bias, due to selection of the cohort based on performance of

the reference standard, makes calculation of negative predictive value meaningless [46].

Finally, there are potential risks related to the use of MRI in obtunded patients, related to the transfer of patients to the MRI suite, and related to the limited ability to monitor patients while in the MRI scanner. In addition, delay in clearance of the cervical spine, with prolonged immobilization, may lead to complications including pressure ulcers, increased intracranial pressure, thromboembolism, and pulmonary aspiration [47–49].

Elderly Patients

Summary of Evidence Elderly individuals are at higher risk of cervical spine injury from both high- and low-energy mechanisms. However, no prediction rules have been validated to identify differential predictors of injury in the elderly. The same predictors in younger patients appear to work in the elderly [50]; however, clinical examination may not be as reliable [51]. Accordingly, the same approach to imaging may be applied in the elderly as in younger patients but with a lower threshold for use of CT due to the higher overall probability of fracture (limited evidence).

Children

Summary of the Evidence The NEXUS clinical prediction rule is a reasonable method of identifying which older children and adolescents should undergo cervical spine imaging after trauma. Imaging should be performed in subjects with (1) altered neurologic function, (2) intoxication, (3) midline posterior bony cervical spine tenderness, and (4) distracting injury (moderate evidence). In children under the age of 3 years, cervical spine imaging may be limited to subjects with high-energy mechanism (motor vehicle crash) or a Glasgow Coma Scale of less than 14 (limited evidence). Radiography can appropriately be used to exclude cervical spine fracture in children, though cervical spine CT may be useful in high-risk subjects. In younger children, when indicated, CT should be limited to the upper cervical spine (limited evidence).

Supporting Evidence Evidence for who should undergo imaging is less complete in children than in adults. Determination of clinical predictors of injury in pediatric subjects is complicated by the decreased incidence of injury in children, requiring larger sample size for adequate study [52–54]. In addition, children may sustain serious cervical cord injuries that are not radiographically apparent [52, 53]. Among adult clinical prediction rules, the Canadian clinical prediction rule development study excluded children [11]. The NEXUS trial included children, but there were only 30 injuries in subjects under age 18 and only 4 in subjects under age 9 [2]. Although no pediatric injuries were missed in the NEXUS study, the sample size was too small to adequately assess the sensitivity of the prediction rule in this group. Further validation of a pediatric version of the NEXUS was performed at a single academic pediatric trauma center in the USA. In 647 trauma victims age 3 or older, injuries were found in approximately 2%, of whom, 4 required operative fixation. No missed injuries were reported [55].

A pediatric adaptation of the NEXUS is a therefore reasonable approach in children over age 3, suggesting that imaging is only indicated when subjects have any of the following: (1) altered neurologic function, (2) intoxication, (3) midline posterior bony cervical spine tenderness, and (4) distracting injury (moderate evidence) [55].

Vanmarcke and colleagues performed a retrospective analysis of trauma registry data from multiple institutions, including 12,537 patients under the age of 3. They found that limiting imaging to subjects with decreased level of consciousness manifest by pediatric Glasgow Coma Scale of less than 14 or high-energy mechanism (motor vehicle crash) identified 78 of 83 (94%) clinically important injuries with a negative predictive value of 99.9%. The overall high negative predictive value was driven largely by the extremely low incidence of injury in this population (0.66%) even in subjects evaluated at major trauma centers [54]. This study has not yet been validated prospectively (limited evidence).

Comparison of CT versus radiography has not been well explored in children. Radiography has accuracy for cervical spine fracture of approximately 94% [56], similar to adults [19]. The odontoid view and flexion-extension radiographs contribute little in young children [57–60]. CT is likely more accurate than radiography but does encompass higher radiation doses and higher costs [61]. Most research studies and cost-effectiveness analyses excluded children [19, 23, 37]. Further, the lower frequency of injury in children [52, 62] and the increased radiosensitivity of pediatric subjects [63] suggest that cost-effectiveness results from adults may not be relevant.

A reasonable approach to pediatric cervical spine imaging is the Harborview protocol (Fig. 11.1 and Table 11.5). Overall, radiography is adequate to exclude cervical spine fracture in most young children (limited evidence) [61, 64]. However, the use of upper cervical CT in high-risk younger children [65] who are getting head CT is probably reasonable, as the time and cost are minimal, and the thyroid can be spared the

CT radiation dose if imaging is limited to the upper cervical spine (insufficient evidence). In addition, upper cervical spine injuries are more common than lower cervical injuries in younger children [62, 66–68].

Who Should Undergo Imaging of the Thoracic and Lumbar Spine After Blunt Trauma?

Summary of Evidence There is no effective, validated clinical prediction rule to guide which patients should undergo thoracolumbar spine imaging. A recently developed prediction rule [69] has potential to identify nearly all fractures and reduce unnecessary imaging but has not yet been validated. Other prediction rules with high sensitivities for detecting thoracolumbar fractures have been reported, but their low specificities and low positive predictive values mean that the effect on imaging in patients without thoracolumbar injuries would be minimal and utilization essentially unchanged (moderate evidence).

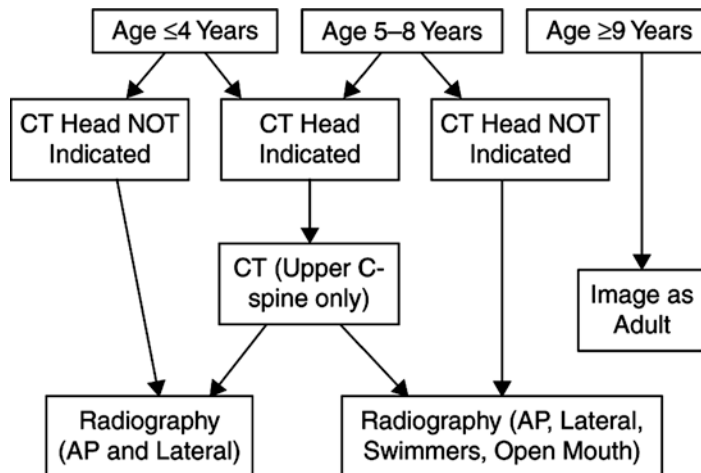


Fig. 11.1 Evidence-based decision tree for imaging of the cervical spine in child victims of trauma. The NEXUS or Canadian prediction rules are used to select patients for imaging. If imaging is appropriate, the selection of CT versus radiography is made based on whether the patient is also to undergo head CT. The radiography and CT pro-

ocols are age dependent (Reprinted with kind permission of Springer Science + Business Media from Blackmore CC, Avey GD. Imaging of the Spine in Victims of Trauma. In Medina LS, Blackmore CC (eds): Evidence-Based Imaging: Optimizing Imaging in Patient Care. New York: Springer Science + Business Media, 2006)

Supporting Evidence Several observational studies have examined potential risk factors for thoracolumbar fracture. These limited studies have identified associations between the risk of thoracolumbar injury and high-speed motor vehicle crash [70, 71], fall from a significant height [60–62], complaint of back pain [72–76], elevated injury score [72, 73], decreased level of consciousness [73–75, 77], and abnormal neurological exam (limited evidence) [74, 75].

Three different clinical prediction rules to guide use of thoracolumbar spine imaging have been developed, although neither prediction rule has been validated. In 2003, Hsu et al. examined the effect of six clinical criteria on two retrospective groups [78]. The first group consisted of a cohort of 100 patients with known thoracolumbar fracture, while the second group consisted of 100 randomly selected multi-trauma patients. The criteria evaluated were (1) back pain/midline tenderness, (2) local signs of injury, (3) neurological deficit, (4) cervical spine fracture, (5) distracting injury, and (6) intoxication. The results of this small-scale, retrospective trial found that 100% of the patients in the known thoracolumbar fracture group would have been imaged appropriately using the proposed criteria. This proposed pathway was then tested retrospectively in the group of randomly selected blunt trauma patients and was found to have a sensitivity of 100%, a specificity of 11.3%, and a negative predictive value of 100%. Implementing these criteria would still require imaging the thoracolumbar spine in 92% of the selected multi-trauma patients.

A second, much larger prospective, single-center study by Holmes et al. evaluated similar criteria in 2003 consecutive blunt trauma patients who underwent thoracolumbar imaging [79]. These clinical criteria (Table 11.5) were (1) complaints of thoracolumbar spine pain, (2) thoracolumbar spine pain on midline palpation, (3) decreased level of consciousness, (4) abnormal peripheral nerve examination, (5) distracting injury, and (6) intoxication. This prediction rule had 100% sensitivity for detecting thoracolumbar fracture, however, with specificity of only 3.9%. Due to this low specificity, implementing this

prediction rule in this patient population would have decreased the rate of thoracolumbar imaging by just 4% (moderate evidence).

More recently, a multicenter study at 13 trauma centers in the USA developed a clinical prediction rule based on clinical exam findings, age over 60 years, and high-energy mechanism. This rule had sensitivity of 98.9% with specificity of 29.0% for clinically important injuries. The authors identified that clinical exam alone, without age and mechanism, was not of sufficient sensitivity. This study has also not yet been validated (Table 11.1) [69].

Though not specifically evaluating a clinical prediction rule, Sava and colleagues did identify that clinical exam may not be sufficiently reliable to exclude fracture in subjects with substantial blunt trauma and altered sensorium [80].

What Is the Optimal Thoracic and Lumbar Imaging Approach in Blunt Trauma?

Summary of Evidence Multiple studies have shown that some CT protocols used for imaging the chest and abdominal visceral organs, when performed with sagittal reformations, are more sensitive and specific for detecting thoracolumbar spine fracture than conventional radiography. In patients undergoing such scans, conventional radiography may be eliminated (limited evidence). The effect of primary screening with CT scan on cost and radiation exposure has not been thoroughly studied for the thoracolumbar spine.

Supporting Evidence Multiple limited evidence studies examine the possibility of eliminating conventional radiography in those patients who are candidates for both conventional thoracolumbar radiographs and CT evaluation of the chest or abdominal viscera; however, many of these trials are hampered by small sample sizes and/or verification bias [81–86]. Studies that combine the results of both CT and conventional radiography as the reference standard suggest that CT has a sensitivity of 78.1–100%, while conventional radiographs have a sensitivity of 29.9–74% for

detecting thoracolumbar fracture (Table 11.1) [82–84, 87]. The clinical importance of thoracolumbar fractures not found with conventional radiography is unknown, as no studies with clinically based outcome measures were located.

A single limited evidence trial examined the use of CT as an initial evaluation in patients for which a CT scan is not indicated for other reasons [83]. This prospective, single-center trial examined 222 trauma patients with both CT and conventional radiographs as initial screening exams. The reported sensitivity was 97% for CT examination and 58% for conventional radiographs. The results of this trial are limited in that only 36 patients were diagnosed with thoracolumbar fracture during the course of the trial.

Applicability to Children

Summary of Evidence There are no clinical prediction rules validated in children for the determination of when imaging is indicated. However, a reasonable approach in older children is to image when any of the following are present: (1) complaints of thoracolumbar spine pain, (2) thoracolumbar spine pain on midline palpation, (3) decreased level of consciousness, (4) abnormal peripheral nerve examination, (5) distracting injury, and (6) intoxication (limited evidence). No reliable data exists on when to image in younger children (insufficient evidence). Compared to adults, younger children are less likely to localize pain and may have pain referred to the spine from intra-abdominal causes, particularly renal (infection and obstruction).

Supporting Evidence Data on appropriate indications for thoracolumbar spine imaging in children is limited. The adult clinical prediction rule from Holmes and colleagues did enroll children. However, the actual number of children in the study is not reported [79]. The youngest patient enrolled in the small clinical prediction rule validation trial by Hsu et al. was 14 years of age [78]. Given the 100% sensitivity in adults, it is reasonable to employ the Holmes clinical prediction rule in older children (limited evidence). In younger children, the criteria would have to be modified ad hoc to meet the clinical perception of the child's

ability to provide reasonable responses and the clinical picture (insufficient evidence). The specificity of the Holmes prediction rule in adults was low (3.9%), so it is not expected that the use of this prediction rule would decrease unnecessary imaging [79]. The Inaba study excluded children [69].

Take Home Tables and Figure

Tables 11.1 through 11.6 and Fig. 11.1 serve to highlight key recommendations, supporting evidence, and imaging decisions.

Imaging Case Studies

Case 1

Figure 11.2a, b presents a victim of a motor vehicle crash who has met criteria for cervical spine imaging with CT scan due to a potentially unstable C6–7 facet and pars interarticularis fracture.

Case 2

Figure 11.3a, b presents a victim for a motor vehicle crash who has met criteria for initial cervical spine imaging with CT scan due to fracture of the right skull base (foramen magnum) and dislocation/dissociation at the atlanto-occipital joint.

Table 11.6 Thoracolumbar spine imaging criteria

1. Pain
2. Tenderness to palpation
3. Neurological deficit
4. Deformity
5. High-risk mechanism ^a
6. Age \geq 60 years

Adapted with permission from Inaba K, Nosanov L, Menaker J, et al. Prospective derivation of a clinical decision rule for thoracolumbar spine evaluation after blunt trauma: An American Association for the Surgery of Trauma multi-institutional trials group study. *J Trauma Acute Care Surg* 2015;78:459–467

^aFall, crush injury, motor vehicle collision with rollover/ejection, unenclosed vehicle crash, automobile versus pedestrian

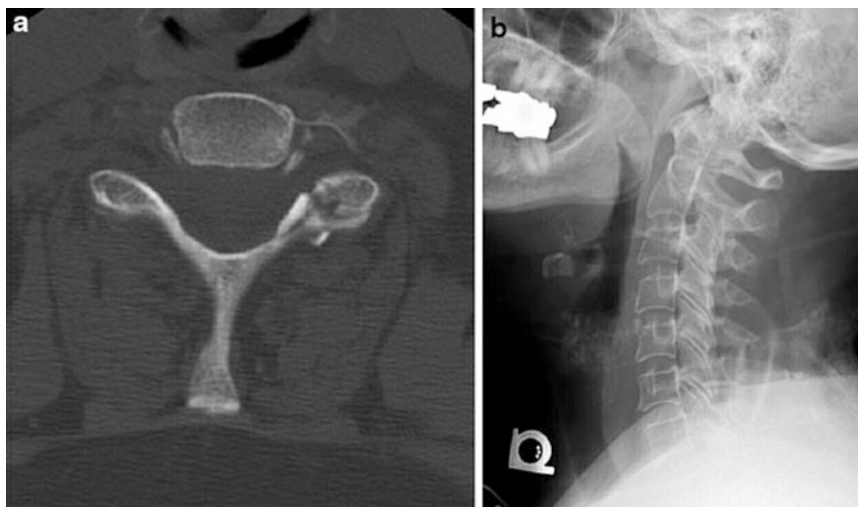


Fig. 11.2 Victim of a motor vehicle crash who met criteria for cervical spine imaging with CT scan. A potentially unstable C6–7 facet and pars interarticularis fracture is apparent on CT (a) but was missed on contemporaneous radiography (b). CT has higher sensitivity for fracture than radiography (Reprinted with kind permission of

Springer Science + Business Media from Blackmore CC, Avey GD. Imaging of the spine in victims of trauma. In: Medina LS, Blackmore CC, editors. Evidence-based imaging: optimizing imaging in patient care. New York: Springer Science; 2006)

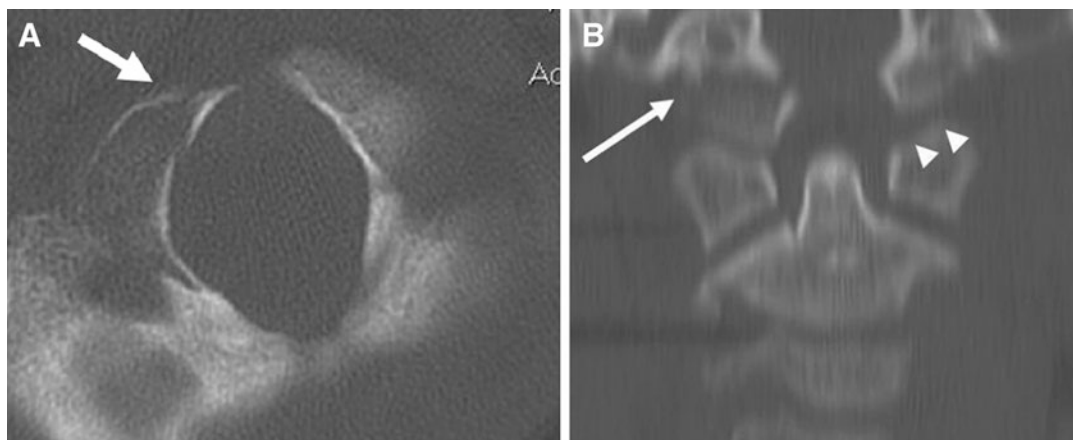


Fig. 11.3 Victim of a motor vehicle crash who met criteria for initial cervical spine imaging with CT scan. A fracture of the right skull base (foramen magnum) (a) and dislocation/dissociation at the atlanto-occipital joint (b) are apparent on CT but were not visible on contemporaneous radiography (Reprinted with kind permission of

Springer Science + Business Media from Blackmore CC. Imaging of the spine for traumatic and nontraumatic etiologies. In: Medina LS, Applegate KE, Blackmore CC, editors. Evidence-based imaging in pediatrics: optimizing imaging in pediatric patient care. New York: Springer Science; 2010)

Recommended Imaging Protocols

Cervical Spine

CT protocol: Multi-detector CT with axial image reconstruction at 2.5 mm or less, in both bone

and soft tissue algorithms, and with sagittal and coronal reformations in bone algorithm at 2 mm collimation.

Radiography protocol: AP, open mouth, lateral, and swimmers. Note that all images must be adequate for evaluation, and the entire region

from skull base to T1 must be visible in both frontal and lateral projections. If adequate films cannot be obtained after repeat imaging, then CT should be performed.

Thoracic and Lumbar Spine

CT protocol: Axial images in bone algorithm through the area of concern, with 2.5 mm collimation. Must include sagittal reformations, and preferable coronal, in bone algorithm, at 2 mm collimation.

Radiography protocol: AP and lateral views covering the entire area of interest.

Future Research

- Studies in both cervical spine and thoracolumbar spine imaging indicate that CT is more sensitive than traditional radiography in detecting fractures. However, further clinical studies addressing the relevance of these fractures are needed.
- The applicability of cervical spine injury clinical prediction rules in pediatric patients is unknown. In addition, the sensitivity, specificity, and cost-effectiveness of the various imaging exams in the pediatric population are not well established.
- Clinical prediction rules for imaging of the thoracolumbar spine have been developed, but further research is necessary to validate such approaches. The effect of implementing these rules on cost, cost-effectiveness, and radiation exposure has not been determined.
- Appropriate imaging to detect unstable ligamentous injury, particularly in clinically unexamined subjects, remains unresolved.

Acknowledgment Dr. Blackmore wishes to acknowledge the chapters below and his coauthors on these chapters, Dr. J. B. Smith (1) and Dr. G. D. Avey (2). These chapters below were drawn upon for this current chapter in the process of presenting thoroughly updated and significantly revised coverage of this subject for emergency imaging. (1) Blackmore CC, Smith JB. Spine Trauma: Evidence-Based Neuroimaging. In Medina LS, et al., eds:

Evidence-Based Neuroimaging Diagnosis and Treatment: Improving the Quality of Neuroimaging in Patient Care. NY: Springer Science; 2013. (2) Blackmore CC, Avey GD. Imaging of the Spine in Victims of Trauma. In Medina LS, et al., eds: Evidence-Based Imaging: Improving the Quality of Imaging in Patient Care. NY: Springer Science; 2011.

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Acute Back Pain in Adults and Children: Evidence-Based Emergency Imaging

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Key Points

- Uncomplicated acute low back pain or radiculopathy is frequently benign and self-limited, and imaging does not improve patient outcomes, exposes the patient to unnecessary harms, and increases costs (strong evidence).
- Reformatted computed tomography (CT) of the cervical spine is the first-line modality for suspected cervical spine injuries in adults, supplanting radiography (moderate evidence).
- There is strong evidence that disk extrusions in symptomatic patients are the etiology for their pain (as this finding is infrequently seen in asymptomatic patients) (strong evidence).
- MRI with contrast is the imaging modality of choice in patients with infection or metastatic disease (strong evidence).

Definitions and Pathophysiology

Acute back pain is a common problem which is frequently seen in emergency rooms. The goal of this chapter is to summarize the available data regarding appropriate imaging for common causes of acute back pain in pediatric and adult patients. Acute back pain in adults and children may be due to a myriad of causes, such as trauma, osteopenic fractures, disk herniation, spondylolysis/spondylolisthesis, cancer, and underlying infectious disease. Acute back pain in children may be due to spondylolysis/spondylolisthesis (most common), infection, and cancer, and a definitive diagnosis is not always found [1].

Epidemiology

Back pain is extremely common, and the majority of adults (reported to be as high as 84%) will experience back pain in their lifetime [2]. In fact, about one fourth of Americans reported back pain in the past 3 months [3]. In children, the prevalence of back pain has been reported to be around 18–36% [4–8].

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Overall Cost to Society

The overall cost to society is billions of dollars annually, as measured to be \$90 billion in 1998 [9]. The overall cost to US patients in 2005 is estimated to be \$6085 per year [10]. The indirect costs of disability or loss of work further increases the cost to the individual.

Goals of Imaging

The goal of this chapter is to help radiologists navigate and advise their emergency room colleagues about the most appropriate imaging modality, if any.

Methodology

A PubMed/MEDLINE search was performed for original articles from 1967 to 2015. A combination of search words was used including imaging/radiology, (acute) back pain, pediatric, spine fracture or injury, cost-effective, spondylolysis, disk herniation, metastatic spine, and spine infection. We excluded case reports, editorials, and articles without an English translation. Some review papers were read to find original references. Those reports were evaluated for our exclusion criteria and were included if deemed relevant to this review. The ACR (American College of Radiology) appropriateness criteria for suspected spine trauma and low back pain were used as part of our analysis [11, 12].

Discussion of Issues

What Is the Role of Imaging in Patients with Acute Back Pain Suspected of Having Fractures?

Summary of Evidence No imaging is necessary in patients who are deemed to be low risk per NEXUS or Canadian C-spine rule criteria (strong evidence). If imaging is required, CT is preferable in patients 14 or older (strong evidence). The ACR

recommends radiographs over CTs in children under the age of 14 (moderate evidence). Spondylolisthesis is best assessed by radiography, although low-dose limited CT is a promising new method.

Supporting Evidence

Radiography

Cervical

Two prospective cohort studies, the National Emergency X-Radiography Utilization Study (NEXUS) and the Canadian C-spine prediction rules, have developed clinical criteria for cervical radiography with reported sensitivity of 99.6–100% (confidence interval (CI) of 99–99.6 and 98–100%, respectively) [13, 14]. The NEXUS study enrolled 34,069, and the Canadian C-spine study also had a large cohort of 8924 patients [13, 14]. The NEXUS study found that patients did not need cervical radiographs if they met all five low-risk criteria: no posterior midline cervical spine tenderness, no intoxication, normal level of alertness, no neurologic deficits, and no painful distracting injuries [13]. The Canadian C-spine rules stated that patients did not need cervical radiography if they did not have a high-risk mechanism, they had low-risk factors that would allow for safe range of motion, and they were able to rotate their neck 45° left and right [14].

A prospective study of 8283 patients later compared NEXUS to the Canadian C-spine rules and found that the sensitivity (99.4% vs 90.7%), specificity (45.1% vs 36.8%), and radiographic rates (55.9% vs 66.6%) were better with the Canadian C-spine rules compared to NEXUS [13, 15]. These rules are helpful to use to determine which patients are “low risk” and do not need imaging.

In patients older than 14 years that do need imaging, CT is preferred over radiographs. Studies have found that 15–61% of cervical spine fractures and 36% spondylolisthesis and dislocations (23% unstable injuries) can be missed with traditional three-view radiographs (AP, lateral, and odontoid images) [16–18]. A meta-analysis of patients with blunt trauma found that

the sensitivity for radiography was 52% compared to 98% sensitivity for CT [19]. Therefore, CT imaging is the first-line modality in patients with clinical features concerning for fracture and the recommended modality by the Eastern Association for the Surgery of Trauma (EAST) practice management guideline committee (moderate evidence) [20].

Flexion and extension views were considered to be part of the “clearing the C-spine” armamentarium but have been falling out of favor, because studies are finding that if they are “positive,” the MRI is negative for ligamentous injury, or they do not change clinical management when the CT scan and neuro exam are negative [21–25]. False-negative flexion/extension radiographs are also problematic especially in patients with true severe instability and subluxation. One retrospective study looked at 49 patients who had both flexion/extension radiographs and MRIs. Eight patients had ligamentous injury on MRI which was not seen on the flexion/extension radiographs (0% sensitivity), and the flexion/extension images were considered incomplete or ambiguous in 20% and 9% of the cases [26] (moderate evidence).

The majority of studies do not recommend performing flexion/extension views in the unconscious, inebriated, or obtunded patients because it is frequently inadequate (up to 96% of the time) and may be dangerous/cause quadriplegia [27–30].

If flexion and extension images are to be performed in patients, the ACR recommends performing the study after a MRI shows normal or equivocal ligamentous pathology with sufficient clinical concern, and waiting until the acute neck pain has resolved so that the study is not limited by insufficient range of motion [11, 31–34].

Thoracolumbar

In patients considered to be low risk for fracture, radiography (AP and lateral) can be the first-line treatment [11]. Otherwise, CT is indicated, as described below.

Computed Tomography

Cervical

In patients with clinical features concerning for cervical spine fracture, CT of the cervical spine is the recommended modality by the Eastern Association for the Surgery of Trauma (EAST) practice management guideline committee [20]. One large prospective trial with 800 patients found that CT has a 98.5% sensitivity for fracture (moderate evidence) [35]. CT is an excellent modality to delineate osseous structures.

Thoracolumbar

If CT of the chest, abdomen, or pelvis is already being performed for clinical reasons, reformatted images should adequately show the thoracolumbar (TL) spine. The data for when to image the TL spine is not as robust as the cervical spine data. Hsu et al. performed a literature review of the available TL spine fracture literature and created guidelines for imaging TL fractures in blunt trauma patients and then retrospectively applied them to 200 patients (100 with fractures and 100 random multi-trauma controls) and found these guidelines to be 100% sensitive and 11.3% specific, with a negative predictive value of 100% [36]. This study suggested that the TL spine should be imaged in patients with back pain/midline tenderness, local signs of thoracolumbar injury, major distracting injury, Glasgow Coma Scale (GCS) <15, abnormal neurological signs, cervical spine fracture, or alcohol/drug intoxication (moderate evidence) [36]. Spinal injury is frequently seen at multiple levels, and 8–27% of patients with cervical fractures also have TL fractures, which is one of the reasons why imaging the TL spine is indicated in patients with C-spine fractures [36–38]. In fact, because it is so common to have noncontiguous spinal fractures, the ACR recommends scanning the TL spine in patients with known cervical fractures [11].

CT is often much faster than MRI and more suitable for patients who are unstable. One study of 1004 patients found that if a CT with coronal

and sagittal reformats was negative for acute fracture in patients with a normal motor exam, an MRI may not be needed for cervical spine clearance (95% CI = 97–100%) [39]. In trauma patients, a CT should be performed to rule out osseous abnormalities prior to MRI as one study found that MRI missed 55% of fractures (moderate evidence) [40]. In any trauma setting it is imperative that sagittal reformatted images are processed and reviewed as one retrospective study found that up to 84% of fractures would be missed if sagittal images are not used [41].

Magnetic Resonance Imaging

MRI is helpful in conjunction with CT if a patient has a suspected spinal cord injury, neurologic deficits, ligamentous injury, concern for soft tissue injury, or radicular pain. MRI is less sensitive for fractures, as one retrospective study found that it was 11.5% sensitive to detect posterior element fractures and 36.7% sensitive to detect anterior cervical fractures (compared to the 75 fractures seen on CT) (limited evidence) [42]. Of note, this study is from 1999, and there has been considerably improved MRI resolution since then. One pediatric study found that MRI was 100% sensitive for fractures, but only six fractures were evaluated (insufficient evidence) [43].

MRI is more sensitive for ligamentous injury. The ACR recommends that MRI for ligamentous injury can be performed at any time, as there is no convincing evidence that it needs to be performed within 48 h [11]. However, if it has been 48 h after the trauma and the patient's neurologic status still cannot be assessed, the ACR recommends proceeding to an MRI, even if the CT was negative [11]. One study looked at 31 patients and compared the MRI ligamentous findings to the surgical findings and found that MRI was 93% sensitive for disk pathology, 93% sensitive for posterior longitudinal ligament injury, and 100% sensitive for interspinous soft tissue injury but less sensitive for anterior longitudinal and ligamentum flavum injury (71% and 67%, respectively) [44].

Applicability to Children

Pediatric patients 14 or older should be treated like adults as their spines are ossified. In children younger than 14, there is insufficient data to support radiographs versus CT. Nonetheless, since CT confers ionizing radiation and the majority of pediatric fractures under 14 are in the occiput to C2 areas, radiography (AP, lateral, and odontoid of the cervical spine or AP and lateral of the thoracic spine) is recommended by the ACR as the first line in pediatric patients [11]. CT is indicated in patients with a high suspicion for fracture or abnormality seen on radiographs [45]. Although the ACR recommends radiography, it seems that pediatric cervical CT requests are on the rise, as a recent study looked at 5148 patients in emergency departments and found that pediatric cervical spine CT usage has increased from 3.5% to 16.1% from 2002 to 2011 [46].

One study retrospectively applied the NEXUS criteria to pediatric patients and found it to have 100% sensitivity (CI = 87.8–100%) [47]. However, this study does have limitations with the low end of the confidence interval, low number of patients with cervical spine injury (only 30), and no children under 2 years of age included (insufficient evidence) [47].

Jaffe et al. performed a retrospective radiographic review of 206 pediatric patients with cervical spine radiographs to see if the following parameters could predict cervical fracture: neck pain, neck tenderness, limited neck mobility, history of neck trauma, abnormal reflexes, strength, sensation, and mental status [48]. Using these criteria, 58 out of the 59 cervical spine fracture patients were correctly identified [48]. The one case that was missed was a 2-year-old who fell off monkey bars and had a dens fracture requiring halo traction [48]. Some studies consider children younger than two with cervical spine trauma automatically “high risk” because they cannot communicate effectively; therefore, imaging is indicated [49].

In pediatric patients with cervical neck pain, radiographs are considered the first-line modality, because cervical spine injuries are uncommon in

this population, and radiographs confer less radiation compared to cervical spine CT [11]. The thyroid is the most radiosensitive structure that is affected by cervical imaging, and one study found the dose to the thyroid with CT was increased 14-fold compared to radiography (26 mGy vs 1.8 mGy), so it is prudent to employ dose reduction strategies and reduce radiation exposure as much as possible in children [50].

Special Cases

Spondylolysis or spondylolisthesis is the most common cause of pediatric back pain [51]. If clinically suspected, a two-view (AP and lateral), four-view (two additional oblique views), or five-view (additional spot lumbar) lumbar radiograph series is requested.

There is some debate about whether those additional oblique and spot lateral views are needed as they more than double the gonadal dose [52]. The effective dose for a two-view study is 0.72 mSv and 1.26 mSv for a four-view study [53]. As the management of most spondylolysis is conservative, the dose imparted from the oblique views or spot lateral images is not insignificant and should be used judiciously [52, 54].

One study looked at 86 patients and found that if the oblique view was eliminated, four unilateral pars fractures would be missed [52]. Another retrospective review of 782 patients found that the spot lateral and the oblique radiographs were only uniquely diagnostic in 2.4% of the cases (13/15 unilateral spondylolysis, 5/45 bilateral spondylolysis, and 1 congenital fusion of L2 facet to L3) [54]. Similarly, Miller et al. found that after retrospective review of 2846 patients, there is no significant difference in sensitivity comparing the two-view study to the four-view study (moderate evidence) [55]. Although these investigators advocate using two views to lower the radiation dose, Libson et al. retrospectively reviewed 1743 cases and found that without the oblique views, 20% of cases would be missed; however, it is unclear if those cases changed clinical management [56]. One solution to this dilemma would be to start with two views (AP and lateral), and if the patient has ongoing pain, add oblique images.

Most commonly, lumbar radiographs are requested when spondylolysis is suspected. However, new data suggests that low-dose limited field of view CT improves interobserver agreement, with kappa improved from 0.24–0.4 with X-ray to 0.8 with CT [57]. There was no significance difference between the dose of the low-dose CT compared to radiographs (0.12 mSv–1.04 mSv for CT versus 0.1–0.3 mSv (for a single radiographic view) [57]. CT is more sensitive than X-rays to diagnose pars defects and more sensitive/specific than bone scanning (CT sensitivity, 90%; bone scanning sensitivity, 84%) [55, 58]. However, one of the caveats of this method is because the CT is limited and focused on the area of concern (most likely L4–S1 area), and it could miss pathology that is outside of the field of view.

Bone scanning and single-photon emission computed tomography (SPECT) can show early stress reaction before spondylolysis, but can be negative in old fractures (up to 83% of the time), and cannot distinguish fractures from stress reaction [59]. Two studies have found that SPECT imaging is more sensitive than bone scans alone in that with the 101 positive SPECT cases, 64 cases would have been missed with bone scan alone (limited evidence) [60, 61]. However, SPECT cannot often provide a specific diagnosis and will need further clarification with another modality (which is why SPECT is occasionally paired with CT).

More recent data has looked into MRI to evaluate for spondylolisthesis as early reaction can be seen and no radiation is needed (although anesthesia may be needed in pediatric patients). One retrospective study of 103 patients with both radiographs and MRI found that MRI was 78% sensitive for spondylolisthesis, compared to the 98% seen on lateral radiographs, suggesting that the upright standing radiographs might change management as the spondylolisthesis was less well seen on the supine MRIs (limited evidence) [62]. A retrospective review found that MRI for spondylolisthesis has a reported sensitivity of 86%, specificity of 82%, PPV of 18%, and NPV of 99% (limited evidence) [59]. Another retrospective study also found that MRI missed 7/11

(64%) of fractures that were seen on CT or plain film [63]. One report found that ancillary MRI findings, such as increased sagittal diameter and wedging of the posterior aspect of the vertebral body, would improve the detection of spondylolisthesis from 30% to 97% (66 patients); it is unclear if the aforementioned studies used these secondary findings [64].

Cost-Effectiveness Analysis

If a trauma patient is already going to undergo a head CT, then adding a cervical CT has been deemed comparatively effective if that patient has 5% or more likelihood of fracture [65]. One study looked at patients who had radiographs that did not show the C7–T1 level and subsequent CTs which did show that level and found that 11/360 fractures were missed on radiography. The cost-effectiveness of requesting CT to look at the C7–T1 level was \$9192 for each fracture seen, \$16,852 for each potentially unstable fracture, and \$50,557 for each definitely unstable fracture, so CT (in this particular situation) was cost-effective [66].

One study retrospectively reviewed 837 radiographs and found that one third of the images were inadequate and only four flexion/extension images were positive (one falsely positive, two borderline, and none requiring surgery) and concluded that flexion/extension radiographs are not cost-effective because about one third of the images were considered inadequate (moderate evidence) [67].

What Is the Role of Imaging in Patients Suspected of Having a Disk Herniation?

Summary of Evidence Recent studies have found that uncomplicated low back pain/radiculopathy usually resolves within 30 days and imaging is not necessary (strong evidence). The difficulty therein is to determine which patients have uncomplicated back pain and who needs imaging.

Supporting Evidence Multiple studies have found the majority of uncomplicated low back

pain/radiculopathy is self-limited and benign and usually resolves within 3–4 weeks [68–72]. In adult patients without specific indication for imaging, routine imaging may not improve outcomes and may result in more unnecessary tests/procedures [73–75]. In adult patients with progressive neurologic deficits or “red flags” of low back pain, imaging is indicated.

The ACR appropriateness criteria define “red flag” symptoms as the following: trauma, (including cumulative trauma), unexplained weight loss, age >50 years (especially women and males with osteoporosis or compression fracture), unexplained fever, difficulty urinating or urinary retention, immunosuppression, age >70 years, diabetes mellitus, prior surgery, history of cancer, intravenous drug use, prolonged use of corticosteroids, osteoporosis, focal neurologic deficit(s) with progressive or disabling symptoms, cauda equina syndrome, or back pain duration longer than 6 weeks [12].

In children, other red flags have been cited such as back pain in prepubertal children, pain lasting more than 1 month, disability, history of malignancy or TB exposure, recurrent or worsening pain, early morning stiffness, night pain, scoliosis, fever, radicular pain, weight loss, limp, or altered gait [76].

Why are these “red flag” symptoms important? A meta-analysis including 1804 patients with acute/subacute low back pain and no red flag symptoms found no improvement of pain, quality of life, or function with imaging compared to those who received conservative management [74]. Furthermore, these patients tend to have considerable improvement in their pain and function after 4 weeks regardless of treatment [77]. Studies have found that no cancer diagnoses would be missed if these criteria were used to evaluate 1170 patients (prospective) and 963 patients (retrospective) (moderate evidence) [78, 79].

Radiographs

Radiographs of the spine are the most helpful to look for alignment, sclerosis, osteophytes, disk space narrowing, compression fractures, and neural foraminal narrowing. Interestingly, the

degree of degenerative changes does not appear to strongly correlate with the degree of symptoms in chronic back pain sufferers (moderate evidence) [80]. Herniated disks cannot be assessed by radiography and MRI is necessary.

Computed Tomography

Intervertebral disks can be seen with CT with reported sensitivity and specificity similar to MRI (59% sensitivity for CT vs 64% sensitivity for MRI and 86% specificity for both modalities) and receiver operating characteristic area under the curve of 0.83–0.86 (CT) and 0.81–0.84 (MRI) (moderate evidence) [81, 82]. The extraforaminal and foraminal nerve roots can be seen on CT, but they are better seen on MRI [83]. CT is not appropriate if intradural or spinal cord pathology is suspected, and MRI is the preferred modality [12]. According to the ACR appropriateness criteria for low back pain, MRI +/- contrast depending on the clinical situation is the most appropriate strategy in patients who are candidates for imaging [12].

CT myelography has fallen out of favor because MRI often provides more information and does not require a lumbar puncture procedure. In patients who cannot have a MRI or have extensive spinal hardware, CT myelography can be helpful to visualize disk herniations and neural foraminal narrowing.

Magnetic Resonance Imaging

In the acute setting, MRI is the imaging modality of choice in patients with complicated back pain, radiculopathy, severe neurologic compromise, or symptoms suggestive of cauda equina syndrome (bilateral leg weakness, urinary retention, fecal incontinence, and saddle anesthesia). In patients who have had prior back surgery or findings concerning for neoplasm or infection, MRI should be performed with contrast [12].

Unfortunately, there is a high prevalence of abnormal disks in asymptomatic people seen on MRI (20–80%), making it difficult to ascertain whether the finding is related to the patient's current pain [84–86]. One prospective study found that disk extrusions were significantly associated with a history of low back pain ($p < 0.01$) and no association was seen with disk protrusions or bulge [87]. Disk extrusions (Fig. 12.1a–d) are uncommonly seen in asymptomatic patients (1%) in contrast to protrusions (27%) and bulges (52%) [88].

What Is the Role of Imaging in Patients Suspected to Have Infection?

Summary of Evidence MRI with and without contrast is the modality of choice in patient's suspected of having an infection (moderate evidence).

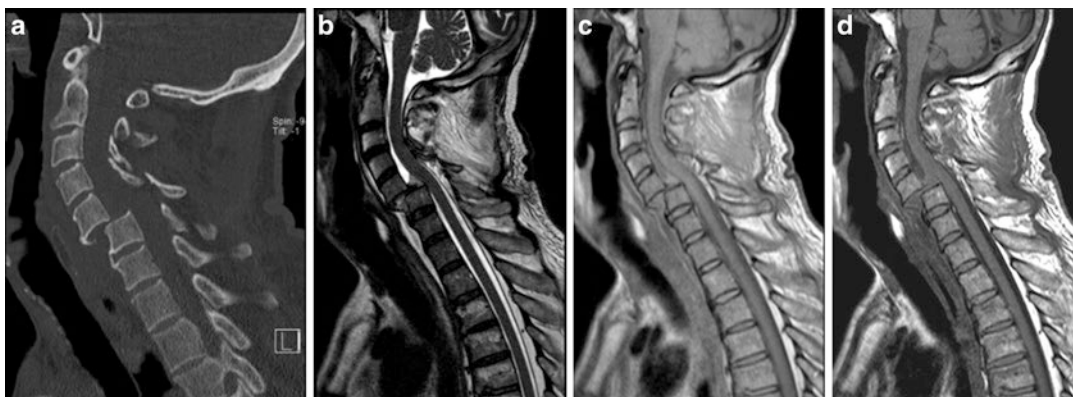


Fig. 12.1 A 65-year-old male who fell 10 feet from a roof, who presented to the emergency room with neck pain and paresthesia in his hands. Sagittal CT (a) demonstrates dislocation C5–C6 with left-sided facet joint dislocation and subluxation of the right facet joint. Sagittal

T2-weighted (b), proton density (PD) (c), and T1-weighted (d) images demonstrate the dislocation between C5 and C6 vertebral bodies, with soft tissue and disk material in the anterior spinal canal, soft tissue injury posteriorly, and paravertebral soft tissue

Supporting Evidence

Radiography

Osseous infections can be occult on radiographs, especially early in the course of disease. The most common early finding is end plate erosion. Manifestations of spine infection can be slow to develop on radiography, and it can take up to 6 weeks to show end plate irregularity. Radiographs have been found to be 82% (sensitive) and 57% (specific) for infection when it is seen (strong evidence) [71]. Typically, radiographs will show end plate irregularity, followed by erosion, decreased disk space, and eventually collapse.

Computed Tomography

There is insufficient data to comment on the accuracy of CT for spinal infection.

Magnetic Resonance Imaging

MRI imaging with contrast is the imaging of choice in patients suspected of having spinal infection as it is the most sensitive and specific modality [12]. Even so, early changes can be difficult to interpret on MRI. One of the earliest findings is bone marrow edema, end plate erosion (best seen on T1W images), increased T2W signal in the disk space, and loss of the internuclear cleft on T2W images [89].

One study retrospectively looked at 44 patients with proven spondylodiscitis and found that paraspinal/epidural inflammation was the most sensitive finding (97.7%), followed by disk enhancement (95.4%) and disk hyperintensity (93.2%) [90]. Erosion of the end plate and effacement of the nuclear cleft had sensitivities of 84.1% and 83.3%, respectively [90].

Sometimes it is hard to distinguish type 1 Modic changes (increased T2 signal in the end plate) from infection on MRI. Patel et al. retrospectively reviewed 73 patients and found that they could distinguish Modic changes from infection using a diffusion-weighted sequence. A well-defined “claw” sign was seen in patients with Modic changes (and 97–100% were

infection-free), and an ill-defined restricted diffusion pattern was seen in the patients with infection (moderate evidence) [91]. Although this is a helpful finding, not all centers use spine diffusion-weighted imaging. Secondary features of spondylodiscitis as described above can also be helpful to differentiate between the two in addition to clinical findings such as fever, white blood cell count, and c-reactive protein elevation (although these clinical findings are not always positive in patients with proven spondylodiscitis) [92].

Bone Scanning, Gallium, and 18F PET/CT

Bone scans and gallium have been found to be 82–92% sensitive for spondylodiscitis, and 94% sensitive when used in combination, but are limited by lack of anatomic detail [93, 94]. These scans can be helpful when trying to assess therapy response, because the gallium scan will become negative during the healing phase of infection and the technetium scan will remain positive [93].

In patients who cannot have an MRI due to implanted devices, spinal hardware, renal failure, or other factors, 18F PET/CT is another option to diagnose spondylodiscitis. One retrospective review looked at 20 pediatric/young patients and found that 18F PET/CT was able to accurately diagnose 6 patients with surgically confirmed infection, and the other patients had noninfectious hardware complications or infections in other locations (limited evidence) [95].

One prospective study of 26 patients compared MRI to 18F PET/CT and found that spondylodiscitis can be accurately detected in both MRI (81% accuracy) and 18F PET CT (84% accuracy) (limited evidence) [96]. As bone scanning, labeled leukocyte, and gallium scanning do not have high sensitivity, specificity, or special resolution, 18F PET/CT is a technique which is showing promise to help diagnose spinal infection in patients who have suboptimal MRIs. Furthermore, similar to gallium scanning, 18F PET/CT can be helpful to assess patient treatment response [97].

What Is the Role of Imaging in Patients Suspected of Having Metastatic Disease?

Summary of Evidence MRI and radionuclide studies are the studies of choice for identifying osseous metastasis as both CT and radiographs are less sensitive (strong evidence).

Radiography

Radiography is not a particularly sensitive modality to detect osseous metastases, as 50–75% of the bone trabecula must be lost before a lytic lesion is seen (limited evidence) [98].

Computed Tomography

There is limited evidence regarding the accuracy of CT for osseous metastasis; nonetheless, studies have found that both MRI and PET/CT are more sensitive methods for evaluating metastatic burden compared to CT alone [99]. One retrospective study looked at 201 osseous spinal metastases and found that CT identified 133/201 and MRI found 198/201 rendering a sensitivity of 66.2% for CT and 98.5% for MRI ($p < 0.0001$) and MRI was also found to be more accurate, 98.7% compared to 88.8% with CT [100].

Magnetic Resonance Imaging

MRI is more sensitive and specific than CT for bone metastasis detection, especially when diffusion-weighted sequences are used. One study retrospectively looked at 17 patients who had whole body diffusion-weighted MRIs, bone scans, and a CT bone survey, and they found that MR identified 22% more metastatic lesions compared to bone scans and 119% more than seen on CT (limited evidence) [101, 102]. One study with 52 metastatic lesions found that when they added diffusion to the whole body MRI, sensitivity and positive predictive value (sensitivity, 96%; PPV, 98%) increased compared to whole body MRI without diffusion (sensitivity, 88%; PPV, 95%) and bone scan (sensitivity, 96%; PPV, 94%) (moderate evidence) [103]. Of note, diffusion imaging is not as sensitive as a bone scan for identifying rib, chest, scapula, and skull lesions but does appear to be particularly helpful to identify axial skeleton metastases [101]. One study

compared diffusion-weighted whole body imaging with bone scanning and found no significant differences in terms of staging; however, in patients with more than ten osseous lesions, diffusion-weighted MRI found more of them (sensitivity 97% compared to bone scan sensitivity of 48%) (limited evidence) [104].

It is unclear if whole body MRI is superior to bone scans. One meta-analysis of 332 patients was unable to show if one modality was clearly better than the other, as both had good diagnostic performance [105]. But, this study excluded studies that used the diffusion-weighted sequence with MRI, which can improve bone marrow metastasis detection [103]. One retrospective study found that when diffusion-weighted sequences were added to MRI in 67 patients, the sensitivity improved from 73% to 95.5% with the addition of this sequence [106].

Bone Scanning and Photon Emission Tomography

PET/CT is more sensitive and accurate at diagnosing osteolytic metastasis compared to bone scanning (92% vs 73%) [107–109]. In patients with osteoblastic metastases, bone scanning is preferred over PET/CT [108].

PET/MR is an emerging modality which has shown some oncologic promise. One study looked at 109 patients with 25 metastases who had same day PET/CTs and PET/MRs and found that the PET/MRI found 12% (or 3) more osseous metastases than PET/CT (limited evidence) [110].

Take Home Table

Table 12.1 reviews the sensitivity and specificity of imaging modalities for acute pain conditions.

Imaging Case Studies

Case 1

In Fig. 12.1a–d, a 65-year-old male who fell 10 feet from a roof presents to the ER with neck pain and paresthesia in his hands.

Table 12.1 Sensitivity and specificity of imaging modalities for acute back pain conditions

	Modality	Study	Sensitivity	Specificity	Limitations/ROC
Fractures	Radiograph	[19, 111]	52–73%	100%	AUC 0.86
	CT	[19, 111]	98–100%	97%	AUC 0.98
	MRI	[42, 43]	11.5*–100%^	97%*^	*Posterior element fracture paper from 1999 ^Pediatric cervical spine
Spondylolisthesis	Radiograph	[53, 55, 62]	53–98%	94–96%	
	CT	[55]	90%		
	MRI	[59, 62]	78–86%	82%	
	Bone scan/ SPECT	[55, 59]	17% (chronic)–84%		
Disk Herniation	CT	[81]	59%	86%	AUC 0.83–0.86
	MRI	[81]	64%	86%	AUC 0.81–0.84
Infection	Radiograph	[112]	82%	57%	
	MRI	[112, 113]	82–100%	16.7–92%	AUC 0.61–0.94
	Bone scanning	[112]	90% (combined with gallium and without)	100% (combined with gallium); 78% alone	
	Gallium	[112]	90% (combined with gallium)	100% (combined with bone scan)	
	FDG-PET	[112, 113]	90–93%	50–82%	AUR 0.75–0.86
Metastatic disease	Radiograph	[114]	73%		
	MRI	[101]	100%	100%	Numbers for MRI with whole body diffusion
	Bone scanning	[107, 114, 115]	67–76%	85–97%	
	FDG-PET	[15, 107]	60–95%	98–100%	

AUC area under the curve, *CT* computed tomography, *FDG-PET* fluorodeoxyglucose positron emission tomography, *MRI* magnetic resonance imaging, *SPECT* single-photon emission computed tomography

Case 2

In Fig. 12.2a–c, we encounter a 47-year-old male with a 2-day history of increased pain and weakness in his right leg and decreased sensibility of the lateral parts of the calf and over his right foot.

Case 3

In Fig. 12.3a–e, a 45-year-old male 3 months post surgery for disk herniation presents with acute low back pain.

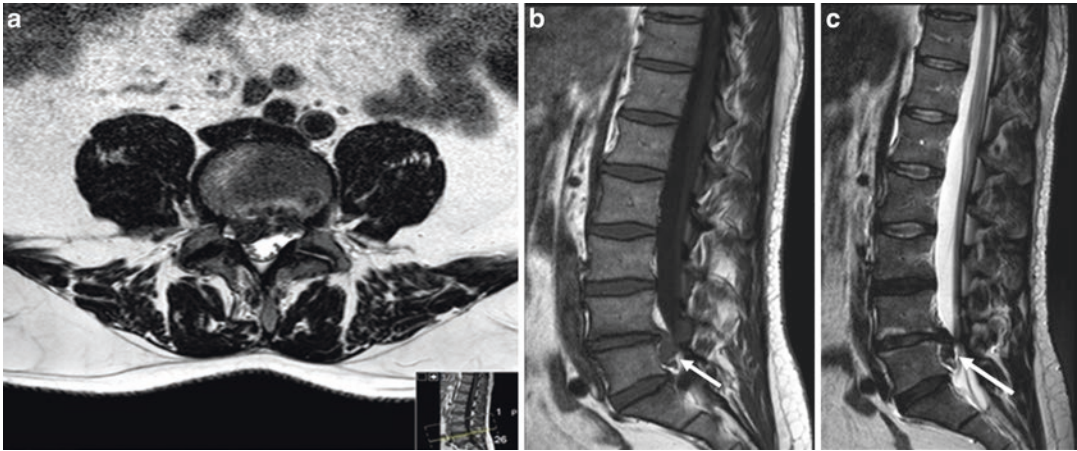


Fig. 12.2 A 47-year-old male with a 2-day history of increased pain and weakness in the right leg and decreased sensibility of the lateral parts of the calf and over the right

foot. Axial T2 (a), sagittal T1 (b), and sagittal T2 images (c) show a disk protrusion (white arrows) at the L4–L5 intervertebral disk level

Case 4

In Fig. 12.4a–c, we encounter a 60-year-old female with a history of breast cancer who presents with acute back pain.

Suggested Imaging Protocols

- Cervical spine fracture: CT is the first-line modality (above foramen magnum to T2, 0.6 mm collimation; axial, 2 mm collimation; and sagittal/coronal reformations, 1.5 mm slice thickness). There is not enough data in the pediatric literature to suggest a first-line modality, but typically radiographs are done first [116, 117].
- Thoracolumbar spine fracture: CT is the preferred method for trauma patients per ACR appropriateness criteria (0.6 mm collimation; axial, 3 mm sections; and sagittal/coronal reformations, 2 mm slice thickness) [117].
- University of Michigan lumbar spine protocol:

- Sagittal T1W FLAIR: TR 1850–3000/TE 24, 288 × 224 matrix, 30 cm FOV, 4-mm slice thickness, 1-mm skip
- Sagittal T2W fat-saturated: TR 3000–5000/TE 110, 384 × 256 matrix, 30 cm FOV, 4-mm slice thickness, 1-mm skip
- Axial T1W: TR 1850–3000/TE 24, 256 × 224 matrix, 20 cm FOV, 5-mm slice thickness, 2.5-mm skip
- Axial T2W: 3000–5000 TR/102 TE, 256 × 224 matrix, 20 cm FOV, 4-mm slice thickness, 2-mm skip

Future Research

- Should children under the age of 14 have cervical spine radiographs or CTs?
- What is the best imaging modality for spondylolisthesis?
- Should diffusion be a standard sequence on spinal MRIs for infection and metastasis?
- Does PET/CT outperform MRI for spinal metastasis?

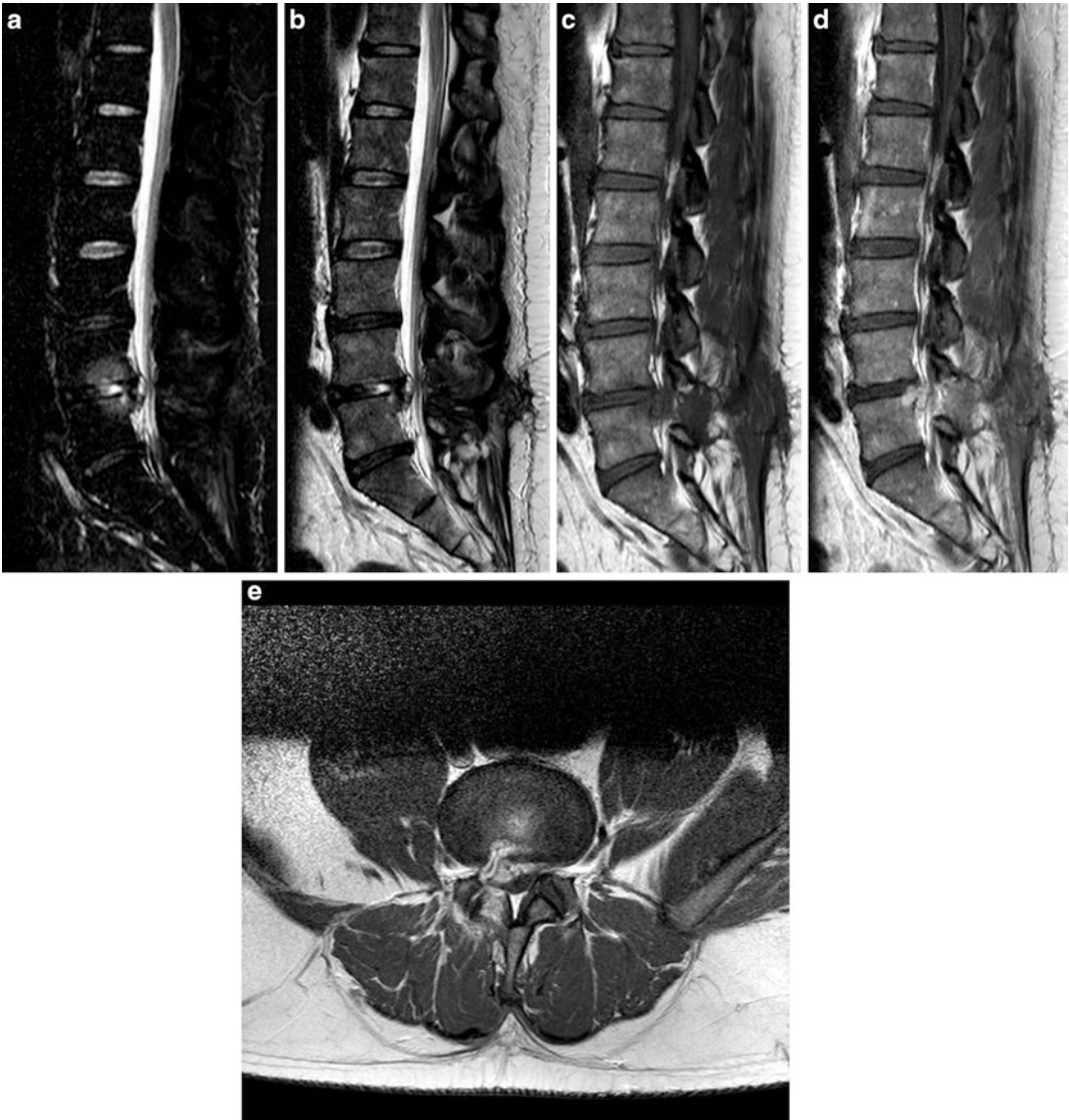


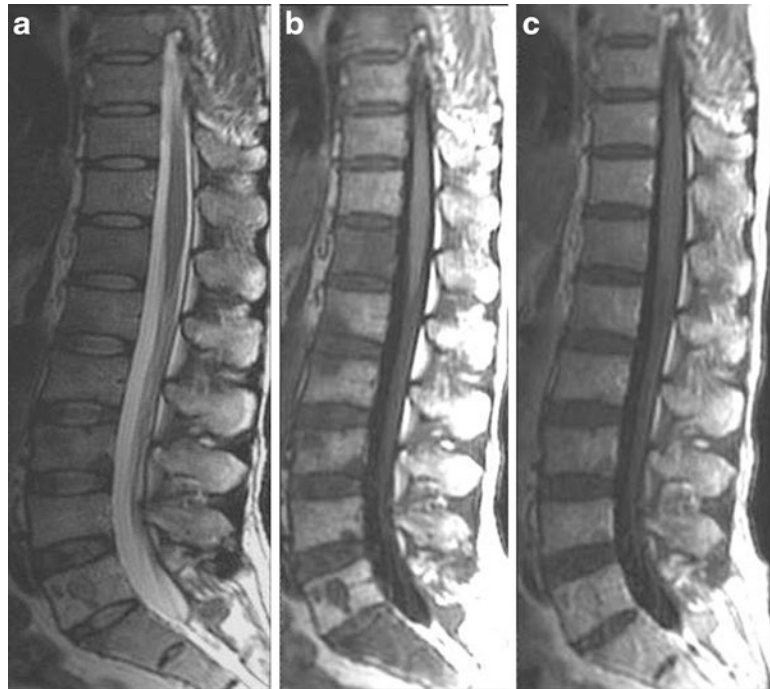
Fig. 12.3 A 45-year-old male 3 months post surgery for disk herniation, who presents with acute low back pain. Sagittal short tau inversion recovery (STIR) (a) and T2-weighted (b) images demonstrate increased soft tissue with hyperintense signal in the anterior aspect of the spinal canal at the level of L4–L5 intervertebral disk space

and in adjacent vertebral bodies. Sagittal T1-weighted image before (c) and sagittal and axial T1-weighted images following intravenous gadolinium injection (d and e) demonstrate pathological contrast enhancement of the soft tissue in the anterior aspect of the spinal canal extending laterally to the right

Summary

- No imaging: low-risk adult patients with cervical spine injury (according to the NEXUS or Canadian cervical rules) or patients who do not have any “red flag” symptoms.
- Radiographs preferred: for spondylolisthesis as a first-line option.
- CT preferred: cervical spine CT is recommended for patients who are considered high risk for cervical spine fracture.

Fig. 12.4 A 60-year-old female with a history of breast cancer who presents with acute back pain. Sagittal T2-weighted pre-intravenous (a), T1-weighted pre-intravenous (b), and T1-weighted images post-intravenous (c) gadolinium administration demonstrate multiple metastases in the vertebral bodies. Note the metastases are less conspicuous on the post-contrast-enhanced T1-weighted sequence



- MRI preferred: over flexion/extension radiographs for ligamentous injury, herniated disks, spine infection (with contrast), and metastatic disease (with contrast).
- NM preferred: metastatic disease, patients with suspected infection who cannot have an MRI.

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Acute Sinusitis in Adults and Children: Evidence-Based Emergency Imaging

13

Laura B. Eisenmenger and Yoshimi Anzai

Key Points

- The clinical signs and symptoms of acute bacterial sinusitis (ABS) overlap with that of nonspecific upper respiratory tract viral infection (strong evidence).
- Sinus radiographs are moderately sensitive to diagnose ABS compared with sinus puncture and culture (moderate evidence).
- Although CT is frequently performed to assist diagnosis of sinusitis, inadequate data exists on the sensitivity and specificity of sinus CT for diagnosis of ABS (limited evidence).
- Imaging criteria include the presence of frothy air-fluid levels or complete sinus opacification but do not include mucosal thickening (limited evidence).
- Despite relatively high sensitivity of CT or sinus radiography, imaging is not indicated in the initial diagnostic workup for acute uncomplicated sinusitis due to cost and radiation dose (strong evidence).
- Imaging is indicated for patients who fail to respond to medical management, have severe symptoms suspicious for complications related to acute sinusitis, or patients planning to undergo surgery (moderate evidence).
- The diagnosis of chronic sinusitis is based on clinical grounds. No gold standard exists to confirm clinical diagnosis. CT findings for chronic sinusitis often do not correlate with patients' clinical symptoms (limited evidence).
- Children under 6 years of age should not undergo sinus radiographs due to their limited sinus development (moderate evidence).
- Imaging (contrast-enhanced CT or MR) is indicated in immunocompromised patients or patients with neurologic symptoms with acute progression of sinus infection in order to assess potential complications from acute sinusitis (limited evidence, strong consensus).

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Definition and Pathophysiology

The term “sinusitis” refers to mucosal inflammation of the paranasal sinuses. The paranasal sinuses are assumed to be sterile under normal circumstances; however, the paranasal sinuses are continuous to the nasal mucosa or nasopharynx that is heavily colonized with bacteria. These bacteria are removed from the paranasal sinuses by the mucociliary function. Normal mucous secretions contain antibodies and, together with mucociliary clearance, work to clear bacteria from the paranasal sinuses. Thus, key host defenses against infection include maintaining normal mucociliary flow and an intact local mucosal surface [1, 2].

Sinusitis is classified as acute, subacute, or chronic based on the duration of the illness. Acute sinusitis refers to sinusitis lasting fewer than 4 weeks, subacute sinusitis refers to sinusitis lasting 4–12 weeks, and chronic sinusitis refers to sinusitis lasting more than 12 weeks. Although initial imaging in the setting of acute uncomplicated sinusitis is not recommended, imaging can play a key role in diagnosis and management of medically refractory disease.

The common predisposing events that set the stage for ABS are an acute viral upper respiratory infection resulting in viral rhinosinusitis (predisposing to approximately 80% of bacterial sinus infections) and allergic inflammation (predisposing to 20% of bacterial infection). Once the mucosa of the paranasal sinuses swells due to either viral infection or allergy, it causes sinus ostia obstruction causing impaired mucociliary clearance. Obstruction and abnormal clearance lead to low pressure within the paranasal sinuses, which exaggerates mucosal thickening and edema, further worsening sinus mucociliary clearance. This can then develop into acute bacterial sinus infection. The presence of “normal” sinus flora is uncertain, as sampling of sinuses in healthy volunteers have revealed both multiple organisms, and also no organism [3]. *Streptococcus pneumoniae* and *Haemophilus influenzae* are two common organisms causing ABS; however, *H. influenzae* has become a more prevalent organism since the widespread use of

the heptavalent pneumococcal conjugate vaccine (PCV7) in 2004 [4, 5]. Other organisms include *Moraxella catarrhalis*, other *Streptococcus* species, and *Staphylococcus*. In the first 7–10 days, sinusitis is typically viral, with progression to predominantly aerobic species, and then a change to anaerobic species in chronic sinusitis.

Epidemiology

Acute sinusitis is one of the most common diagnoses in primary care setting in the USA affecting 28.5 million individuals diagnosed each year [6]. Twelve percent of Americans claim to have had a previous diagnosis of sinusitis down from the previously reported 14% a decade earlier [6]. Between 1998 and 2007, the average visit rate for children with acute sinusitis remained steady at approximately 11–14 visits per 1000 children despite the introduction of the PCV7 vaccine in 2000 [7]. Women were more likely than men to have sinusitis with reported incidence of 9.1% in men and 15% in women. Asian and Hispanic adults reported lower rates of sinusitis than Caucasian and African-American adults. Sinusitis is more common in the south and least common in the west coast [6]. Acute sinusitis more often affects patients with a history of allergy or asthma. Other patients with high risk of developing acute sinusitis include individuals with defects in immunity (HIV, agammaglobulinemia), delayed or absent mucociliary activity (Kartagener’s syndrome, cystic fibrosis), structural defects (cleft palate), and white blood cell functional abnormalities chronic granulomatous disease, granulomatosis with polyangiitis (Wegener’s granulomatosis) [8]. Dental infections may cause 5–10% of all cases of maxillary sinusitis, as the roots of the upper back teeth (second bicuspid, first and second molars) abutting upon the floor of the maxillary sinus.

Sinusitis affects all age groups. The prevalence of sinusitis among children is even higher than adults and may be as high as 32% in young children [9–11]. The average child has between six and eight “cold” episodes annually, and it is estimated that 5–10% of all upper respiratory

infections are complicated by sinusitis. Children under 6 years of age are the most likely to have ABS [12].

Acute maxillary sinusitis in adults is characterized with purulent nasal discharge, facial tenderness, headache or toothache, and fever. Children, however, may have less specific symptoms, such as a prolonged daytime cough lasting more than 10 days. The development of paranasal sinuses in children also contributes to diagnostic challenges. The maxillary and the ethmoid sinuses are present at birth. The sphenoid sinuses generally start to pneumatize by age 5 years; the frontal sinuses start to develop around aged 7–8 years [12, 13]. Both frontal and sphenoid sinuses continue to develop until late adolescence. Sinus tenderness is not a typical sign observed in children with acute sinusitis.

Diagnosis of chronic sinusitis is even more challenging. No gold standard, i.e., pathological diagnosis, exists for chronic sinusitis. Diagnostic workups and treatment are often driven by patients' symptoms.

Overall Cost to Society

Sinusitis has a significant economic impact on healthcare organizations. In 1992, Americans spent \$200 million on prescription medications and more than \$2 billion for over-the-counter medications to treat sinusitis [14]. There were 11.7 million doctor visits and 1.3 million outpatient visits due to sinusitis in 2009 [15]. Approximately 500,000 sinus surgeries are performed each year. Direct costs of chronic sinusitis were an estimated \$8.6 billion in 2007, likely decreasing from previous years after adjusting for inflation [16]. Approximately 31% of the direct costs were attributed to treatment expenditures for children 12 years or younger [17]. In 2014, Smith reported the systematic review of the annual direct cost of management of adult chronic sinusitis to the US healthcare system, and they concluded the direct cost was estimated to be \$6.9 to \$9.9 billion and indirect cost from lost work or productivity reached to \$13 billion [18]. They concluded that sinusitis

needed to be recognized as a serious, debilitating, costly disease that warrants precise diagnosis and effective specific therapy [19]. A study using data from the Agency for Healthcare Research and Quality (AHRQ) 2011 Medical Expenditure Panel Survey estimated that chronic rhinosinusitis represents an annual economic burden of 60–64.5 billion dollars, mainly from ambulatory expenses followed by prescription and inpatient expenses [20]. Clearly, sinusitis imposes a considerable economic burden for the patients and families. Therefore, improved diagnosis and the use of the most effective treatment with the highest tolerability profile will improve outcomes and lower the overall cost of therapy.

One of the cost components related to treatment of sinusitis is the use of antibiotics. It is important to keep in mind that the majority of “sinusitis” is caused by upper respiratory tract viral infection. The symptoms of acute viral sinusitis and allergic rhinitis overlap with those of ABS, leading to overdiagnosis (in as many as 50–60% of cases), and therefore antibiotics are overprescribed in the primary care setting. Clinical studies showed that as many as 60% of patients with colds are prescribed antibiotics [21]. Antibiotics were more likely to be prescribed in younger patients and by primary care providers [18]. Despite the lack of clear evidence supporting antibiotic use in sinusitis, approximately 85.5% of acute sinusitis and 69.3% of chronic sinusitis office visits resulted in an antibiotic prescription [22]. The overprescription of antibiotics potentially contributes to a widespread of antibiotic-resistant infection. Antibiotic-resistant infections are an increasing problem in hospitals in terms of the number of resistant organisms and their prevalence. Consequently, the cost of care is increased, in addition to increasing length of stay, admissions to intensive care unit, and more intensive resource use.

Goals of Imaging

Sinusitis is diagnosed and managed based on clinical grounds, and imaging is not indicated for initial diagnosis of uncomplicated sinusitis.

In patients presenting with symptoms of acute sinusitis, the goal is to differentiate those with ABS who benefit from antibiotics from those with nonspecific virus infection. Imaging is not indicated for the initial diagnostic workup for acute sinusitis due to nonspecific imaging findings, cost, and radiation. Diagnosis and treatment decision, particularly prescribing antibiotics or not, should be made based on clinical examination for uncomplicated sinusitis.

Imaging is indicated for patients who fail to respond to medical management. CT remains the primary imaging study of choice. CT is considered when patients do not respond to medical management as patients may have a structural abnormality or obstructive lesion. Imaging is also indicated in patients who are suspected of having sinusitis related to orbital and intracranial complications, to immunocompromised state, or for pre-operative surgical planning. The goal of imaging in this setting is to exclude (or include) diagnosis of ABS. Imaging is also used to assess for potential causes of poor mechanical drainage of the paranasal sinuses due to a potential obstructive lesion and complications of ABS such as orbital cellulitis or abscess formation (i.e., orbital subperiosteal abscess and anterior cranial fossa abscess).

The goal of sinus CT for chronic sinusitis is to provide objective information to support the clinical diagnosis, to provide detailed anatomy for surgical planning, and to predict which patients would most benefit from endoscopic sinus surgery.

Methodology

The authors performed a MEDLINE search using PubMed (National Library of Medicine, Bethesda, MD) for data relevant to the diagnostic performance and accuracy of both clinical and radiographic examinations of patients with acute sinusitis. The diagnostic performance of clinical examination (history and physical exam) and clinical outcome was based on a systematic literature review performed in MEDLINE from January 1966 to May 2015. The clinical exami-

nation search strategy used the following statements: (1) acute rhinosinusitis, (2) ABS, (3) diagnosis, (4) clinical examination, and (5) outcomes. The review of the current diagnostic imaging literature was done with MEDLINE covering from January 1966 to December 2015, with the following key statements and words: (1) rhinosinusitis, (2) sinusitis, (3) radiograph, and (4) CT, as well as combinations of these search strings. We excluded animal studies and non-English articles.

Discussion of Issues

Is There a Role for Imaging in the Initial Diagnosis of Acute Bacterial Sinusitis?

Summary of Evidence Diagnosis of acute sinusitis should be made on clinical criteria (strong evidence). Imaging as an initial diagnostic workup not only substantially increases the cost but also is potentially harmful from radiation exposure.

Although sinus radiographs cost little and are readily available, the ability to evaluate intracranial or intraorbital complications is limited. CT is the preferred imaging modality for diagnostic workups for patients with suspected intracranial or intraorbital complications or recurrent or chronic sinusitis. The American College of Radiology Appropriateness Criteria (ACRAC©) guidelines state that the diagnosis of uncomplicated acute sinusitis should be made on clinical grounds alone and reserve the use of imaging for situations of medically refractory cases or worsening during the course of antibiotic treatment [23, 24] (<http://acsearch.acr.org/>) (moderate evidence).

Radiographic imaging studies are not recommended to diagnose acute sinusitis or to confirm clinical diagnosis of acute sinusitis in children (strong evidence) [13, 25].

Supporting Evidence Acute sinusitis is a common clinical condition. Diagnosis of acute sinusitis should be made on clinical criteria in patients who present with uncomplicated upper respira-

tory symptoms (strong recommendation) [26]. Clinical guidelines and criteria have been developed to distinguish ABS from acute viral rhinosinusitis. For adult maxillary sinusitis, William's criteria are often used, which include (1) maxillary toothache, (2) poor response to decongestants, (3) history of colored nasal discharge, (4) purulent nasal secretion on physical examination, and (5) abnormal transillumination result. On the other hand, Gonzales et al. reported that purulent nasal secretions alone neither predict bacterial infection nor benefit from antibiotic treatment [19]. Transillumination is a useful technique in the hands of experienced personnel, but only negative findings are useful (limited evidence).

Respiratory symptoms related to acute viral sinusitis may not have completely resolved but almost always have peaked in severity and begun to improve by the tenth day. Therefore, persistence of respiratory symptoms without any signs of improvement beyond the tenth day suggests the presence of bacterial infection [26]. If fever is present in uncomplicated viral infection, it is usually at the earlier phase of illness and accompanied by other constitutional symptoms such as headache. Purulent nasal discharge does not appear for several days for uncomplicated viral infection. The concurrent presentation of fever and purulent nasal discharge for at least three to four consecutive days helps diagnose ABS [25]. The most recent guidelines issued in 2015 have summarized the clinical criteria of ABS as (1) persistent symptoms of purulent nasal discharge with nasal obstruction, facial pain/pressure/fullness, or both, without improvement for at least 10 days after the onset of upper respiratory symptoms, or (2) worsening within 10 days after initial improvement (strong recommendation based on moderate evidence) [27].

Physical examination does not contribute to the diagnosis of ABS. Sinus aspiration is the gold standard for the diagnosis of ABS; but it is invasive, painful, and time-consuming that should only be performed by a specialist (otolaryngologist) [28]. Nasal swab and culture from the middle meatus or nasopharynx is also reported, but the correlation with nasal swab with sinus punc-

ture remains weak. Endoscopic-guided swab culture is more accurate to sample secretion from a sinus of interest. However, this is usually performed by otolaryngologists in the operating room or office, resulting in higher cost, and thus is not feasible for routine use for management of acute sinusitis [29].

Imaging should not be obtained for patients who meet clinical diagnostic criteria for ABS. When an alternative diagnosis is considered, imaging might be useful. Normal radiographs or CT is powerful objective information that bacterial sinusitis is not the cause of the symptoms [30] (limited evidence). A practical guideline by the Agency for Healthcare Research Quality (AHRQ) indicates that imaging is not warranted when the likelihood of acute sinusitis is either high or low, but imaging is useful when a diagnosis is in doubt (limited evidence).

Sinus CT is indicated for patients with acute sinusitis symptoms in the following three conditions: (1) when complications related to sinusitis are suspected, (2) when symptoms persist without response to medical management, or (3) surgery is considered (strong recommendation based on moderate evidence). Complicated sinusitis is suspected when patients present with ptosis, cranial nerve palsies, and facial and orbital swelling. Contrast-enhanced CT of the sinuses and orbit is recommended when orbital cellulites or periorbital abscess as a complication of sinusitis is suspected [23, 31, 32]. Contrast-enhanced MRI is recommended when intracranial extension, such as epidural empyema or brain abscess, is suspected [24, 33–37] (limited evidence).

Applicability to Children

The revised clinical practice guidelines for ABS in children are (a) persistent symptoms including nasal or postnasal discharge (of any quality) and daytime cough lasting more than 10 days without improvement, (b) worsening nasal discharge, daytime cough, or fever after initial improvement, or (c) severe onset (concurrent fever $>39^{\circ}\text{C}$) and purulent nasal discharge for at least three consecutive days in a child who seems ill or toxic [13]. Facial pain is rare and an unreliable symptom in children.

The paranasal sinuses are still under development in younger children. Therefore, lack of aeration of the sinuses may be physiological rather than infection, limiting the accuracy of radiography [33]. In children younger than 6 years of age, clinical history correlates with sinus radiography 88% of the time [38]; therefore, radiography can be safely omitted for children under age 6 (strong consensus based on limited evidence). For children over 6 years of age with persistent symptoms, the need for radiograph as a confirmatory test of acute sinusitis remains controversial but is not supported in the latest guidelines. The culture of middle meatus secretion also remains a questionable value, as the middle meatus in healthy children is commonly colonized with *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*, major pathogens for acute bacterial sinusitis [39].

What Is the Diagnostic Performance of Sinus Radiography and Sinus CT in Acute Bacterial Sinusitis? What Diagnostic Criteria Should We Use?

Summary of Evidence Although the diagnosis of acute sinusitis should be made on clinical grounds, the accuracy of such clinical diagnosis is not well documented compared with the gold standard of direct sinus puncture. Compared with sinus radiography as the gold standard, clinical diagnosis has moderate accuracy (moderate evidence) [26]. Summary receiver operating characteristics (SROC) curve is used to represent the accuracy of a diagnostic test, where 1 is perfect accuracy and 0.5 is no better than the flip of a coin. The area under the curve (AUC) of clinical diagnosis compared with sinus radiograph is 0.74 [40].

Sinus puncture performed by an otolaryngologist is the gold standard; however, it is rarely performed due to its invasiveness and cost. An inexpensive, simple, and accurate diagnostic test is needed to better differentiate patients who need antibiotics from those with nonspecific viral illness. Compared with sinus puncture as the gold standard, sinus radiography offers moderate abil-

ity to diagnose acute sinusitis (SROC area 0.83) (moderate evidence) [41–45]. No single study comparing CT or MR with sinus puncture to evaluate accuracy of CT or MR for acute sinusitis was found (limited evidence). Given CT and MRI's superior spatial and soft tissue resolution to radiography, both are likely more sensitive for detection of acute sinusitis, but specificity is questionable. Lack of definitive diagnostic criteria for sinus disease makes it difficult to interpret studies investigating specificity of sinus CT or MRI.

Supporting Evidence The accuracy of such clinical diagnosis is not well documented. Engels performed a meta-analysis of diagnostic tests for acute sinusitis that showed clinical history, and physical examination had moderate ability to identify patients with positive radiography (SROC area 0.74) [44].

Using sinus opacity or the presence of an air-fluid level as the criterion for sinusitis, sinus radiography had a sensitivity of 0.73 and specificity of 0.80. Compared with sinus puncture and aspiration as the gold standard, sinus radiography offers moderate ability to diagnose acute sinusitis (SROC area 0.83). Another systematic review performed by Varonen published concurrently with Engels's study focused on adult patients suspected of acute maxillary sinusitis. They compared sinus radiography, ultrasound, and clinical examination with sinus puncture as the gold standard and concluded that sinus radiography was a more accurate method for diagnosing acute sinusitis (SROC area of 0.82) than clinical examination. Clinical examination even by experienced physicians was less reliable (area under SROC is 0.75) [45]. Using sinus puncture as the gold standard, Berg reported that clinical examination had a sensitivity of 66% and specificity of 79% in the emergency setting [46]. Even though a sinus radiograph is more accurate than clinical examination for diagnosis of ABS, a sinus radiograph as part of the initial diagnostic workup is not justified due to its costs and radiation exposure.

In Europe, A-mode ultrasound is used to diagnose acute maxillary sinusitis in primary care setting with moderately strong accuracy (SROC area of 0.80) [41, 45, 47]. Savolainen reported among 234 patients suspected of maxillary sinusitis that ultrasound had a sensitivity of 81% and specificity of 72%, as compared with sinus puncture [48]. Ultrasound waves are transmitted to the sinus and then reflected back from the interface of two different media. A sinus cavity filled with secretions results in an echo in the display screen. It is insensitive for mucosal thickening of the sinus [49].

Computed tomography (CT) provides superior assessment of all paranasal sinuses compared with sinus radiographs [50]. However, CT has not been directly compared with sinus puncture for assessment of diagnostic accuracy [44, 45]. Given the invasiveness of sinus puncture and need for otolaryngology referral (additional cost), sinus CT can be used as a proxy for sinus puncture. Sinus CT is considered more sensitive than sinus radiographs for diagnosis of acute sinusitis. A study comparing sinus radiography and CT in 47 consecutive patients showed that sinus radiography had a high specificity but markedly low sensitivity for disease in the ethmoid, frontal, and sphenoid sinuses [51]. The sensitivity of sinus radiograph for maxillary sinus was 80% in this study. In another study that enrolled 134 patients with suspected sinusitis who underwent a single Waters' view of sinus, CT revealed that radiography has markedly low sensitivity for disease outside of the maxillary sinus. The sensitivity and specificity of Waters' view compared with CT for maxillary sinus disease were 68% and 88%, respectively [52], with this study recommending the use of low-dose, high-resolution CT of the paranasal sinuses (moderate evidence). The problem is a lack of specificity data for sinus CT compared with sinus puncture. CT may overdiagnose sinusitis [53].

Another reason that accuracy of sinus CT remains uncertain and controversial is lack of definitive diagnostic criteria. Diagnostic criteria of sinus radiography for acute sinusitis are complete opacification or sinus air-fluid level.

Diagnostic criteria for acute sinusitis on sinus CT are not well defined but usually include mucosal thickening greater than 4 mm, any degree of sinus opacification, and any type of fluid level (Fig. 13.1a–d). Mild mucoperiosteal thickening can be found on head CT in up to 40% of individuals without any sinusitis-related symptoms [54]. Gwaltney reported CT scan of 31 patients with self-diagnosed common cold. They found that 87% of 31 patients had occlusion (or mucosal thickening) of ethmoid infundibulum, and 65% of patients had mucosal abnormality in maxillary sinuses including air-fluid levels [55]. It is of paramount importance to define what CT findings constitute ABS. The only reportedly specific CT finding to indicate acute sinusitis is a frothy, bubbly (frothy) air-fluid level, which indicates purulent secretion within the sinuses [33]. Waterish smooth air-fluid level may be nasal secretion without bacterial infection or clear secretion related to allergic rhinitis [56]. Complete opacification of a sinus with bone thickening may indicate chronically obstructed sinus rather than acute sinusitis [57].

Applicability to Children

Imaging study is not indicated for children with uncomplicated sinusitis (strong recommendation) [13]. This is due to high frequency of non-specific findings seen in patients with viral sinusitis as well as bacterial sinusitis. Normal sinus radiography or CT ensures that symptoms are not due to sinusitis, abnormal imaging findings cannot confirm its diagnosis or differentiate bacterial from viral sinusitis (moderate evidence) [13].

Due to underdevelopment of the paranasal sinuses in younger children, lack of aeration of the sinuses may be physiological rather than infection, limiting the accuracy of radiography [33]. In children, clinical history correlates with sinus radiography 88% of the time [38]; therefore, radiography can be safely omitted for children (strong consensus based on limited evidence). Imaging study should be reserved for children with suspected complications of sinusitis.



Fig. 13.1 Various imaging findings and suggested diagnoses. (a) Air-fluid level in the right maxillary sinus on coronal CT: findings highly suspicious for acute bacterial sinusitis. (b) Near-complete opacification of the right maxillary sinus on coronal CT in a patient suspected of acute sinusitis. (c) Diffuse mucosal swelling and opacification of bilateral maxillary and ethmoid sinuses with thickening of bone walls on coronal CT in a patient with sinonasal polyposis. (d) Nonspecific mucosal swelling of

the maxillary sinus bilaterally on coronal CT. This could be viral infection, allergy, or common cold. (All: Reprinted with kind permission of Springer Science + Business Media from Anzai Y, Paladin A. Diagnosis and management of acute and chronic sinusitis in children. In Medina LS, Applegate KE, Blackmore CC, editors. Evidence-based imaging in pediatrics: optimizing imaging in pediatric patient care. New York: Springer; 2010.)

When Are Imaging Studies Indicated for the Diagnosis and the Management of Patients with Acute Sinusitis?

Summary of Evidence Sinus CT is indicated for patients with acute sinusitis symptoms (1) when complications related to sinusitis are suspected, (2) when symptoms persist without response to

medical management, or (3) surgery is considered (strong recommendation based on moderate evidence). Ptosis, cranial nerve palsies, and facial and orbital swelling suggested complicated sinusitis. Contrast-enhanced CT of the sinuses and orbit is recommended when orbital cellulitis or periosteal abscess is suspected (strong recommendation based on moderate evidence) [23, 24, 31, 32]. Contrast-enhanced MRI is occasionally recommended when intracranial extension (epi-

dural empyema, subdural empyema, venous sinus thrombosis, or intracranial abscess) is suspected [33–37] (limited evidence).

Sinusitis is a self-limiting disease with complete cure in most cases. However, serious complications still do occur in a small percentage (3.7–11%) of these patients with acute sinusitis [58]. When patients with sinusitis symptoms present with orbital swelling, ptosis, visual changes, cranial nerve palsies, and mental status changes, contrast-enhanced CT and/or MR is recommended to diagnose orbital cellulitis/abscess, epidural or subdural empyema, cavernous sinus thrombosis, and intracranial extension of infection (limited evidence) [37]. When patients do not respond to medical management, the patients may have mechanical obstruction that prevents restoration of mucociliary clearance, such as a polyp or tumor of the nasal cavity and sinuses. Sinus CT is a valuable imaging study for evaluating the pattern of sinus obstruction and assessing extrasinus soft tissue or bone destruction, in particular, immunocompromised patients (limited evidence) where invasive fungal sinusitis is suspected [24] where invasive fungal sinusitis is suspected.

When surgery is considered for patients with recurrent where invasive fungal sinusitis is suspected or medically refractory disease, detailed sinus CT is indicated to define the bone anatomy including the osteomeatal complex, dangerous anatomical variations that impose complication risk during endoscopic sinus surgery, as well as correlate with patients' clinical symptoms (limited evidence) [26, 59–61].

Supporting Evidence Sinusitis is a common, self-limited disease with complete resolution with appropriate antibiotic therapy in most cases. Patients with complicated acute sinusitis may have symptoms including high fever, pressure over the face, intense headache above or behind the eye, or periorbital swelling. Complicated acute sinusitis results from a delay in initiating treatment, antibiotic-resistant infection, and incomplete treatment.

The true incidence of sinusitis-related complications remains indeterminate as peer-reviewed publications are primarily case series or case

reports. These include intraorbital complications such as orbital cellulitis, subperiosteal abscess, cavernous sinus thrombosis, epidural empyema, meningitis, cerebritis, and brain abscess (Figs. 13.2a, b, 13.3, 13.4a–c). A retrospective review from a single institution revealed that 5.3% of ear, nose, and throat (ENT) emergencies were sinusitis complications. Among them, orbital complications were the most common (62%) followed by acute subdural empyema (23%) and meningitis (15%) [62]. Among the transplant patients, patients with graft-versus-host disease (GVHD) were 4.3 times more likely than patients without GVHD to develop sinusitis posttransplant [63]. Therefore, contrast-enhanced CT or MR is indicated when patients with sinusitis symptoms present with orbital swelling, proptosis, visual changes, and cranial nerve palsies [36, 64, 65]. Clary investigated the accuracy of sinus CT for orbital abscess as compared with surgical exploration in 19 patients and reported that CT had a sensitivity of 93% and specificity of 67% [66].

With the advent of antibiotics, the incidence of orbital cellulitis has decreased. Approximately 3% of sinusitis progresses to orbital cellulitis [50]. This can be divided into pre- and postseptal cellulitis. The septum is defined as the medial orbital periosteal reflection attaching to the medial eyelid at the tarsal plate. The majority of orbital cellulitis is due to either direct spread from ethmoid sinusitis through porous lamina papyracea or through the valveless anterior and posterior ethmoid veins [50]. The periosteum of the medial orbital wall is loosely attached to the lamina papyracea; as such it often forms subperiosteal abscess or phlegmon. Clinically, these patients may present with deviation of the globe or proptosis.

Cavernous sinus thrombosis results from infection of the midface, orbit, and sinonasal cavity. This may lead to periorbital edema, cranial nerve paralysis, and in some cases blindness due to venous congestion of retinal vein. In the setting of orbital cellulitis, the presence of cranial nerve paralysis involving cranial nerves III, IV, V, and/or VI raises the suspicion of cavernous sinus thrombosis or thrombophlebitis. Contrast-enhanced CT or MR shows an engorged superior ophthalmic vein. Enhancing cavernous carotid

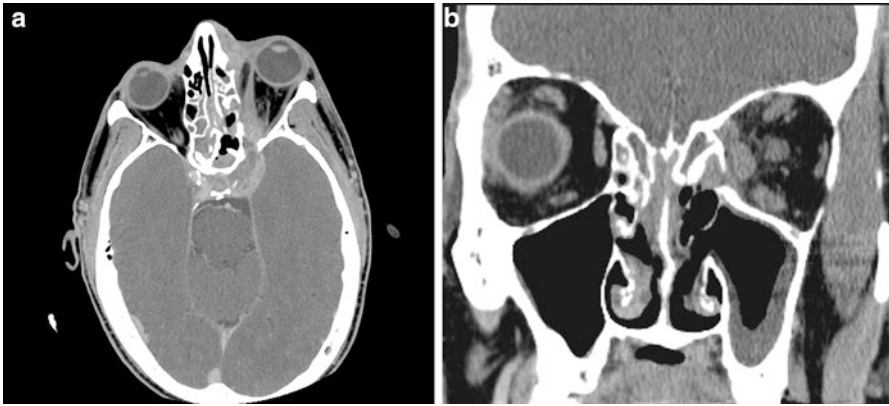


Fig. 13.2 (a) Axial contrast-enhanced CT in a patient with fungal infection involving ethmoid sinuses complicated with left cavernous sinus thrombosis. (b) Coronal CT image of the same patient shows extension of infection to the medial left orbit associated with focal bone erosion. (All: Reprinted with kind permission of Springer

Science + Business Media from Anzai Y, Paladin A. Diagnosis and management of acute and chronic sinusitis in children. In Medina LS, Applegate KE, Blackmore CC, editors. Evidence-based imaging in pediatrics: optimizing imaging in pediatric patient care. New York: Springer; 2010.)

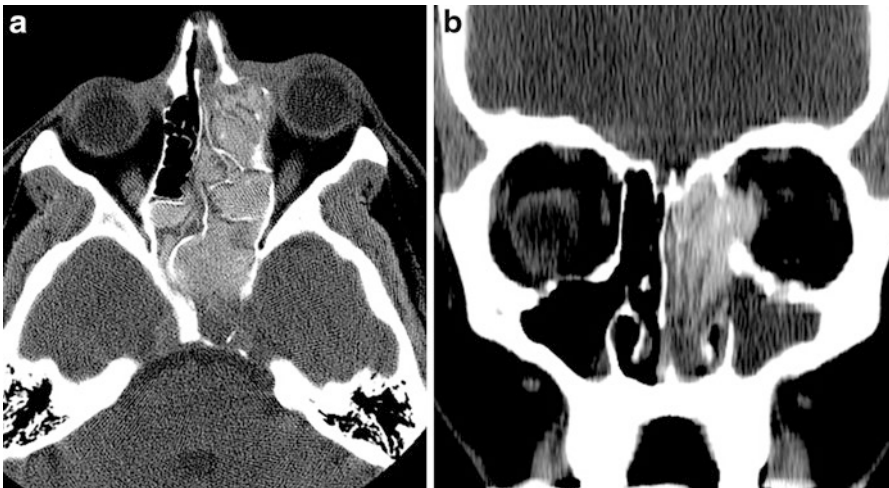


Fig. 13.3 (a) Axial CT of a patient with allergic fungal infection involving the bilateral ethmoid sinuses with medial orbital extension. Notice the content of sinus opacification is markedly increased in attenuation with low attenuation edematous mucosa. (a: Reprinted with kind permission of Springer Science + Business Media from Anzai Y, Neighbor, Jr. WE. Imaging evaluation of sinusitis: impact on health outcome. In Medina LS, Blackmore CC, editors. Evidence-based imaging: opti-

mizing imaging in patient care. New York: Springer; 2006.); (b) Coronal reformatted image of the same patient shows medial orbital extension with displacement of medial rectus muscle. (b: Reprinted with kind permission of Springer Science + Business Media from Anzai Y. Imaging evaluation of sinusitis: impact on health outcome. In Medina LS, Blackmore CC, Applegate KE, editors. Evidence-based imaging: improving the quality of imaging in patient care. New York: Springer; 2011.)

artery may stand out from the surrounding thrombosed cavernous sinus [67–70].

Intracranial spread of sinus infection most commonly originates from frontal or sphenoid sinusitis [64, 71]. Behcet's plexus, the abundant valveless emissary venous plexus of the posterior frontal

sinus, facilitates intracranial extension of infection. Infection spreads through the sinus to dura, meninges, and parenchyma resulting in epidural or subdural empyema, meningitis, and in severe cases cerebritis, and brain abscess [67]. Contrast-enhanced brain MR is recommended when intra-

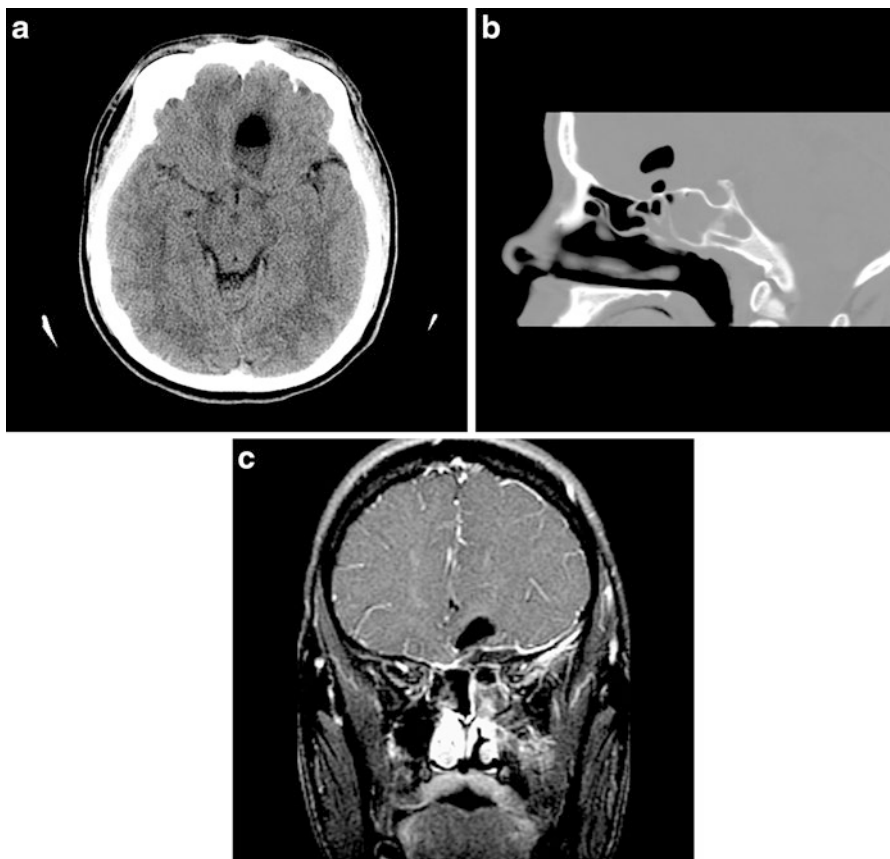


Fig. 13.4 (a) A young patient presented with headache and mental status change. Non-contrast head CT shows focal air near the fluid collection in the base of left frontal lobe. (b) Sagittal reformatted image shows an expansive sphenoid sinus with adjacent pneumocephalus. (c) Contrast-enhanced T1-weighted fat-suppressed coronal MR image shows a focal epidural abscess adjacent to the left sphenoid sinus, underneath the air pocket. This patient

was thought to have left sphenoid mucocele with intracranial ruptured, resulting in epidural abscess (All: Reprinted with kind permission of Springer Science + Business Media from Anzai Y, Paladin A. Diagnosis and management of acute and chronic sinusitis in children. In Medina LS, Applegate KE, Blackmore CC, editors. Evidence-based imaging in pediatrics: optimizing imaging in pediatric patient care. New York: Springer; 2010.)

cranial spread of sinusitis is suspected [64, 67]. One study comparing diagnostic accuracy of CT, MR, and clinical diagnosis for sinusitis-related complications revealed that the diagnostic accuracy was 82% for clinical assessment compared with 91% for CT for orbital complications. For patients with intracranial complications, meningitis was the most common diagnosis, and MRI was more accurate (97%) in determining the diagnosis than CT (87%) or clinical findings (82%). Both CT and MR have improved the management and outcomes of patients who have sinusitis related complications [72].

Endoscopic sinus surgery may be considered for patients who do not respond to maximum medical management. Sinus CT is the primary imaging test and provides detailed images of sinus anatomy in multiple planes. Patients with chronic sinusitis often receive the maximum medical therapy before CT scan in order to evaluate the bony details. Thus, mucosal disease is often minimal or absent for those patients. A detailed sinus CT with reformatted images is recommended for patients with chronic sinusitis who undergo endoscopic sinus surgery as “limited CT” does not provide

detailed anatomical information that are critical for preoperative assessment and planning [73].

Sinus CT often reveals various common anatomical variations, such as nasal septum deviation or concha bullosa. A study evaluating anatomical variations of sinuses on CT revealed that 64.9% of 202 patients had anatomical variations. It is commonly taught to evaluate the bony anatomy related to osteomeatal complex with attention to the curvature and superior extension of the uncinate process [74]. Moreover, dangerous anatomical variations such as dehiscence of optic canal or carotid canal, low-lying fovea ethmoidalis, uncovered anterior ethmoidal artery or Onodi cells may also be found. It is important for ENT surgeons to be aware of these findings prior to surgical intervention.

Applicability to Children

The above recommendations are applicable to children although special consideration should be paid to reducing radiation when appropriate such as radiation reducing techniques on CT studies. Radiographic imaging should not be obtained for patients who meet clinical diagnostic criteria for ABS. A study of 147 children with no clinical evidence for sinusitis demonstrated 61% had mucosal thickening [75].

The most recent consensus guidelines from the American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) mirror the recommendations of the ACR, recommending against the routine use of imaging in the initial evaluation for uncomplicated sinusitis in the pediatric population [76].

Imaging study is indicated for three conditions: (1) suspected sinusitis-related complications, (2) persistent or worsening symptoms despite medical management, and (3) preoperative evaluation for endoscopic sinus surgery.

What Is the Most Cost-Effective Strategy for the Diagnosis and the Management of Acute Sinusitis?

Summary of Evidence The most cost-effective method to manage patients presenting with mild to

moderate symptoms of acute sinusitis is to use clinical guidelines and treat with first-line antibiotic therapy. For patients with severe symptoms or high disease prevalence population, empirical antibiotic treatment is cost-effective. However, this leads to many unnecessary antibiotic prescriptions that lead to antibiotic-resistant infection.

Cost-effectiveness analysis (CEA) comparing four different management strategies (empirical antibiotics, no antibiotics, clinical diagnosis, or sinus CT-based treatment) of adult acute sinusitis revealed that empirical antibiotic therapy is most cost-effective from the societal perspective, as patients return to normal life more quickly, offsetting the up-front cost of antibiotics [77, 78]. From the payer's perspective, clinical diagnosis-based treatment was the most cost-effective strategy [77]. The effectiveness of antibiotic therapy in children remains controversial. The study results highly depend on the inclusion criteria of the study population. Antibiotic therapy was effective for patients with radiographically confirmed pediatric acute sinusitis, but little or no effect is seen when patients were selected based on clinical diagnosis [11]. This is likely due to the fact that some of these patients had viral infection, therefore potentially diluting the effectiveness of antibiotic therapy.

Supporting Evidence A diagnostic workup strategy for any disease should be directly connected to its management of the disease. Although sinusitis is a self-limiting disease in most cases, undertreating acute sinusitis may lead to rare but serious complications. Patients remain sick longer, thus requiring time away from work, loss of productivity, and increase use of over-the-counter medications [78]. Overtreating sinusitis may result in unnecessary costs and adverse effects from antibiotic therapy, such as allergic reaction or gastrointestinal disturbance, as well as future development of antibiotic-resistant infection. Treating a viral illness with antibiotics leads to no benefit but potential adverse drug effects, increasing cost, and future development of antibiotic resistance infection. Accurate diagnosis by CT scan improves effectiveness of antibiotic therapy, by selecting patients who benefit from antibiotics. However, such additional benefit is

too small to justify the additional cost of CT scan and the additional risks from radiation exposure. Therefore, imaging-based management of acute sinusitis is not cost-effective.

Applicability to Children

The effectiveness of antibiotic therapy in children remains controversial, especially when combined with a reported 44% adverse reaction rate to antibiotics compared to 14% adverse event rate for a placebo [79]. The results highly depend on the study inclusion criteria. The study results highly depend on the inclusion criteria of the study population. Patients treated with antibiotics recovered more quickly than those under placebo [38]. On the third day of treatment, 83% of children receiving antibiotics were cured or improved compared with 51% of the children in the placebo group. However, little or no effect is seen in antibiotic treatment when patients were selected based on clinical diagnosis alone. A study by Garbutt challenged the notion that children having acute sinusitis based on clinical ground will benefit from antibiotic therapy. Antibiotic therapy was effective for patients with radiographically confirmed pediatric acute sinusitis, but little or no effect is seen when patients were selected based on clinical diagnosis [11]. This is likely due to inaccuracy of clinical diagnosis of acute sinusitis, diluting the effectiveness of antibiotic therapy.

The American Academy of Pediatrics clinical guidelines have evolved since the original 2001 guidelines [79]. The recommendation for initiation of antibiotic therapy for children presenting with severe or worsening symptoms remains unchanged. However, for otherwise healthy children who present with persistent symptoms for 10 days, without improvement, the new guidelines allow for a 3-day observation period before starting antibiotics. Children with underlying conditions (such as asthma, cystic fibrosis, immunodeficiency, previous sinus surgery, or anatomic upper respiratory tract abnormalities) should receive with antibiotics instead of waiting an additional observation period.

Guidelines for the management of sinusitis show that children with mild and moderate symptoms who do not attend day care should receive

the usual dose of amoxicillin [25]. Those patients who (a) do not improve while receiving the usual dose of amoxicillin, (b) have recently been treated with antibiotics, (c) have illness that is moderate to severe, or (d) attend day care should receive high-dose amoxicillin with clavulanate. Alternative guidelines published by the Infectious Disease Society of America (IDSA) recommend initial empirical treatment to be with amoxicillin with clavulanate, instead of starting with amoxicillin alone [80]. Higher doses of amoxicillin are effective for *S. pneumoniae* species that are intermediate in resistance to penicillin, and potassium clavulanate is effective against beta-lactamase-producing *H. influenzae* and *M. catarrhalis*. In the event that children appear acutely ill or toxic on presentation, intravenous cefotaxime or ceftriaxone can be initiated as an inpatient. The AAP guidelines make no recommendations about the use of antihistamines, decongestants, intranasal steroids and saline irrigation based on limited or controversial data [13].

What Is the Imaging Role for Patients with Chronic Sinusitis?

Summary of Evidence Clinical diagnosis of chronic sinusitis is even more difficult than that of acute sinusitis. Patients with chronic sinusitis have relatively vague symptoms that overlap with viral upper respiratory infection, allergy, and migraine. Imaging plays an important role for excluding diagnosis or identifying anatomical causes leading to sinusitis (moderate evidence). When CT is completely normal, diagnosis of sinusitis can be excluded without prior treatment. Once a treatment decision is made to offer sinus surgery, CT is the modality of choice as it provides bone details far better than radiography or ultrasound (strong recommendation based on moderate evidence). MR with contrast is recommended if there is suspicion of serious complications such as intracranial or orbital abscess as well as to cavernous sinus thrombosis (limited evidence).

Supporting Evidence Chronic sinusitis is defined as sinusitis symptoms lasting more than 12 weeks.

The diagnosis of chronic sinusitis is difficult because of relatively nonspecific signs and symptoms that overlap with viral upper respiratory infection and allergy, migraine, gastroesophageal reflux, and temporomandibular joint arthritis. Imaging plays a major role for assisting or excluding diagnosis or assessing the sinus anatomy leading to recurrent or chronic infection [81]. Sinus CT provides detailed anatomy as well as extent of disease better than sinus radiography and remains the imaging study of choice for patients with chronic sinusitis. CT is often performed in patients who remain symptomatic following multiple courses of antibiotics in order to diagnose or rule out the presence of obstructive lesion interfering mucociliary clearance.

If sinus CT is completely normal without treatment in patients who are suspected of having chronic sinusitis, the diagnosis can generally be excluded. A focal intranasal mass with unilateral sinus opacification on CT necessitates endoscopic evaluation for surgical resection. When sinus CT shows mild, nonspecific, diffuse mucosal thickening without correlation with clinical symptoms, i.e., facial pain or tenderness, it is difficult to determine if sinusitis contributes to patients' clinical symptoms. Certain anatomical variations are thought to contribute causality of chronic sinusitis as these variations may interfere with sinus drainage pathways. These include, but are not limited to, nasal septum deviation, concha bullosa, and Haller cells. As these findings can be seen in asymptomatic subjects, the caution should be paid to interpret anatomic variations [82].

A single prospective study published in 2013 evaluated 115 patients who had failed conventional medical management [83]. A higher quality of life as measured by the Chronic Sinusitis Survey and Rhinosinusitis Disability Index scales was identified in patients undergoing endoscopic sinus surgery compared to continued medical management [83]. The decision regarding the need for sinus surgery should not be solely based on imaging abnormalities. A study that investigated the impact of sinus CT on therapeutic decision by otolaryngologists showed that concordance of abnormality on imaging and patient's symptoms and

obstruction of ostiomeatal complex are the main predictors for favorable surgical treatment [84].

Applicability to Children

Children or adolescents with chronic headache are often misdiagnosed as having sinus headache and receive sinus medication [85]. In terms of the choice of imaging for children with chronic sinusitis, sinus radiography was reported to overestimate abnormalities. In a study performed using sinus radiography and CT in 34 children with chronic sinusitis, sinus radiography (Waters and occipitomeatal views) overestimated ethmoid sinus disease in 24% and maxillary sinus disease in 56% [86].

CT has also been used for chronic sinus evaluation in children. A multi-institutional prospective dual-cohort study comparing the severity of CT findings using Lund-MacKay staging system in 66 pediatric patients with chronic sinusitis and control showed that the AUC of CT is 0.92 ($p < 0.01$), indicating excellent diagnostic accuracy [87]. A study comparing CT scan findings of 60 children aged 2–12 with chronic sinusitis with 50 control subjects who underwent CT scan for indications other than sinusitis found that mucoperiosteal thickening is a highly prevalent finding seen in 60% of patients and 46% of control groups. Early-stage (mild) mucoperiosteal thickening was present in the majority of children who had sinus CT (98% of control and 85% of children with chronic sinusitis) [88]. Although rare, for children suspected for serious complications, such as intracranial or orbital abscess, MR with contrast is recommended to assist surgical treatment planning [81].

Medical management remains the cornerstone for children with chronic sinusitis. Indication for sinus surgery is controversial. Sinus surgery may be performed in children with nasal obstruction from sinonasal polyposis or refractory sinusitis aggravating asthma [89]. Outcome assessment for 308 children with chronic sinusitis after sinus surgery revealed that endoscopic sinus surgery improved outcomes in 2-year follow-up in the intermediate stages of chronic sinusitis (stages II and III out of stages I–IV) [90]. Some studies

suggested the use of IV antibiotics for children who have failed to respond to traditional oral antibiotics therapy [91].

Special Situation: What Is the Role of Imaging in Immunocompromised Patients?

Summary of Evidence Invasive fungal sinusitis (IFS) has been increasingly seen in immunocompromised and poorly controlled diabetic patients, in part due to increasing use of antibiotics, steroids, chemotherapy, and radiation treatment. IFS is a rapidly progressive aggressive fungal infection with a high mortality rate. Yet, IFS is a difficult disease to diagnose and manage. CT findings for IFS are mucoperiosteal thickening associated with bone erosion or extrasinus soft tissue invasion to the orbit, pterygopalatine fossa, or retroantral fat pad [92]. CT is helpful for planning of surgical debridement; however, diagnosis of IFS based on imaging can be challenging in its earlier course. Bone erosion or extrasinus invasion is often very subtle or absent in an earlier stage of disease [93] but rapidly progresses without proper management. With a high clinical suspicion, rigid nasal endoscopy with biopsy is recommended for early diagnosis (moderate evidence) [93]. MR imaging can be used to assess for findings suggestive of IFS as well as assess for extent of involvement including complications such as intracranial invasion [94]. IFS lesions appear hypointense on both T1- and T2-weighted images with very little, if any, contrast enhancement (Fig. 13.5a, b) due to the presence of necrotic tissue. These fungi spread along blood vessels, leading to hemorrhage or vascular occlusion. Complete surgical resection and reversal of neutropenia are critical elements for improved outcomes.

Supporting Evidence IFS is a rare but life-threatening disease in patients with an underlying immunocompromised state or poorly controlled diabetes particularly those with diabetic ketoacidosis. The incidence has been increasing with the expansion of transplant medicine and advances in chemotherapy for hematological malignancies.

Common fungal organisms seen in immunocompromised patients include aspergillosis, mucormycosis, and zygomycosis. IFS often spreads directly to the brain via vascular channels or is blood-borne from pulmonary infection. Abscess formation along blood vessels can cause thrombosis leading to neurological deficit [95]. Therefore, when immunocompromised patients present with stroke like symptoms, intracranial involvement of IFS should be considered as a potential cause.

Imaging studies such as sinus CTs play an important role in demonstrating the extent of disease, degree of bone destruction, orbital invasion, extrasinus soft tissue invasion, presence of non-enhancing soft tissue and vascular encasement. Classic CT findings of IFS, however, are often absent in an earlier stage of disease. Retrospective review of CT findings in 23 immunocompromised patients with confirmed IFS showed that many patients had mucoperiosteal thickening of sinuses (21/23), but bone erosion (8/23) or orbital invasion (6/23) was seen only in more advanced IFS. They found that the disease was frequently unilateral (21/23) [93]. Thus, clinicians should not rely solely on imaging to make a diagnosis of IFS. With a high index of clinical suspicion, early nasal endoscopy and surgical debridement as well as initiation of antifungal therapy is critical to improve prognosis.

When intracranial involvement is suspected, brain MR with and without contrast is essential to make a diagnosis and plan appropriate surgical management. MR allows differentiation of direct cerebral invasion from epidural abscess/phlegmon, cerebritis, multiple brain abscesses, or septic emboli. Venous sinus thrombosis is another serious complication that can be diagnosed with MR and MR venography. Some fungal disease has markedly low T2 signal mimicking well-aerated sinuses on T2-weighted images. These lesions may appear slightly hyperdense on non-contrast CT examination. Contrast enhancement is useful in order to assess extrasinus extent of disease.

Treatment for IFS includes surgical debridement followed by high-dose antifungal treatment and attempts to correct underlying immunocompromised state are essential for improved survival.

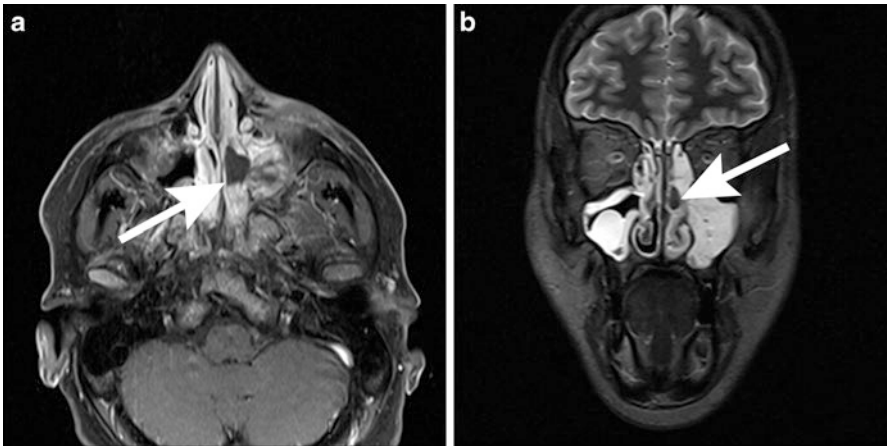


Fig. 13.5 A 23-year-old male with acute myeloid leukemia presented for workup of suspected invasive fungal sinusitis. **(a)** An axial T1-weighted postcontrast fat-saturated MR demonstrating a region of nonenhancement involving the midportion of the left middle nasal turbinate. The mucosa otherwise enhances normally. There is near-complete opacification of the bilateral maxillary sinuses

and nasal cavities from mucosal thickening, left greater than right. **(b)** A coronal STIR MR demonstrating a region of low signal intensity involving the midportion of the left middle nasal turbinate. The mucosa otherwise demonstrates expected high T2 signal. The patient is status post prior uncinectomies and ethmoidectomies. Endoscopy and biopsy demonstrate invasive fungal sinusitis

Applicability to Children

IFS in immunocompromised children has a high mortality rate and requires early diagnosis and treatment. Imaging findings are similar as in adults with imaging providing a role in the diagnosis and evaluating the extent of disease; however, early nasal endoscopy, surgical debridement, and initiation of antifungal therapy are critical to improve prognosis.

Recent work in evaluating post-bone marrow transplant (BMT) patients has been inconclusive. A lack of immune response similar to that in adult immunosuppressed patients reduces the utility of CT for detection of sinusitis. In a study of pediatric hematopoietic stem cell transplant patients with clinical identification of sinusitis, CT imaging findings including mucosal thickening, fluid levels, frothy secretions, near-complete opacification, and multiple positive findings had sensitivities of 19%, 26%, 37%, 56%, and 37%, respectively [96]. Another study demonstrated that following BMT procedures in children, patients presenting with rhinorrhea, nasal congestion, or cough had a 4.46 times greater chance of having moderate/severe opacification compared to asymptomatic patients. Immunocompromised patients had a 6.24 times

greater chance of sinus opacification with the presence of these symptoms [97].

Take-Home Tables

Table 13.1 gives the definition of acute sinusitis. Table 13.2 presents the clinical signs/symptoms of acute bacterial sinusitis vs. viral upper respiratory infection. Table 13.3 is a summary table of diagnostic performance of imaging and clinical examinations for diagnosing acute sinusitis in children.

Take-Home Points

- The clinical signs and symptoms of acute bacterial sinusitis (ABS) overlap with that of non-specific upper respiratory track viral infection (strong evidence).
- Sinus radiographs are moderately sensitive to diagnose ABS compared with sinus puncture and culture (moderate evidence).
- Although a CT scan is frequently performed to assist diagnosis of sinusitis, inadequate data

Table 13.1 Definition of acute bacterial sinusitis (acute sinusitis) in children

Infection of the paranasal sinuses lasting less than 30 days that presents with either *persistent or severe symptoms*

Persistent symptoms are those that last longer than 10–14 days. Sinusitis symptoms include nasal discharge, nasal congestion, maxillary or facial pain, or toothache. Such symptoms for children include nasal or postnasal discharge, daytime cough (which may be worse at night), or both

Severe symptoms include a temperature of at least 102 °F, and purulent nasal discharge presents concurrently for at least three to four consecutive days

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Table 13.2 Acute bacterial sinusitis versus viral upper respiratory infection: clinical signs and symptoms in children

Acute bacterial sinusitis		Viral URI
Duration of illness	Longer than 10–14 days	Usually less than 5–7 days
Symptoms	Persistent or worsening after mild resolution (double sickening)	Improved or resolved by 10 days
Fever	Concurrent presentation of high fever and nasal discharge	Earlier in illness and later nasal discharge
Headache	Severe headache behind eyes	Mild headache
Facial pain	Unilateral pain	Mild or absent
	But not reliable for small children	

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exists on the sensitivity and specificity of sinus CT for diagnosis of ABS (limited evidence).

- Imaging criteria include the presence of frothy air-fluid levels or complete sinus opacification but do not include mucosal thickening (limited evidence).

- Despite relatively high sensitivity of CT or sinus radiography, imaging is not indicated in the initial diagnostic workup for acute uncomplicated sinusitis due to cost and radiation dose (strong evidence).
- Imaging study is indicated for patients who fail to respond to medical management, have severe symptoms suspicious for complications related to acute sinusitis, or patients planning to undergo surgery (moderate evidence).
- The diagnosis of chronic sinusitis is based on clinical grounds. No gold standard exists to confirm clinical diagnosis. CT findings for chronic sinusitis often do not correlate with patients' clinical symptoms (limited evidence).
- Children under 6 years of age should not undergo sinus radiographs due to their limited sinus development (moderate evidence).
- Imaging (contrast-enhanced CT or MR) is indicated in immunocompromised patients or patients with neurologic symptoms with acute progression of sinus infection in order to assess potential complications from acute sinusitis.

Imaging Case Studies

Case 1

Figure 13.1a–d shows various imaging findings and suggested diagnoses.

Case 2

In Fig. 13.2a, b, CT scans of a patient with fungal infection in the sinuses extending to the medial left orbit, with left cavernous sinus thrombosis, and exhibiting focal bone erosion are shown.

Case 3

Figure 13.3a, b shows a patient with an allergic fungal infection in the sinuses, medial orbital extension, and displacement of medial rectus muscle.

Table 13.3 Summary table of diagnostic performance of imaging and clinical examinations for diagnosing acute sinusitis in children (only those using sinus puncture as gold standards)

	Sensitivity (95% CI)	Specificity (95% CI)	References
Physical exam only	0.66 (0.58–0.73)	0.79 (0.73–0.87)	[15, 34–36]
Radiographs	0.87 (0.85–0.88)	0.89 (0.85–0.91)	[32–35]
Ultrasound	0.85 (0.84–0.87)	0.82 (0.80–0.83)	[23, 26, 31, 37, 38]
CT: no study assessing accuracy of CT using sinus puncture as the gold standard			
CT (orbital abscess)	0.93	0.67	5

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Case 4

In Fig. 13.4a–c, a young patient presents with headache and mental status change.

Case 5

In Fig. 13.5a, b, a 23-year-old man with acute myeloid leukemia presents for workup of suspected invasive fungal sinusitis.

both not indicated and technically difficult to perform. The revised guidelines released by the AAP agree, noting further that healthy patients and patients with viral upper respiratory infections demonstrated sinus abnormalities on radiographs, advising against the use of imaging for children under 6 years old.

Suggested Imaging Protocols for Children Clinically Suspected of Acute Sinusitis

Sinus Radiographs

Sinus radiographic series has been rapidly replaced by screening sinus CT for evaluation of sinusitis. Despite this, some physicians still order sinus radiographs often due to either lower costs or easier access to radiographs than CT. At least three views of the sinuses are required to visualize and assess all paranasal sinuses including the Waters' view, Caldwell view, and lateral view. For recurrent infection, some clinicians order a single Waters' view to evaluate the maxillary sinuses.

Applicability to Children In children under 6 years of age, the ACR Appropriateness Criteria state that radiographs of the paranasal sinuses are

Low-Dose Screening Sinus CT

Low mA and low kVp is most widely used for assessment of sinus infection in our institution, when available, reducing radiation dose compared with the standard CT [78, 98]. MDCT allows rapid acquisition of axial images through paranasal sinuses with thin collimation (≤ 3 mm), in the supine position using 100 mAs and 120 kVp. Reconstruction of these images in the coronal plane is routinely performed. No intravenous contrast is necessary unless there is a suspected complication such as orbital abscess or epidural empyema. No sedation is needed for these rapidly acquired CTs. Low-dose screening sinus CT may demonstrate air-fluid levels, sinus opacification, mucosal thickening, “foamy” secretions, nasal polyps, nasal masses, adjacent soft tissue abnormalities, and mastoid and middle ear fluid collections.

Applicability to Children Radiation saving techniques should always be used for children who receive a sinus CT including low mA, low kVp, and increased slice thickness.

MRI

When MR is needed to assess intracranial complications or fungal infection, the following sequences should be included: axial FLAIR, axial diffusion, axial T2-weighted FSE, pre- and postcontrast T1-weighted multiplanar images. Fat suppression should be used for assessment of postcontrast images in order to better visualize the cavernous sinuses, orbital apex, skull base, as well as epidural and subdural spaces.

Applicability to Children No additional special sequences are recommended. With an exam time approaching 1 h, children may require sedation adding to the potential risk of an MRI. MRI also gives less osseous anatomic information than at CT scan.

Future Research

- Develop noninvasive strategies to accurately diagnose acute sinusitis, particularly imaging that differentiates bacterial infection from viral infection or allergic inflammation.
- Determine better staging strategy using sinus CT for patients with chronic sinusitis.

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Part III

Cardiothoracic Imaging



Acute Aortic Syndrome in Adults: Evidence-Based Emergency Imaging

14

Larry A. Latson Jr. and Jill E. Jacobs

Key Points

- Acute aortic syndrome encompasses four (nontraumatic) acute aortic pathologies: aortic dissection, intramural hematoma, penetrating atherosclerotic ulcer, and aortic rupture.
- CT angiography is the gold standard for rapid diagnosis and treatment planning in patients with suspected acute aortic syndrome (strong evidence).
- MRI/MRA of the aorta is an appropriate alternative to CT angiography in selected clinical situations (strong evidence).
- The “triple-rule-out” CT angiogram can be performed safely and effectively, but its increased radiation dose, contrast burden, and higher nondiagnostic image quality preclude its widespread acceptance as a first-line imaging modality in patients presenting to the emergency department with undifferentiated chest pain (limited evidence).

Definition and Pathophysiology

The term “acute aortic syndrome” (AAS) encompasses a variety of different but related conditions, including aortic dissection (AD), acute intramural hematoma (IMH), penetrating atherosclerotic ulcer (PAU), and frank aortic rupture [1]. Definitions and descriptions of these varied syndromes in the medical and surgical literature in general, and the radiologic literature in particular, are challenging, as they are related and overlapping syndromes. Also, various authors have used variable descriptors in the literature. Our understanding of the underlying pathophysiology of these interrelated diseases has also evolved over the decades and centuries since aortic dissection was first described in 1819 by Rene Laennec [2].

The terms “aneurysm” and “dissection” have become irrevocably intertwined [2], although they represent two separate but intimately related disease processes. An aortic “aneurysm” is a fixed dilatation of the vessel greater than 1.5 times its expected diameter, which is usually asymptomatic, and, if asymptomatic, is followed over time until it reaches a size large enough that warrants intervention. An aortic “dissection,” on the other hand, is a tear in the intimal lining of the aorta, which allows blood to dissect into the media (middle layer) of the wall of the aorta. It is usually exquisitely painful when it initially occurs, and is a life-threatening emergency,

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which requires emergent medical and/or surgical or endovascular therapy. Once a dissection occurs, the separation between the intima and media can extend retrograde (back toward the heart) and result in coronary artery occlusion, hemopericardium, and tamponade and/or antegrade throughout the thoracoabdominal aorta and its branches, resulting in occlusions of the head and neck vessels (and subsequent stroke), and renal and visceral arteries, resulting in end-organ ischemia.

The presence of an aortic aneurysm increases the risk of subsequently developing a dissection or rupture. Aneurysms exceeding 6 cm in size have a yearly rate of these complications of at least 7% [3]; aortic dissection similarly increases the risk of subsequent aneurysm formation, but they are distinct entities. Aortic aneurysms can exist without dissection, and dissection can occur without aneurysmal dilatation [4]. Dissections are typically classified using the Stanford or DeBakey classification systems. In the more commonly used Stanford system, a “Type A” dissection is any dissection that involves the ascending aorta (whether it extends into the arch and/or descending thoracic aorta), whereas a “Type B” dissection does not involve this portion of the aorta [4].

One proposed common pathway for the development of aneurysm and/or dissection, particularly in the ascending aorta, has been medial degeneration (previously called “cystic medial necrosis”), which represents loss of the extracellular matrix and smooth muscle in the media of the aortic wall [4, 5]. Cystic medial degeneration can occur idiopathically or in association with systemic hypertension, connective tissue disorders (such as Marfan syndrome and Ehlers-Danlos), aortitis (such as giant cell arteritis), and bicuspid aortic valve [6, 7].

Acute intramural hematoma is defined as acute (thrombosed) blood within the wall of the aorta, without the presence of an intimal flap or tear [8, 9]. The pathophysiology is typically attributed to rupture of the vasa vasorum (the small vessels which supply the wall of the aorta) leading to hemorrhage into the wall of the aorta, without associated intimal disruption [10]. This can occur spontaneously (e.g., in association with hypertension) or in conjunction with a penetrating athero-

sclerotic ulcer. A classic aortic dissection with thrombosis of the false lumen is a separate clinical entity, but distinguishing between these two entities on imaging studies is often difficult if not impossible [10]. Features of IMH that place the patient at higher risk for complications (aneurysmal dilatation, dissection, or rupture) include the presence of an ulcer-like projections, aneurysmal enlargement, pronounced thickness of the hematoma (>11–16 mm), and intramural blood pools [11]. While often treated in a similar manner to acute dissection, the natural history of acute IMH is uncertain, with regression seen in approximately 10% of patients, progression to classic dissection in 28–47% of patients, and an estimated risk of rupture of 20–45% [12].

Penetrating atherosclerotic ulcers (PAUs) represent an atherosclerotic plaque that has disrupted the internal elastic lamina and extends into the media of the aortic wall [13–16], without a visible intimal dissection flap. This disruption of the intima by the PAU can lead to development of an acute IMH, classic dissection, pseudoaneurysm formation, or frank rupture. Symptomatic PAUs are included in the acute aortic syndrome spectrum and are generally treated urgently, with rates of rupture as high as 38% [15]. However, with the increasing use of cross-section imaging, more asymptomatic PAUs or “ulcer-like” projections of the aorta are being discovered in otherwise asymptomatic patients. These patients are often elderly and are imaged for other reasons entirely. They have lower rates of rupture and disease progression [15, 17].

The imaging features of these complex diseases often overlap and coexist, but some general patterns and radiographic definitions exist. Aortic dissection appears as a distinct intimal flap within the lumen of the aorta, with a “true” and “false” lumen, which typically enhances following intravenous contrast administration unless thrombosed. The site of intimal tear (fenestration) may or may not be visible. Acute intramural hematoma is characterized on CT (and MRI) by the presence of crescentic high attenuation in the wall of the aorta (which is often more conspicuous prior to intravenous contrast administration) and lack of enhancement following intravenous contrast administration. Aortic rupture and impending

rupture are present when there is stranding and ill-defined soft tissue surrounding the aortic wall, mediastinal or pleural hemorrhage, or frank extravasation of contrast outside the wall of the aorta (Fig. 14.5a, b). Penetrating atherosclerotic ulcers are seen as focal contrast-filled outpouchings through the wall of the aorta, without a visible dissection flap, in the presence of diffuse aortic atherosclerotic disease [13, 15, 17].

Epidemiology

According to a large autopsy series from Sweden including almost 30 years of data, the incidence of aortic dissection is 3.2 per 100,000, with an incidence of aortic rupture of 0.9–1.0 per 100,000 [18]. Risk factors for aortic aneurysm and dissection are similar, and include age, systemic hypertension, atherosclerosis, vasculitides such as Takayasu's and Giant cell arteritis, bicuspid aortic valve, and inherited connective tissue disorders such as Marfan, Loeys-Dietz, Ehlers-Danlos, and Turner syndromes [5, 6, 19]. Pregnancy is also a risk factor for aortic dissection [20]. In the large International Registry of Acute Aortic Dissection (IRAD) database, established in 1996 and encompassing 17 years and 28 centers, 67% of patients enrolled presented with Type A dissection and 33% with Type B dissection, with mean ages of 62–64 years [21]. Two thirds of the patients were men [21]. Over 17 years of the study, in-hospital mortality for Type A dissection improved significantly from 31% to 22%, and in-hospital mortality for Type B dissection remained stable at 12–14% [21]. In the classic paper by Hirst et al. in 1958, Type A dissections have a mortality rate of 1–2% per hour and are thus treated with emergent surgery [22]. Type B dissections (without evidence of end-organ compromise) are generally treated with medical management (see below).

Overall Cost to Society

Limited data exists on the overall costs to society of the acute aortic syndromes. While mortality from AAS is high, the overall

incidence is orders of magnitude less compared to more common causes of chest pain. For example, the IRAD investigators note that coronary artery disease is 100–200 more common than aortic dissection, with an estimated incidence of three aortic dissections for every 1000 patients presenting with chest and/or back pain [12].

Goals of Imaging

The primary goal of imaging in patients with acute aortic syndrome is to (1) diagnose the underlying aortic pathology, (2) identify any associated conditions or complications which may be present, and (3) provide adequate information for subsequent medical, open surgical, and/or endovascular aortic repair.

Methodology

A comprehensive PubMed search for articles published between 1990 and July 2015 using the PubMed search engine was performed using a combination of the following key terms: acute aortic syndrome, aortic dissection, aortic aneurysm, penetrating ulcer, CT, MR, angiography, and triple rule out.

Discussion of Issues

What Is the Imaging Modality of Choice in Patients with Suspected Acute Aortic Syndrome?

Summary of Evidence Computed tomography angiography (CTA) is the gold standard for imaging of suspected acute aortic syndrome. It is readily available in most if not all emergency departments in the developed world, can be obtained relatively rapidly, and provides excellent spatial resolution not only for diagnosis but also for subsequent treatment planning (strong evidence).

Supporting Evidence

Chest Radiography

Chest radiography is often performed in patients presenting to the emergency department with chest pain and is recommended in all patients presenting with symptoms suspicious for acute aortic syndrome [19, 23]. However, it is used primarily as a means of discovering alternative causes of acute chest pain (such as pneumothorax). It is specifically noted that the chest radiograph should not to be the definitive test for acute aortic syndromes. Historically, findings of aortic dissection and aneurysm were described on chest radiographs as mediastinal widening, displaced intimal calcifications, and changes in the configuration of the aorta over successive radiographs [24]. A study, performed in the modern era, assessed mediastinal width on posteroanterior (PA) and anteroposterior (AP) radiographs in 100 patients with confirmed nontraumatic thoracic aortic dissection and 120 patients with confirmed normal aortas [25]. The authors found that PA radiographs were both more sensitive and specific than AP radiographs, as would be expected due to less magnification on PA radiographs, and found utility in both the maximal mediastinal width (a cutoff of 7.5 cm on PA films was 90% sensitive and 88% specific), as well as the maximal left mediastinal width (a cutoff of 5 cm was 90% sensitive and 90% specific) [25]. Chest radiography is therefore useful in uncovering other causes of acute chest pain and may suggest the diagnosis of aortic dissection. However, in any patient with suspected AAS, further cross-sectional imaging is required to definitely exclude AAS [19, 23]. CT and MRI also have the ability to guide surgical and/or endovascular management in confirmed cases of AAS.

CT Angiography

CT angiography has become the mainstay for diagnosis of suspected AAS in the United States. In the IRAD, data from 4428 patients revealed that over a span of 17 years, the frequency of CT utilization increased from 46% to 73% for the detection of Type A dissection, while the use of transesophageal echocardiography (TEE)

decreased from 50% to 23% [21]. CT angiography is fast, with scanners readily available in most modern emergency departments. CT can provide an overview of the entire thoracic (and abdominal) aorta in one data set, along with information about potential complications. A CT angiogram provides excellent spatial resolution for 3D reconstructions, which can be critical in planning surgical and endovascular repair of AAS.

Much of the data on sensitivity and specificity of CT for the diagnosis of aortic dissection and other AAS comes from older literature, with studies performed on older equipment with less resolution and slower scan times compared to modern machines. Previously reported sensitivities of 90–100% and specificities of 87–100% [23] are now likely close to 100% with current multi detector CT scanners [26].

When performing a CT angiogram for suspected AAS, a precontrast exam of the thorax is often obtained to assess for the presence of IMH. Intramural hematoma has classically been described as crescentic high attenuation in the wall of the aorta, which can potentially be mistaken for wall thickening (or even overlooked) on post-contrast images. However, a newer retrospective study by Lovy et al. found a sensitivity of 100% for IMH on the post-contrast material-enhanced CTA exam, suggesting that unenhanced imaging may not always be necessary [27]. In addition, a retrospective study by Knollmann et al. similarly found that IMH was visible on post-contrast CTA images in all 31 of their cases [28]. Whether pre-intravenous contrast material-enhanced images are obtained routinely for all suspected AAS patients is generally a matter of institutional preference. If they are routinely performed, they should be limited in z-axis coverage, extending from the top of the arch to the bottom of the heart to limit radiation exposure.

After the precontrast exam is performed, a CT angiogram is performed, typically extending from the thoracic inlet to the diaphragmatic hiatus. Optimal contrast enhancement of the aorta (>250 Hounsfield units) can be obtained utilizing either a timing run or bolus tracking, with an injection rate of 4–5 mL/s [29]. The volume of iodinated contrast utilized will depend on several

factors, including patient size and the pitch of the CT machine, but is typically in the range of 60–120 mL. Reconstructed images should include coronal and sagittal images, for evaluation of the aortic arch, and axial data sets at no more than 1–2 mm thickness to allow for adequate multiplanar and 3D volume rendering. CT technology has advanced rapidly in the last few decades. Newer technologies, such as EKG synchronization, high temporal resolution “high-pitch” acquisition modes, and dual-energy imaging, are discussed in more detail below.

As with most radiological exams, detection and subsequent management of incidental findings are an important issue to consider. CT angiograms of the chest include not only the aorta but the heart, lungs, chest wall, and upper abdomen, where incidental (but potentially life-altering) findings can occur. In a recent retrospective review of 370 CTAs performed to evaluate for AAS, 329 patients (89%) had at least one incidental finding, and 106 (29%) had recommendations for some form of follow-up [30]. Most of these (44%) were for pulmonary nodules, but other findings included pneumonia, pleural and pericardial effusions, and cancer and/or metastases [30].

Magnetic Resonance Imaging

MR angiography, while an excellent modality for evaluating the aorta, is not typically the first test of choice in suspected AAS, for several reasons [21]. First, MRI is not nearly as readily available as CT, and even when available, may not be available 24 h a day. MR angiograms take significantly longer to perform than CT angiograms, which is an issue in potentially unstable patients with suspected AAS. Patient cooperation is required, as most MR sequences require breath-holding to minimize artifact. Claustrophobia can limit the patient’s willingness to cooperate with the exam. When it is available and the patient deemed appropriate, a focused MR exam including steady-state free precession (SSFP) axial and coronal images, cine SSFP oblique sagittal images, and contrast-enhanced 3D MRA (CE-MRA) could be performed in 4 minutes, with reported 100% accuracy for determining the presence or absence of dissection or aneurysm

[31]. In cases of suspected acute IMH, T1-weighted black blood (BB) images can demonstrate intermediate or high signal within the wall of the aorta [32].

In patients who cannot reliably hold their breath or who cannot receive gadolinium-based contrast agents due to significant renal dysfunction, the development of unenhanced SSFP MR angiography is a viable alternative [33–35]. With these sequences, the patient breathes freely while a special “navigator” sequence monitors the position of the diaphragm, only utilizing data when the diaphragm is within a certain narrow window [33]. These sequences can also be performed with EKG gating, allowing for visualization of intracardiac structures and the proximal coronary arteries, which are typically not well seen on conventional non-EKG-gated MR angiography. In a comparison of 30 consecutive patients who underwent both EKG-gated free-breathing SSFP MRA and conventional MRA, the SSFP sequence performed excellently [36].

Echocardiography

Echocardiography is a useful modality in the diagnosis of aortic dissection. Transthoracic (TTE) and transesophageal (TEE) echocardiography offer real-time acquisition, which can be obtained at the bedside, a significant advantage over CT and MRI in hemodynamically unstable patients. Reported sensitivities for detection of dissection range from 59 to 85% and specificities from 93 to 96% [23]. In a large meta-analysis of 16 studies involving 1139 patients, Shiga et al. found that TEE, CT, and MRI all yielded equally reliable diagnostic accuracy for confirming or excluding thoracic aortic dissection [37]. However, there are some important limitations with echocardiography. An experienced operator must be available to obtain and interpret the images, as echocardiography can suffer from a number of potential artifacts. Transthoracic echocardiography is limited by the availability of acoustic windows and can be affected by abnormal chest wall configuration, obesity, and pulmonary emphysema [38, 39]. Transesophageal echocardiography is a more invasive procedure and can image nearly the entire thoracic aorta,

but there is a known “blind spot” in the anterior portion of the aortic arch, caused by artifact from the trachea and left main stem bronchus as they pass between the probe (in the esophagus) and aorta [38]. The full extent of a dissection, including involvement of the abdominal aorta, iliac vessels, and visceral branches, is not as readily apparent compared to CT or MRI. Despite these limitations, echocardiography remains a key modality in the management pathway, both in the United States and Europe [23, 39].

PET/CT

While metabolic imaging of the aorta, with ^{18}F FDG PET/CT, is not a first-line diagnostic test for patients with suspected AAS, there is limited evidence that PET/CT of the aorta can be useful in a few specific clinical situations. In a small study by Reeps et al., imaging findings of nine patients with known acute dissection and two patients with symptomatic progressive dissection were compared with those of seven patients with known chronic stable Type B dissection. The standardized uptake value (SUV) of the aortic wall or dissection membrane was found to be significantly higher in all of the acute or progressive dissection cases compared to the chronic dissection cases [40]. Thus, PET/CT could have a role resolving whether a newly diagnosed aortic dissection is in fact acute or chronic, in patients who present with atypical or nonclassic symptoms. Metabolic imaging may also have a role in assessing prognosis; a study of 28 patients by Kato et al. demonstrated that higher SUV values in the wall of the aorta in dissection patients were significantly associated with an increased risk for progression and rupture [41]. However, larger scale studies would be required before either of these assertions could be generalized for routine clinical practice.

What Newer CT Technologies Are Being Utilized in Imaging of Suspected Acute Aortic Syndromes?

Summary of Evidence Most modern CT scanners are capable of EKG synchronization, which can reduce or eliminate pulsation artifact in the

ascending aorta and allow accurate assessment of the coronary arteries and aortic valve. However, CTA protocols utilizing EKG synchronization should be carefully tailored to minimize the increased radiation dose. Dual-source scanners are capable of high-pitch acquisition modes, which can eliminate pulsation artifact while minimizing radiation dose. Dual-energy techniques are available for generation of virtual noncontrast (VNC) images, potentially eliminating the need for a precontrast scan (thereby reducing radiation dose), but their routine use in suspected AAS may be complicated by higher levels of artifact (limited evidence).

Supporting Evidence

EKG Synchronization

EKG synchronization refers to placing electrodes on the patient’s chest during the CT exam and acquiring and reconstructing images during specific phases of the cardiac cycle (one R-to-R interval). EKG synchronization can be performed retrospectively, in which data from all cardiac cycles (systole and diastole) is acquired and then “retrospectively” reconstructed at specific phases (usually in 10% increments from 0% to 90% of the R-to-R interval). Alternatively, EKG synchronization can be performed utilizing prospective triggering, in which data only from specific parts of the cardiac cycle (typically at about 30% of the R-to-R interval for systole or about 70% of the R-to-R interval for diastole) is acquired “prospectively” at preselected locations, and imaging is optimized or acquired for some phases of the cardiac cycle. Prospective EKG triggering results in significant dose reduction to the patient [42], but is more likely to result in artifact at higher heart rates and in patients with cardiac ectopy.

The primary advantage of EKG synchronization over conventional CT angiogram is the reduction or elimination of cardiac motion and pulsation artifact in the ascending aorta. With EKG synchronization, the lumen of the coronary arteries can be assessed, and aortic valve leaflets can be visualized [43]. A study by Roos et al. showed a clear reduction in motion artifact with EKG-synchronized CTA compared to conventional CTA, but did not comment on the difference in

radiation dose [44]. A more recent study by Scherthaner et al. showed a significant reduction in motion artifact, an increase in diagnostic confidence, with EKG-synchronized CTA performed with the same radiation dose as conventional CTA [45]. The routine use of EKG synchronization for suspected AAS is not universal, however, and while some consider it an integral part of their protocol [29], its use varies among institutions.

High Pitch

With the introduction of dual-source CT scanners, high-pitch acquisition protocols (with pitch up to 3.2) have been developed which allow for very fast imaging of the entire chest, in under one second [46, 47]. These can be performed with EKG synchronization (i.e., timed for a specific phase of the cardiac cycle), but even without EKG synchronization, the sub-second scan time is enough to significantly reduce or eliminate pulsation artifact in the ascending aorta, which is a common pitfall that can mimic a Type A dissection flap [29, 43]. In a study of 51 consecutive patients with undifferentiated acute chest pain, an EKG-synchronized high-pitch protocol provided excellent image quality with low radiation dose (average 3.8 mSv) [46]. Beta-blockers were not routinely administered prior to the exam. When patients had heart rates of 65 beats per minute or less, the image quality was excellent, but did degrade significantly at higher heart rates. Importantly, image noise can increase significantly when using high-pitch protocols in patients with a large body habitus [47].

Dual Energy

With the introduction of dual-source CT scanners, the concept of dual-energy CT emerged [48]. By operating the two tubes at different kVp (typically one at a low energy of 80–100 kVp and the other at a higher energy of 140–150 kVp) and comparing the differences in X-ray attenuation within a voxel between the two sources, the amount of iodine within the voxel can be quantified [49]. This is particularly useful when imaging the aorta, because it allows for the creation of virtual non-contrast (VNC) images (potentially avoiding a precontrast scan and reducing radiation dose) [50, 51]. The replacement of a precontrast scan with

VNC images from a dual-energy scan has been studied in the setting of follow-up imaging after thoracic endovascular aortic repair (TEVAR), with excellent results [52, 53]. However, its routine use in the setting of suspected AAS is less well established. One recent study comparing VNC images of the thoracic aorta to the abdominal aorta found VNC images tend to be prone to pulsation artifact [54]. In fact, while VNC images were deemed an acceptable replacement for conventional precontrast images in 93% of cases of the abdominal aorta, they were acceptable in only 12% of thoracic aorta cases [54].

What Is the Role of the “Triple-Rule-Out” Examination?

Summary of Evidence The “triple-rule-out” (TRO) CTA typically requires higher radiation dose and more iodinated contrast and is more difficult to perform, compared to conventional coronary CTA or CTA of the aorta or pulmonary arteries alone. While it may be quite useful in selected clinical situations, its routine use in patients with undifferentiated chest in the emergency department is not yet justified (limited evidence).

Supporting Evidence Patients presenting to the emergency department with chest pain present a significant diagnostic challenge. With the introduction of some of the techniques discussed above, including EKG synchronization and high-pitch acquisition modes, the development of a single CT exam that could simultaneously evaluate the aorta, the pulmonary arteries (for PE), and the coronary arteries is an appealing goal. Rogg et al. found that patients who underwent workup for one of these conditions were more likely to receive simultaneous testing for one of the others [55], suggesting that a single test to evaluate for all through would be useful. Special considerations for the TRO CTA include the amount and timing of contrast administration, to ensure adequate opacification of both the aorta and coronary arteries, as well as the pulmonary arteries [56].

While this examination is now readily feasible and safe with modern CT scanners [57], its routine

use in undifferentiated chest pain remains somewhat controversial, as the TRO CTA requires more contrast than standard CT angiography and use of EKG synchronization (with increased radiation dose) [58]. In a large meta-analysis of 11 studies with 3539 patients, Ayaram et al. found that while image quality was excellent for detecting coronary artery disease, the low prevalence of PE and dissection in these patients was not enough to recommend routine usage [59]. Similarly, in a very large review of 12,834 patients who underwent TRO CTA, Burris et al. found a slightly higher yield of PE and aortic disease, but at the expense of image quality, radiation dose, and contrast dose [60]. They too concluded that, while it certainly has value in individual cases, “its indiscriminate use is not warranted” [60]. A retrospective study of 2068 patients by Madder et al. found that TRO CTA resulted in higher radiation dose, but was not associated with improved diagnostic yield, reduced clinical events, or diminished downstream resource use, compared to conventional coronary CTA [61]. A retrospective study by Al Qahtani et al. of 467 patients presenting with atypical chest pain found the prevalence of acute coronary syndrome (ACS) and AAS was limited (0.5–5.5%) in those patients clinically suspected of having a pulmonary embolism, but the prevalence of ACS and PE was much higher (18% and 5.6%, respectively) among suspected AAS patients [62]. Finally, in the prospective, randomized CAPTURE trial of 59 patients, the authors concluded that, while helpful in certain circumstances, the TRO CTA “should not be used routinely with the expectation that it will improve efficiency or reduce resource use” [63].

Imaging Case Studies

Case 1

In Fig. 14.1, a 57-year-old man presents to the emergency department with “crushing” chest pain.



Fig. 14.1 57-year-old man presenting to the emergency department with “crushing” chest pain. Axial contrast-enhanced CT angiogram demonstrates an acute Type A aortic dissection. The false lumen (*) often has slower flow and will enhance less than the true lumen. The true lumen is typically smaller and more central in location. A fenestration or intimal tear is seen (*black arrow*), with communication between the true and false lumens

Case 2

In Fig. 14.2a, b, a 94-year-old man presents to the emergency department with chest pain.

Case 3

A 60-year-old man presents in Fig. 14.3a–d with a known history of penetrating atherosclerotic ulcer, arriving as an outpatient for presurgical planning.

Case 4

In Fig. 14.4a–d, a 63-year-old male with uncontrolled hypertension presents for a noncontrast CT thorax for preoperative planning prior to a CABG procedure.

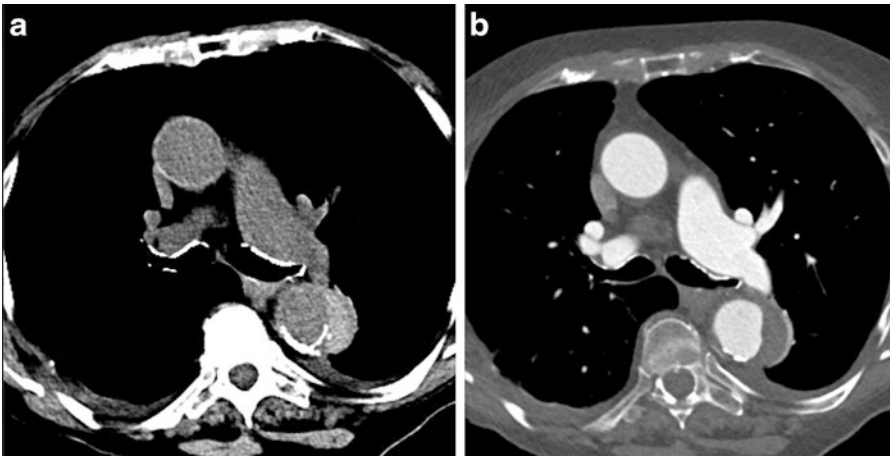


Fig. 14.2 94-year-old man presenting to the emergency department with chest pain. Precontrast images (a) are useful for demonstrating crescentic high attenuation along the wall of the descending aorta, consistent with Type B acute IMH. On post-contrast CT angiogram images (b),

this region appears relatively low in attenuation compared to the adjacent contrast-enhanced aortic lumen and could potentially be misinterpreted as low attenuation (chronic) atherosclerotic plaque, rather than acute blood in the wall of the aorta

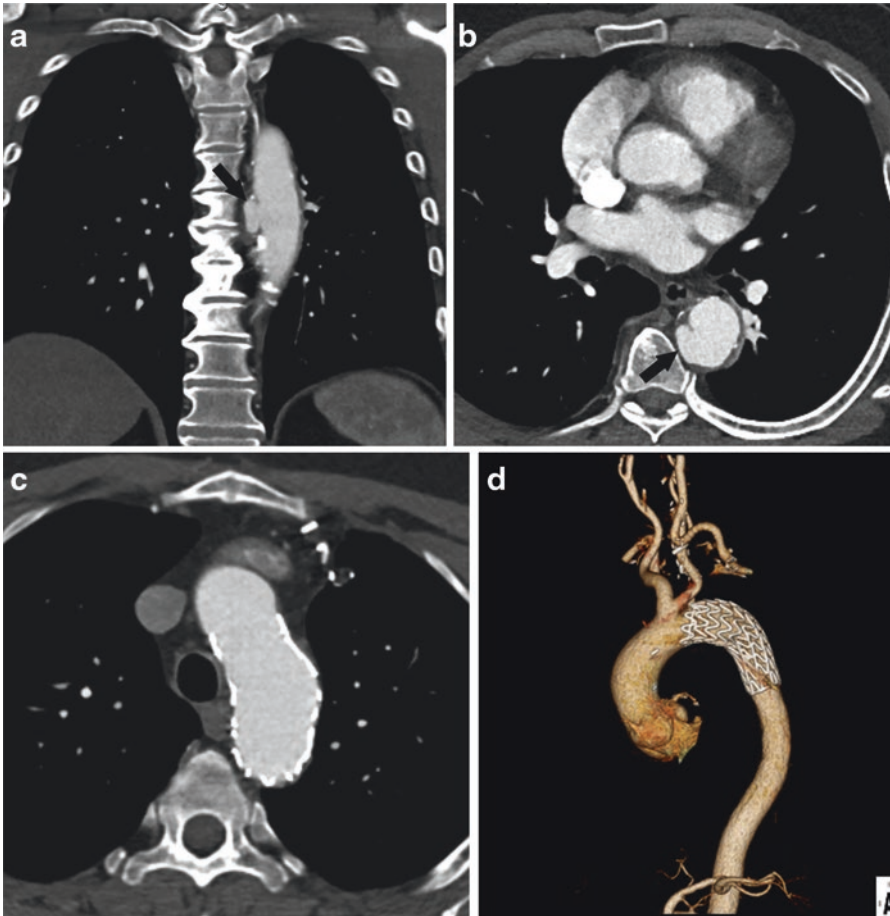


Fig. 14.3 60-year-old man with a known history of penetrating atherosclerotic ulcer, presenting as an outpatient for presurgical planning. Coronal (a) and axial (b) CT angiogram demonstrates a focal penetrating atherosclerotic ulcer

(black arrow) in the mid-descending thoracic aorta. The patient underwent successful thoracic endovascular aortic repair (TEVAR), with resolution of the PAU (c, d)

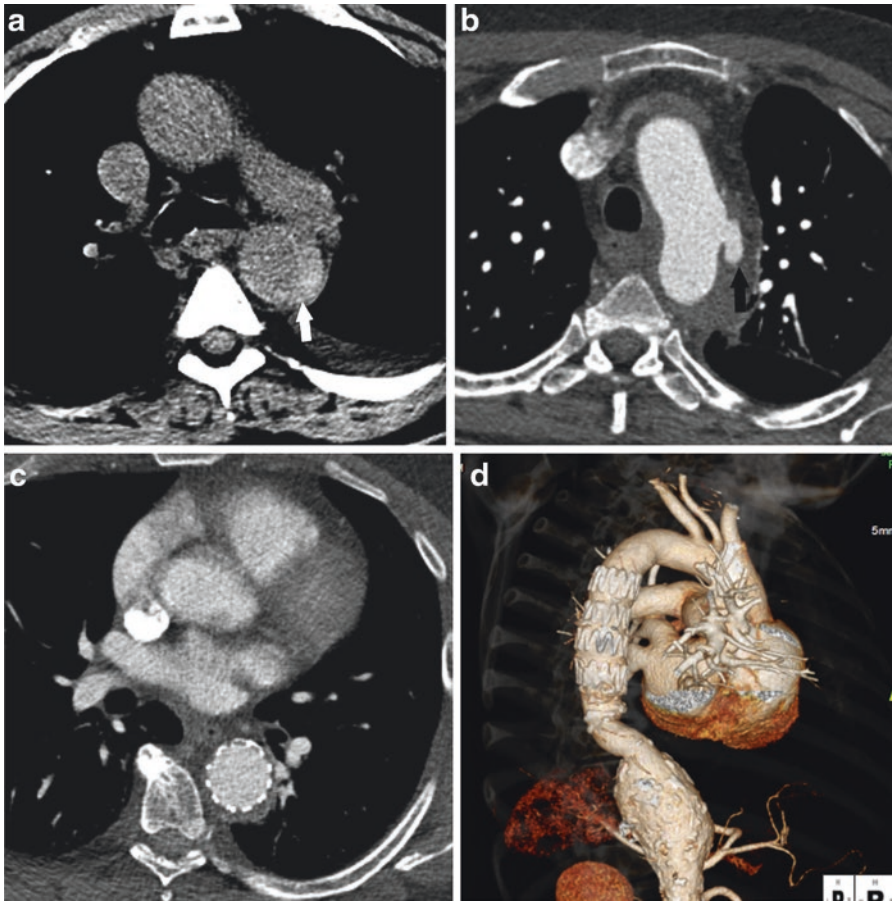


Fig. 14.4 63-year-old male with uncontrolled hypertension, presenting for a noncontrast CT thorax for preoperative planning prior to a CABG procedure. Noncontrast image (a) demonstrates crescentic high attenuation in the wall of the descending aorta (*white arrow*), consistent

with acute IMH. Subsequently performed CT angiogram (b) in region of the distal aortic arch demonstrates a PAU as the cause of the IMH (*black arrow*). The patient underwent successful TEVAR, with resolution of the PAU (c, d)

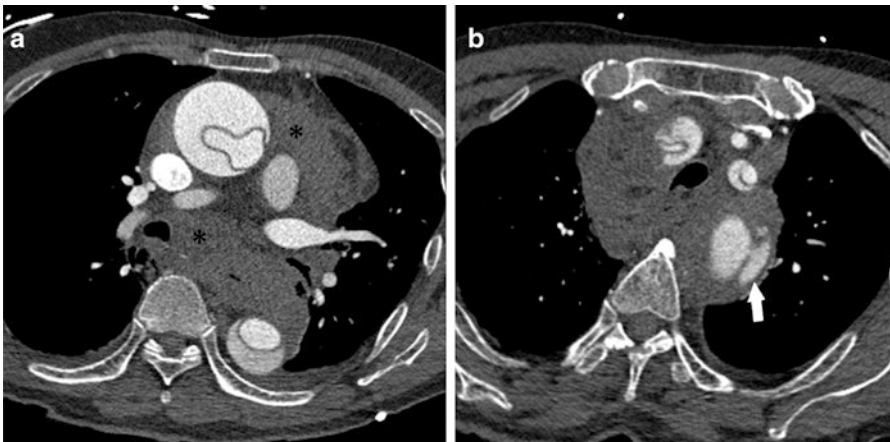


Fig. 14.5 81-year-old male presented to the emergency department with sudden onset of chest pain and was hypotensive. CT angiogram (a) demonstrates an acute Type A dissection involving the ascending and descending aorta,

with a large amount of blood (hematoma) in the mediastinum (*). There is active extravasation from proximal descending aorta (b, *white arrow*). Findings consistent with aortic rupture

Case 5

An 81-year-old male presents in Fig. 14.5a, b to the emergency department with sudden onset of chest pain and was hypotensive.

Suggested Imaging Protocols

Chest radiography:

- Indicated for all patients presenting with suspected acute aortic syndrome
- Primary use is to exclude other etiologies that may mimic symptoms of AAS
- Normal chest radiographs do not exclude AAS and should not delay cross-sectional imaging in patients with symptoms of AAS

CTA Chest:

- Indicated for all patients presenting with suspected acute aortic syndrome
- Noncontrast images can be obtained to assess for acute intramural hematoma
- CT angiogram of the chest performed
- Consider EKG synchronization and/or high-pitch mode to reduce motion artifact in the ascending aorta and aid in assessing the coronary artery origins

MRI/MRA Chest:

- Indicated when patient is hemodynamically stable and able to cooperate
 - MRA with contrast of the thoracic and abdominal aorta
- If gadolinium contrast is contraindicated (renal failure, allergy)
- Noncontrast 3D SSFP respiratory-gated navigator sequences

Transesophageal echocardiography indicated as a viable alternative to CTA or MRA when an experienced operator is available to perform/interpret the images.

Future Research

- Role of dual-energy CT angiography in the setting of suspected acute aortic syndrome, and specifically the role of virtual noncontrast (VNC) images to detect acute intramural hematoma.
- Continued advancements in CT technology will allow faster gantry rotation times and higher pitch, to reduce/eliminate cardiac pulsation artifact without the need for EKG gating.
- Continued study of the role of the “triple-rule-out” exam in patients presenting to the emergency department with undifferentiated chest pain.

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Acute Coronary Syndrome in Adults: Evidence-Based Emergency Imaging

15

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Key Points

- A strong recommendation can be made for utilizing dedicated coronary CTA in patients who present with acute chest pain but are at low risk for a cardiac event (strong evidence).
- Coronary CTA should not be utilized in patients presenting with acute chest pain that have intermediate to high risk for a coronary event (strong evidence).
- The utilization of a triple rule out coronary CTA has been shown to improve the disposition of patients with acute chest pain. However, there is limited data in the added value over a dedicated coronary CTA (insufficient evidence).
- Coronary CTA has been proven to be cost-effective in the assessment of low-risk patients who present with acute

chest pain to exclude a cardiac origin. However, the utilization in high-risk patients should not include coronary CTA (strong evidence).

- The utilization of coronary CTA in asymptomatic high-risk patients has not been shown to be beneficial (strong evidence).

Definition and Presentation

Acute chest pain is a complex symptom. While management and disposition is relatively streamlined and straightforward in patients who present with classic signs and symptoms of acute coronary syndrome (abnormal EKG, elevated troponins, or appropriate clinical presentation), atypical acute chest pain can encompass a wide range of diagnostic entities ranging from a catastrophic aortic dissection to a muscle strain [1–6].

In patients with atypical chest pain or who are at low risk for acute coronary syndrome, the workup and disposition becomes more complex. These individuals present with atypical symptoms and a normal EKG and normal initial serum troponins. In this patient population, there remains a small but real risk of morbidity as well as medical legal risk that could result from missing a major

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adverse cardiac even [7–10]. Classically, this patient would be admitted for an extensive cardiac workup. Often, the workup would include a stress test with or without imaging and/or a cardiac catheterization. The greater percentage of the time no cardiac source for the patient's pain would be identified. As such, a great deal of resources would be directed toward this patient population without identifying a cardiac cause of pain.

Coronary CTA, performed on a 64-slice scanner (or above) has made it possible to rapidly evaluate this low-risk patient population in the acute setting without impacting clinical outcome or requiring invasive diagnostic testing such as cardiac catheterization [11, 12].

Epidemiology

Chest pain is the second most common complaint among patients presenting to the emergency department (ED) [13]. This number has steadily increased since 2004. Currently, approximately 9 million patients each year present to the ED with chest pain, increased from approximately 6 million in 2004 [14, 15] and is expected to increase further given our society's diet and sedentary lifestyle. In individuals who are at low risk (no prior history of a cardiovascular event and absence of risk factors), the likelihood of having an acute coronary syndrome (as evidenced by an abnormal EKG or abnormal serum biomarkers) is less than 8% [1–7].

Overall Cost to Society

Missed myocardial ischemic/infarction events account for approximately 40% of malpractice judgments against EDs. In addition to the cost of malpractice judgments, the direct cause from patients with acute chest pain presenting to the ED is estimated between \$13 and \$15 billion [14, 15].

With such extensive resources placed toward this patient population, there are still at least 2% of these individuals who present to the ED that will have their diagnosis of acute coronary syndrome overlooked [16, 17]. This points to the

need for a work flow and/or testing algorithm that minimizes risk and decreases cost.

Goals of Imaging

The overall goal in evaluating the patient with acute chest pain particularly in the ED is to isolate those who are at high risk for acute coronary syndrome (ACS) from those who are not. As part of this risk stratification, the purpose is to efficiently evaluate and diagnose the presenting patient's etiology of acute chest pain while minimizing cost, diagnostic procedures, and hospitalizations without negatively impacting the diagnosis of potentially life-threatening diseases.

Methodology

Outcome studies, cost-effectiveness literature, and current professional guidelines and recommendations were reviewed with a MEDLINE search ranging from January 2005 to June 2015. The keyword searching included acute chest pain, coronary CTA, and cost-effectiveness. Over 500 reports were identified in the literature search. Approximately 50 specifically addressed acute chest pain cost-effectiveness and/or outcomes.

A similar literature search was performed with a date range between 2005 and 2015 that included acute chest pain, diagnostic evaluation, and cost-effectiveness/outcomes. Approximately 2000 reports were identified with less than 100 specifically addressing outcomes and cost-effectiveness.

Discussion of Issues

Is Coronary CTA Useful in Acute Chest Pain?

Summary of Evidence There has been a multitude of imaging trials that support the utilization of coronary CTA as an initial diagnostic tool in individuals who present to the ED with acute chest pain. In addition, these studies have shown that the

use of coronary CTA in low- to intermediate-risk patients is cost-effective (strong evidence).

Supporting Evidence The initial observational studies which compared the diagnostic capabilities of coronary CTA to invasive coronary angiography (ICA) showed that 64-slice CT scanners had a high sensitivity in diagnosing coronary artery stenoses of greater than 50% diameter [4, 5, 18–22]. This suggests that coronary CTA has the ability to detect stenoses which would be of clinical significance and possibly requiring intervention (Table 15.1).

Multiple randomized controlled trials have been performed comparing standard of care versus coronary CTA in patients who were low risk for acute coronary syndrome demonstrating that there was no long-term impact on patient outcome while preserving diagnostic capabilities and limiting costs. However, in several trials it has been shown that patients who have moderate to high risk of coronary artery disease will have a greater likelihood of having greater than 50% stenosis on a coronary CTA [4, 5, 18–22]. These patients will often go on for additional functional testing or cardiac catheterization, in order to evaluate for a physiologic degree of ischemia.

An important point when evaluating coronary CTA versus ICA results is that the sensitivity and specificity as well as positive predictive values change depending on whether the data is assessed on a per patient basis (patient level data) or a 17 segment AHA comparison (vessel segment level data). When evaluating the results of multiple studies, the performance of coronary CTA on a per patient basis results in a high sensitivity (at least 96%) but low specificity (approximately

74%) [20, 23]. However, an evaluation on a per segment basis, negatively impacts sensitivity (approximately 80%) but positively impacts specificity (92%). This should be kept in mind when developing and implementing coronary CTA in the evaluation of chest pain. The utilization of coronary CTA is very favorable when assessing CAD presence on a per patient basis [20, 23]. The high negative predictive value of coronary CTA makes it an ideal diagnostic study to exclude coronary artery disease especially in the low- to intermediate-risk population. Thus, a negative study in this patient group would almost certainly exclude any significant coronary artery disease.

Based on Patient Risk, When Should Coronary CTA Be Applied?

Low-Risk to Intermediate-Risk Patients

Summary of Evidence The current recommendations for the evaluation of low-risk patients in the ED, established by the American Heart Association and the American College of Radiology, encompass a wide range of diagnostic modalities including stress testing with or without imaging, echocardiography, and coronary CTA [22–24]. However, due to lack of immediate resources, these patients are often admitted for their clinical evaluation in order to improve diagnostic accuracy. In the acute setting, coronary CTA is a potential method for evaluation given its high negative predictive value and its ability to diagnose other causes of acute chest pain, such as pneumonia, aortic dissection, or pulmonary embolism [24, 25].

Table 15.1 Comparison of performance characteristics of coronary CTA in the detection of coronary artery disease across multiple imaging trials

Trial	Patient risk	Sensitivity	Specificity	PPV	NPV
ACCURACY	Low to intermediate	94%	83%	48%	99%
CORE-64	High	94%	44%	93%	50%
CORE-64	Low	91%	87%	90%	88%
ROMICAT I	Low	77%	87%	48%	98%

Note: The gold standard is based on cardiac catheterization with a 50% or greater stenosis on coronary CTA being considered a significant degree of stenosis. *PPV* positive predictive value, *NPV* negative predictive value

Supporting Evidence There has been a multitude of studies evaluating coronary CTA in this patient population. The most recent trials are ROMICAT II and ACRIN-PA. ROMICAT II randomized patients to either standard of care (stress test with or without imaging, stress echocardiography or no diagnostic testing) or to coronary CTA. The utilization of coronary CTA resulted in a statistically significant reduced length of stay in the hospital of 8.6 h for the coronary CTA group versus 26.7 h for the standard of care group [6]. In addition, there were no adverse cardiac events in either the standard of care group or the coronary CTA group within 30 days. The ACRIN-PA study supported these findings and demonstrated a higher rate of direct discharge from the ED [26]. These studies supported the initial findings of the ROMICAT I trial [21].

In the low-risk population, the vast majority of patients will not have coronary artery disease, and only a small proportion, approximately 10%, would require additional testing or intervention. Therefore, the use of coronary CTA as a noninvasive tool with a high negative predictive value could be recommended [12, 27]. However, some researches have argued that the risk of events in this group is so low that no immediate imaging would be needed [28, 29].

Moderate- to High-Risk Patients

Summary of Evidence The utilization of coronary CTA in acute chest pain patients at moderate to high risk for coronary artery disease is not supported by the evidence (strong evidence). Those patients will have some degree of coronary atherosclerosis. Thus, because of the limited specificity and the high sensitivity of coronary CTA, additional testing would be required. In addition, the presence of coronary artery calcium often results in overestimation of the degree of stenosis also resulting in additional diagnostic testing. As a result, the American Heart Association, the American College of Radiology, the American College of Cardiology, and other professional organizations have recommended that coronary CTA is not suggested as the first-line management in this patient population (strong evidence) [4–6, 30, 31].

Supporting Evidence Individuals who are at high risk for or have been diagnosed with coronary artery disease have a high initial likelihood that their acute chest pain will be cardiac in origin. In patients with a high likelihood of disease, the initial workup should focus on establishing ischemia via either functional testing or ICA. The positive predictive value, especially for flow limiting lesions, is less than ideal (Table 15.1) [27, 32, 33]. Positive predictive values have been noted as low as 76% in a high-risk population. This leads to further testing and increased cost [23, 34]. Research suggests that coronary CTA in the high-risk groups has no additional benefit.

In addition, these high-risk patients have other limitations that make coronary CTA a less than ideal study for initial evaluation. This patient population has a high prevalence of obesity which makes the performance of the study technically challenging, resulting in a greater proportion of examinations that are either limited in quality or that are nondiagnostic. Moreover, a high incidence of diabetes places these patients at risk for contrast induced nephropathy [35–38]. It would be more appropriate in these patients to utilize contrast for the definitive study, i.e., catheter-based angiography.

Coronary CTA Compared with Other Imaging Modalities

There are multiple imaging modalities that can be utilized in the evaluation of acute coronary syndrome. Catheter angiography is the traditional modality for the evaluation of patients who have chest pain of presumed cardiac origin. However, angiography is an invasive and expensive test and not ideal in the low- to intermediate-risk patient population. However, it remains the gold standard for the diagnosis of coronary artery disease although utilizing it does not always result in lower cost or improved diagnosis. Studies have shown that coronary CTA has a greater sensitivity compared to catheter angiography (80% vs. 67%) but a decreased specificity (67% vs. 75%) when using intravascular ultrasound as the gold standard [39]. Furthermore, in patients with a low pretest likelihood ($\leq 50\%$) of coronary artery disease, coronary CTA has been found to result in

lower cost which is not the case in the high-risk group (likelihood of 70% or greater).

Historically, single photon emission computed tomography (SPECT) has been the noninvasive method for the evaluation of chest pain and coronary artery disease. Multiple studies have shown the superiority of coronary CTA in the detection of coronary artery stenosis. Coronary CTA has been shown to have a superior sensitivity compared with SPECT (92–100% vs. 76–81%) and greater specificity (78–89% vs. 57–78%) [40, 41]. In conjunction with the efficiency and speed of performance, this makes coronary CTA the preferential method in patients with acute chest pain.

Taking all evidence into account, coronary CTA would be the preferred diagnostic tool over catheter angiography and SPECT in moderate- to low-risk patients presenting with chest pain.

What Are Special Considerations for the Utilization of CTA in Acute Chest Pain?

Summary of Evidence The utilization of coronary CTA in the diagnosis of acute chest pain often brings up special considerations. This is centered on the pathology of other entities that are associated with acute chest pain. As such, protocols have been developed for the simultaneous evaluation of the coronary arteries, aorta, and pulmonary arteries. This so-called triple rule out CT examination is an attempt to evaluate not only the coronary arteries but also the aorta for dissection and the pulmonary arteries for pulmonary thromboembolism. However, currently, the evidence does not support the widespread use of triple rule out for the evaluation of patients with chest pain [42, 43] (insufficient evidence).

Supporting Evidence There are, however, several small studies that have shown that triple rule out may be useful in the evaluation of acute chest pain. In these studies, the triple rule out has reduced additional testing in up to 75% of the patients who have low to intermediate risk for acute coronary syndrome [4]. Further, the triple rule out has been able to detect non-coronary

causes of chest pain in between 10 and 30% of the time [4].

Apart from the fact that the routine use of a triple rule out CT examination has not been assessed in large multicenter trials, the actual performance also raises some limitations. When a triple rule out study is performed, the radiation dose will be higher than in a standard coronary CTA because of the additional volumetric coverage that is required [36, 44]. The amount of contrast that is needed to perform the study is also increased. However, despite the performance limitations and the lack of evidence for of the utility of the triple rule out CT examination, the increased risk of litigation in the ED for acute coronary syndrome (25% of all liability) often results in the use of this examination, resulting in increased patient risk [45].

What Are the Risks of Utilization of Coronary CTA in Acute Chest Pain?

Summary of Evidence The utilization of coronary CTA in acute chest pain poses a unique set of risks. The ease of performance and availability of the study may result in overutilization. This overutilization results in increased costs and may place the patient at risk for increased radiation exposure and over testing from incidental findings (moderate evidence).

Supportive Evidence The biggest risk of coronary CTA in those presenting with acute chest pain is exposure to radiation [36, 44]. This is exacerbated by the likelihood that there is a very low pretest probability of having a positive study. In the ROMICAT I trial, the results indicated that because of the high negative predictive value (NPV) of coronary CTA, patients with a negative coronary CTA could avoid a repeat study for at least 2 years [21].

For a retrospectively gated coronary CTA, the radiation exposure is approximately 12 mSv, and for a prospectively gated examination the exposure is approximately 5 mSv [46, 47]. Since there is concern of unnecessary medical radiation exposure to patients, these studies need to be

appropriately applied in the clinical setting to minimize potential long-term risks.

The patients who are typically evaluated are often low risk for cardiac disease. Up to 30% of these examinations will have non-cardiac findings. The vast majority of these findings (approximately 80%) will be incidental findings such as a pulmonary nodule [48, 49]. Most of them will have no clinical relevance but yet will require additional workup and testing leading to further costs and stress on the patient.

What Are the Costs of Utilization of Coronary CTA for Acute Chest Pain?

Summary of Evidence There have been multiple multicenter trials that have demonstrated cost benefits of using coronary CTA in low-risk patients presenting with chest pain. These studies have demonstrated cost savings, decreased hospital admissions, and decreased lengths of stay (strong evidence).

Supporting Evidence ROMICAT I was the first large trial to show improved efficacy using coronary CTA in the evaluation of chest pain without compromising patient outcomes [21]. This was followed by several other studies including ROMICAT II, ACRIN-PA, and CT-STAT trials (Table 15.2) [4, 6, 21, 26, 50]. Overall, these studies demonstrated between \$200 and \$1100 savings by utilizing coronary CTA in the ED. The CT-STAT trial compared coronary CTA to a rest stress perfusion study. In this study, the investigators were able to demonstrate a decrease in emergency time stay and lower cost without any impact on the diagnosis of acute coronary syndrome [4]. The ROMICAT II trial supported these findings by demonstrating shorter hospital length of stay, a more rapid time to diagnosis, and an increase in the number of patients were discharged directly from the emergency room [6]. ROMICAT II showed that coronary CTA compared to standard of care could be performed without any impact on the outcome or diagnosis of acute coronary syndrome.

Table 15.2 Comparison of cost savings and length of stay in multiple trials

Trial	CCTA (cost)	SOC (cost)	Length of stay (CCTA)	Length of stay (SOC)
CT-STAT	\$1586	\$1872	3.4 h	15.0 h
ACRIN-PA			18.0 h	25.0 h
STAT-CT	\$2137	\$3458	2.9 h	6.3 h
ROMICAT II	\$4026	\$3874	8.6 h	26.7 h

Note: The trial utilized standard of care (SOC) as determined by the clinician or a fixed modality that was SOC for the evaluation of acute chest pain. CCTA coronary CTA

ACRIN-PA was able to demonstrate shorter length of stay and higher rates of direct ED discharge when comparing coronary CTA to standard of care. There was a difference in the ability to detect acute coronary syndrome between the coronary CTA and standard of care groups [26]. The follow-up of this patient cohort demonstrated that even after 1 year and a negative coronary CTA, there was less than a 1% risk of a cardiac event [51].

Take Home Tables

See Tables 15.1 and 15.2 for comparison of performance characteristics of coronary CTA in the detection of coronary artery disease across multiple imaging trials and for comparison of cost savings and length of stay in multiple trials, respectively.

Take Home Points

- Several large multicenter trials have evaluated the application of coronary CTA in the diagnosis of acute chest pain in low- to intermediate-risk patients and have demonstrated that, because of its high NPV, coronary CTA can be applied in the initial acute chest pain workup in this patient population.
- When the use of coronary CTA is limited to low- to intermediate-risk patients with acute chest pain, there is a proven benefit including decreased hospital length of stay and overall

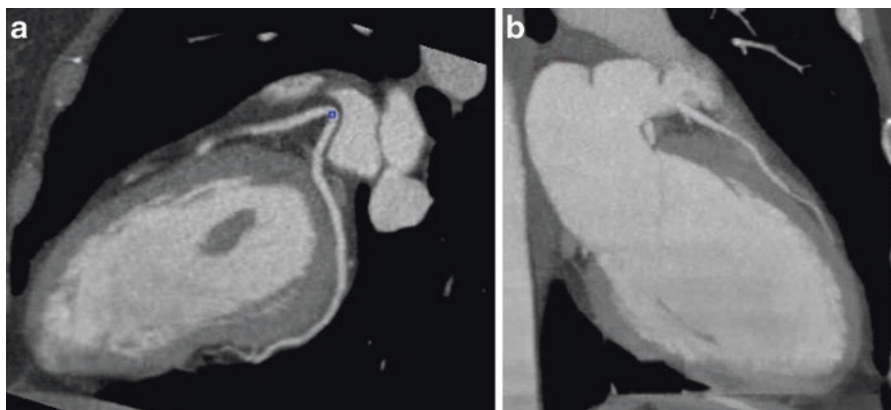


Fig. 15.1 A 35-year-old man with no family history of cardiac disease. Normal ECG and negative troponin. No clinical risk factors. Coronary CTA was performed as the patient was low risk. Coronary CTA demonstrated no coronary artery disease (a and b). There were no areas of

calcification or stenosis. Image b depicts a short segment of myocardial bridging. This is not associated with the patient's presentation for chest pain. The utilization of coronary CTA in a low-risk patient averted a cardiac catheterization and led to a discharge directly from the ED

costs, without major adverse cardiac events within 30 days of discharge.

Imaging Case Studies

Case 1

In Fig. 15.1a, b, a 35-year-old man with no family history of cardiac disease and a normal ECG and negative troponin undergoes a coronary CTA.

Case 2

In Fig. 15.2, a 63-year-old man who presents with acute chest pain and a strong history of coronary artery disease undergoes a coronary CTA.

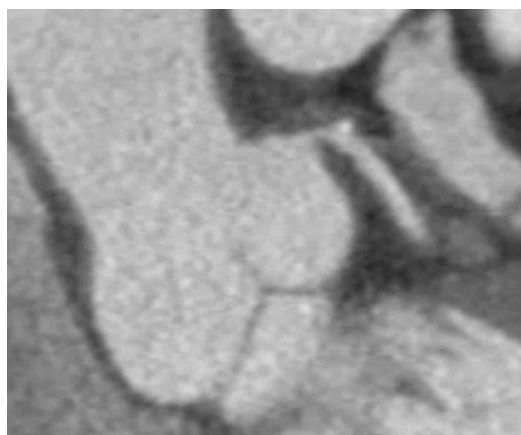


Fig. 15.2 A 63-year-old man presented to ED with acute chest pain. There was a strong family history of coronary artery disease, elevated cholesterol, and diabetes. An initial coronary CTA was performed in the ED which demonstrated significant coronary artery disease. The coronal reconstruction depicts a greater than 70% narrowing of the left main coronary artery. The image depicts both a calcified and non-calcified plaque. This was followed up with a catheterization and stenting of the left main coronary artery for a high-grade stenosis. Given the patient's history and presentation, the pretest probability for coronary artery disease is greater than 70%. Therefore, the initial study that should have been performed was a cardiac catheterization

Future Research

The evaluation of acute chest pain is an ever evolving arena of research. There are multiple modalities for the diagnosis of coronary artery disease, but researchers need to focus on exploring which diagnostic modalities are best applied to the various patient populations. In addition,

research needs to focus on methods to limit cost of evaluations without impacting long-term outcome.

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Acute Pulmonary Embolism in Adults and Children: Evidence-Based Emergency Imaging, Evaluation, and Diagnosis

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Key Points

- Validated structured clinical assessments such as the Wells score, the Pulmonary Embolism Rule-out Criteria, and the Geneva score, as well as an experienced physician's gestalt evaluation, are vital for determining the clinical

probability of pulmonary embolism and the appropriateness of imaging.

- CT pulmonary angiography is currently the most commonly performed imaging modality when pulmonary embolism is suspected. However, ventilation-perfusion scintigraphy performs comparably with a lower radiation dose and is especially suitable for patients with normal chest radiographs and those with contraindications to intravenous contrast.
- An underlying risk factor is found in most pediatric patients ultimately diagnosed with pulmonary emboli on computed tomography pulmonary angiography.
- A clinical threshold of two or more risk factors should likely be used to optimize imaging for pediatric pulmonary emboli.
- Although dual-energy CT pulmonary angiography/CT lung perfusion is attractive and shows promise for increased sensitivity of pulmonary emboli detection, evidence, and clinical experience is currently lacking.

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Abbreviations

CT Computed tomography
V/Q Ventilation/perfusion study

Definition and Pathophysiology

Pulmonary embolism is a common disease with a high morbidity and mortality burden. Its clinical presentation is quite variable, making accurate diagnosis challenging. In this chapter, we examine how clinical assessment determines pretest probability and then guides the diagnosis and management of acute pulmonary embolism. The important role of imaging in work-up is summarized, and various imaging modalities are compared and evaluated based on up-to-date medical literature. Pulmonary embolism diagnosis in pregnancy is also briefly reviewed and evidence-based diagnostic algorithms for evaluation of acute pulmonary embolism are presented.

Acute pulmonary embolism (PE) occurs when thrombus travels to the pulmonary arteries from the deep veins of the lower extremities and less commonly from other central veins. In situ thrombosis of the pulmonary arteries is rare and can present similarly. The pathophysiology of PE is variable and depends on the size of the emboli and the patient's clinical condition [1]. In a healthy patient, a small PE may not be of clinical significance because a physiological function of the pulmonary capillary bed is to filter and lyse small thrombi that regularly develop in the legs [2]. In patients with limited cardiopulmonary reserve or those with larger pulmonary emboli, the compromise of the pulmonary vascular bed can result in acute right heart dysfunction and even death [1].

Risk factors for PE fall into several categories including situational, intrinsic, and related to comorbidities. Situational risk factors include recent prior surgery, prolonged travel especially long-haul airplane flights, oral contraceptive and hormone replacement therapy, and smoking. Intrinsic hypercoagulable states are a major risk factor for pulmonary embolism and a focus of ongoing research and new insights. These include inherited thrombophilias which are present in 5–8% of the population such as protein C and S and antithrombin deficiencies, factor V Leiden mutations, increased clotting factors such as factor VII, sickle cell trait, and acquired conditions such as antiphospholipid antibody syndrome.

Other patient related-risk factors include malignancy, heart and kidney disease, immobilization, obesity, and advanced age [3].

In contrast to adults where up to 31% of pulmonary emboli are idiopathic, an identifiable risk factor is found in 96–98% of pediatric patients with pulmonary emboli [4, 5]. Specific risk factors vary across the pediatric age range. In 80% of infantile PE cases, a thrombus associated with a central venous catheter is present [4, 6, 7]. Other risk factors in infants include dehydration, peripartum asphyxia, and septicemia. In older children, presence of a central venous catheter remains the greatest risk factor for pulmonary embolism. However, other risk factors such as immobilization, hypercoagulable states, excess estrogen, and a prior history of PE and/or deep vein thrombosis begin to take on a more prominent role [8].

Epidemiology

Venous thromboembolic disease encompasses both deep vein thrombosis and pulmonary embolism. About 500,000 people are diagnosed with thromboembolic disease in the United States annually although these estimates are inexact due to ascertainment, reporting, and national database limitations. The incidence is 1–2 per 1000 overall but increases tenfold in the elderly aged 80 years and older. About one-third of thromboembolic disease presents clinically with pulmonary embolism, and up to a quarter of all patients with pulmonary embolism have sudden death as their initial presentation. Among those who survive the initial event, the mortality is roughly 10%, with the highest risk of death for those with underlying malignancy or morbidities associated with poor cardiopulmonary reserve. Ten percent of patients with thromboembolic disease are expected to have a recurrence within 10 years [9]. However, the long-term survival of patients diagnosed with acute pulmonary embolism is quite low. A Mayo Clinic series [10] describes a 37% 10-year survival for patients who survived to reach the hospital and undergo CT pulmonary angiography.

The true incidence of pediatric pulmonary embolism remains unknown as many patients are likely misdiagnosed and, thus, not imaged, given the often subtle or nonspecific clinical presentation of children with pulmonary emboli. Therefore, pediatric epidemiologic estimates largely rely on autopsy series or retrospective studies looking at patients who were clinically suspected of having a pulmonary embolus and, as such, received imaging. In the most recent of these published works, Kristaneepaiboon et al. found a PE incidence of 15.5% in patients who underwent pulmonary CT angiography for clinically suspected PE [11]. These findings led the authors to conclude PE to be more common than previously reported.

Overall Cost to Society

Cost to society is a broad and difficult to quantify concept that may encompass the costs of diagnosis and treatment of the illness, loss of wages and future earnings due to disability, and death. The in-hospital costs of caring for patients admitted with the diagnosis of pulmonary embolism have been estimated to be \$8764 [12]. The annual medical costs the year after diagnosis with pulmonary embolism is in excess of \$18,000 compared with \$680 for a control group. These are direct cost-of-care estimates that do not take into account the more difficult to estimate costs related to lost wages, disability, and death [13].

Goals of Imaging

The goal of medicine is to improve the care of our patients. Diagnostic tests, including imaging, are performed in order to diagnose or exclude the diagnosis of clinically relevant disease and to serve as a guide to management. For patients who are suspected of having pulmonary embolism and have an intermediate or high probability of disease, imaging is generally recommended in order to diagnose or exclude the diagnosis of pulmonary embolism. If pulmonary embolism is diagnosed, the usual treatment is anticoagulation.

Alternative diagnoses that may explain the patients' symptoms can be demonstrated on chest radiography or CT [14]. However, there has been a rapid increase in imaging utilization over the past two decades. Medical imaging, especially from CT, has become a substantial contributor to the annual US population radiation exposure, along with background radiation levels [15]. In fact, among patients diagnosed with pulmonary embolism, Stein et al. [16] described a substantial increase in radiation exposure for a cohort of recently diagnosed patients compared with a pulmonary embolism cohort diagnosed more remotely, reflecting increased imaging utilization. Therefore, it is of utmost importance to select the most appropriate patients to undergo imaging and identify those for whom imaging can safely be obviated.

Methodology

The medial literature was searched using PubMed (National Library of Medicine, Bethesda Maryland) and Google for articles published between 2005 and 2015. The search was limited to English language articles and human studies. Pulmonary embolism and thromboembolic disease were searched alone and in combination with diagnostics, D-dimer, imaging, computed tomography pulmonary angiography, CT, ventilation perfusion scintigraphy, lung scan, echocardiography, duplex, lower extremity ultrasound, and cost. Additional classical literature on pulmonary embolism was included when recently referenced and deemed to be pertinent. A priority was given to original research focusing on clinical outcomes, national databases, high-quality reviews, and evidence-based guidelines. The articles were rated based on the quality of the evidence.

Comment

Because studies reporting clinical outcomes in patients who receive diagnostic testing for pulmonary embolism can only report false-negative val-

ues and rates of false-negative results, false-positive results and positive predictive values are not determinable. A false-negative result is recognized when a patient initially diagnosed as not having pulmonary embolism returns with symptoms and imaging findings of pulmonary embolism or deep vein thrombosis within a pre-specified time period, usually 90 days (recurrence rate). Patients diagnosed as positive for pulmonary embolism at presentation are typically treated, thus precluding systematic study of false-positive results.

Discussion of Issues

What Is the Role of Clinical Assessment in the Evaluation of Pulmonary Embolism?

Summary of Evidence Initial consideration of the diagnosis of pulmonary embolism occurs prior to any formal clinical assessment. Once the diagnosis has been considered, its probability can be assessed clinically either in an unstructured, gestalt manner or by using a validated structured clinical assessment. The Pulmonary Embolism Rule-out Criteria (PERC) developed in the United States, the Wells score developed in Canada, and the Geneva score developed in Europe have all been validated in their respective populations and can be used to assign a probability of pulmonary embolism to a given patient [17–20]. Interestingly, a gestalt evaluation by an experienced physician performs at least as well as the structured clinical assessments (moderate evidence) [21, 22]. If the clinical probability of pulmonary embolism is low, a serum D-dimer assay is recommended and if the results are negative, imaging can be safely obviated (moderate evidence). If the D-dimer is elevated then imaging is recommended. If a patient has a high clinical probability of pulmonary embolism, imaging is typically the first appropriate step. When imaging is performed, the results should be evaluated in the context of the pretest probability of disease and have the best predictive value when the clinical probability and imaging findings are concordant (Fig. 16.1).

Supporting Evidence Practice patterns in medicine vary geographically, and consequently the prevalence of pulmonary embolism in patients who are suspected of having the disease varies greatly. Penalzoza et al. [23] aggregated data from three prospective clinical trials of 11,114 patients with suspected pulmonary embolism from the United States and Europe. They found that the pretest probability of pulmonary embolism was significantly higher in Europe when the patients were evaluated by clinical gestalt or using the Wells or Geneva scores. The prevalence of pulmonary embolism was 27% in European patients and only 8% in US patients (moderate evidence). The Canadian practice pattern is intermediate; Anderson et al. [24] in a level 1 evidence study described an overall prevalence of pulmonary embolism of 17.7% in their randomized trial of 1417 patients with suspected pulmonary embolism who were imaged with CT pulmonary angiography versus ventilation perfusion scintigraphy. In the United States, which has a low disease prevalence among those imaged, the Pulmonary Embolism Rule-out Criteria perform well as a stand-alone probability assessment [25]. However, in populations with a higher disease prevalence, Hugli et al. [26] described a 5.4% prevalence of pulmonary embolism among PERC-negative patients. Penalzoza et al. [27] combined a gestalt assessment with the Pulmonary Embolism Rule-out Criteria in a prospective series of 959 patients from Europe who had a pulmonary embolism prevalence of 29.8% and found that the combined approach had a high negative predictive value, although these limited to moderate evidence results that require confirmation in larger clinical trials.

What Is the Role of the D-dimer Assay in the Evaluation of Suspected Pulmonary Embolism?

Summary of Evidence D-dimer is a fibrin degradation product and is not normally present in blood. Blood clots are degraded by fibrinolysis; therefore, D-dimer is typically present in the blood of patients with deep vein thrombosis or

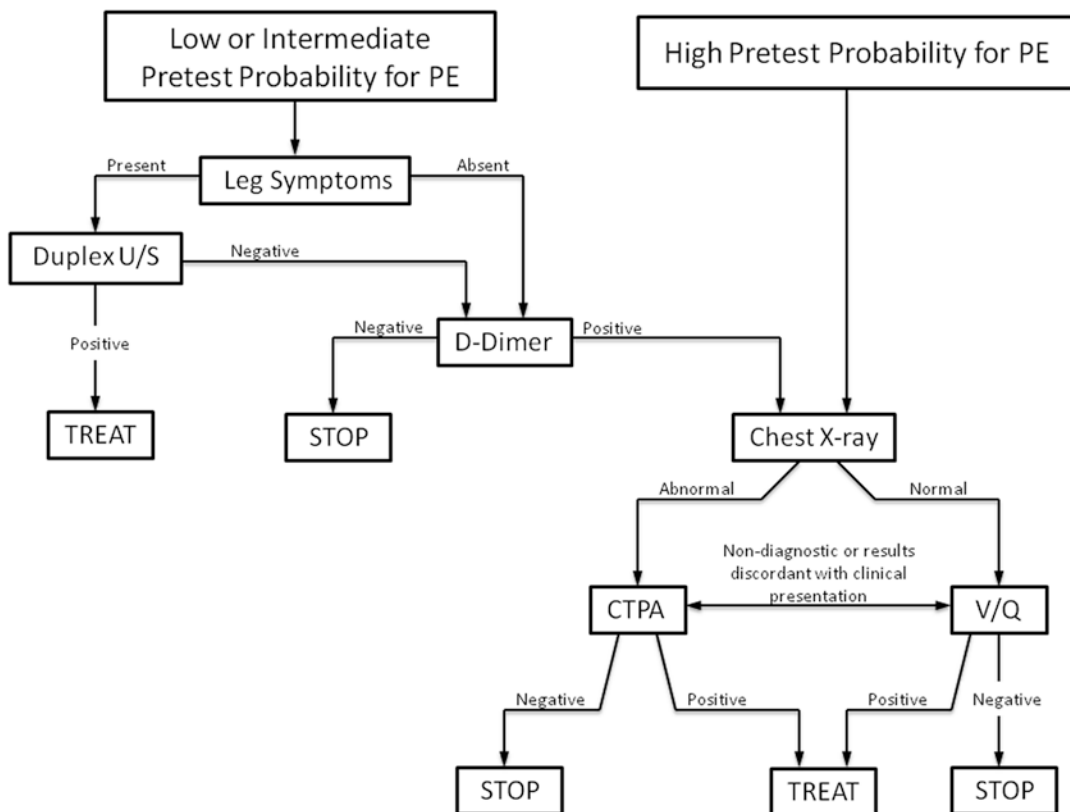


Fig. 16.1 Diagnostic algorithm for evaluation of pulmonary embolism based on clinical pretest probability. *PE* pulmonary embolism, *U/S* ultrasound, *CTPA* computed tomographic pulmonary angiography, *V/Q* ventilation/perfusion study

pulmonary embolism. However, it is not specific for thromboembolic disease, and D-dimer is present in the blood in a variety of circumstances and illness including but not limited to trauma, surgery, pregnancy, inflammation, malignancy, liver disease, and disseminate intravascular coagulation [28]. D-dimer concentrations are also normally higher as people age [29]. The D-dimer assays represent a variety of monoclonal antibody tests of differing sensitivities and rapidity. The rapidity of the assay impacts its clinical utility in the acute setting, and higher thresholds may be appropriate for older patients. The high sensitivity D-dimer assays have been found to be most useful in ruling out pulmonary embolism when the results are negative. Imaging can safely be obviated for those patients who have a low clinical probability of pulmonary embolism and a negative D-dimer assay (moderate evidence) [30, 31]. In contrast, the D-dimer assay does not have

a role in evaluating patients who have a high clinical probability of pulmonary embolism; those patients should directly undergo imaging.

Supporting Evidence Carrier et al. [31] in a level 1 evidence, systematic review evaluated the safety of withholding anticoagulation in patients with suspected pulmonary embolism who had a low or intermediate pretest probability of disease and a negative VIDAS D-dimer—a highly sensitive automated D-dimer assay. The review included 5622 patients from seven studies who had pretest probabilities assessed using clinical gestalt, Wells, or Geneva scores that were non-high clinical probability. Forty percent (2248) had a negative VIDAS D-dimer. This group's rate of thromboembolic disease at 3-month follow-up (a commonly used metric for the false-negative rate) was very low at 0.14%, with a 1–2% false-negative rate as the general target (strong evidence).

However, it is known that the serum concentration of D-dimer increases with age. Schouten et al. [32] performed a meta-analysis of 13 studies comprised of 12,497 older patients with suspected pulmonary embolism who had clinical probability assessments and D-dimer testing (strong evidence). For those with non-high clinical probability, conventional D-dimer thresholds demonstrated decreased specificity with age at 57% for 51–60 years, 39% for 61–70 years, 25% for 71–80 years, and 15% for those older than 80. However, age-adjusted D-dimer thresholds much improved the specificity, which increased at every decade and ranged from 62% to 35% with good sensitivities of over 97% for each age group.

What Is the Role of Various Imaging Modalities in Establishing a Diagnosis of Pulmonary Embolism?

Chest Radiography

Summary of Evidence Chest radiography plays a useful but limited role in patients suspected of having pulmonary embolism. The radiograph may depict an alternative diagnosis that explains the patient's symptoms such as a pneumothorax, mucus plugging with lobar collapse, rib fracture, or an unsuspected tumor. Results of chest radiography have also proven to be useful in triaging patients who require further imaging to either ventilation-perfusion scintigraphy (V/Q scan)—when the radiograph is normal—or to CT in the presence of a significant radiographic abnormality. The performance characteristics of V/Q scans are enhanced in the setting of a normal radiograph [33].

A number of chest radiographic abnormalities have been described in the setting of pulmonary embolism. These include a prominent central pulmonary artery (Fleischner sign) due to either a central embolus or pulmonary hypertension and regional lung oligemia at the site of the embolus (Westermark sign). Ischemic injury to the lung from a pulmonary embolism can manifest as atelectasis secondary to decreased surfactant production or pulmonary parenchymal hemorrhage or infarction. Hemorrhage and infarction both pres-

ent with broad-based peripheral parenchymal opacification abutting a pleural surface often with a truncated apex (Hampton's hump). The truncated apex, typical of a pulmonary infarct, differs from wedge-shaped infarcts in other organs, due to the bronchial arterial supply of the lung which nourishes the more central lung subtended by the pulmonary embolism, protecting it from infarction. Pleural effusion, usually small and hemorrhagic, is common in patients with pulmonary embolism and infarction. However, none of these radiographic signs reliably distinguish between patients with and without pulmonary embolism in the relevant population.

Supporting Evidence Worsley et al. [33] reviewed the chest radiographs for 1063 patients from the original PIOPED study [34], which compared V/Q scanning with conventional pulmonary angiography. The prevalence of pulmonary embolism in PIOPED was 36%, and the majority of patients (68%) were inpatients. The chest radiograph was normal in only 12% of patients with pulmonary embolism (moderate evidence). Atelectasis and parenchymal opacities were the most common findings, but the prevalence of these abnormalities did not differ significantly between those with and without pulmonary embolism. More specific radiographic findings of pulmonary embolism such as the Westermark and Fleischner signs and Hampton's hump were also poor predictors of pulmonary embolism. The authors therefore concluded that the main role of chest radiography was to exclude alternative diagnoses and to guide the interpretation of the V/Q scan.

Stein et al. [35] evaluated the impact of an emergency department protocol that triaged patients with suspected pulmonary embolism who merited imaging on clinical grounds to V/Q scan or to CT pulmonary angiography based on the results of chest radiography; V/Q scans were recommended for patients with normal radiographs. Over the 2-year study period which included the year before and the year after initiation of the chest radiographic triage protocol, 4115 imaging examinations were performed. Before the protocol was initiated, 62% of imaging for suspected pulmonary embolism was with

CT, while the year after the protocol was initiated, 57% of imaging was with V/Q. This trend toward more V/Q studies has increased over the ensuing years up to the present. The false-negative rate as measured by 90-day venous thromboembolism recurrence was in the 1% range for each year and for both imaging modalities (moderate evidence).

Ventilation-Perfusion Scintigraphy (V/Q Scan)

Summary of Evidence V/Q scans served as the dominant noninvasive imaging test for suspected pulmonary embolism until the development of CT pulmonary angiography, which overtook V/Q in 2001 in the United States for imaging patients with suspected pulmonary embolism. Since then, V/Q scans have remained a first line imaging modality for patients with renal insufficiency or contraindications to intravenous contrast. V/Q scans confer a substantially lower radiation dose to the patient than CT and demonstrate excellent performance characteristics in patients with normal chest radiographs [36]. When patient outcomes are used as the reference standard, clinically significant pulmonary embolic disease is just as effectively demonstrated and excluded with V/Q scans as with CT (strong evidence) [24, 37]. One of the confusing aspects of V/Q scanning was the probability language used in reporting the results, in contrast to the “positive” or “negative” results of CT. Recently, some centers have adopted a trinary interpretation scheme for V/Q scans as follows: “positive for PE,” “no evidence for PE,” and “nondiagnostic.” This trinary interpretation scheme has similar diagnostic value to the probability interpretation scheme but has the advantage of easily understandable results [38]. A negative V/Q scan has a negative predictive value in the 98–99% range, similar to the negative predictive value of CT (strong evidence) [34].

Supporting Evidence Anderson et al. [24] performed a randomized clinical trial of V/Q scan versus CT pulmonary angiography in 1417 patients with suspected pulmonary embolism who had an intermediate or high pretest probability of pulmonary embolism using the Wells score

or a positive D-dimer assay. The primary outcome was development of thromboembolic disease within 3 months after a negative work-up for suspected pulmonary embolism (false-negative rate). Results of the study showed no significant difference between the V/Q scan and CT groups in the false-negative rate, which was $\leq 1\%$ for both (strong evidence). However, pulmonary emboli were diagnosed 50% more frequently among patients who were imaged with CT compared with those imaged with V/Q scanning (17.7% vs. 11.7%). This raised concern that a substantial proportion of the excess pulmonary emboli diagnosed on CT compared with V/Q scanning were not of clinical significance and represented over diagnosis which in turn, led to overtreatment with anticoagulation in these patients.

V/Q scanning confers a substantially lower radiation dose to the patient than does CT. Mettler et al. [36] in their catalogue of estimated doses published in 2008 described an estimated effective dose of 2.2 mSv for V/Q scanning. In contrast, mean CT pulmonary angiography dose estimates have been as high as 10 mSv in the real-world, nonoptimized setting [39]. When Stein et al. [35] used the chest radiograph to triage patients with normal chest radiographs to V/Q scanning and those with abnormal radiographs to CT, they documented a drop in average annual estimated radiation exposure from 8 mSv to 6.4 mSv among their population of emergency department patients who were imaged for suspected pulmonary embolism. This decrease in radiation exposure was more pronounced among women younger than 40 years (from 7.2 mSv to 4.9 mSv) who are more biologically susceptible to the detrimental effects of radiation exposure. However, advances in CT technology and rigorous adherence to CT dose reduction strategies have begun to shift the dose curve downward for CT [40].

CT Pulmonary Angiography

Summary of Evidence CT pulmonary angiography is currently the most commonly performed imaging modality in patients suspected of having pulmonary embolism. CT superbly demonstrates pulmonary emboli when present, and physicians

readily appreciate the direct demonstration of the pulmonary artery anatomy and pulmonary emboli. The heart can and should be evaluated on every positive CT pulmonary angiogram in order to diagnose or exclude the diagnosis of right heart dysfunction (strain), which is associated with an increased 30-day mortality in patients with pulmonary emboli [41]. Pulmonary infarction, when present, is also well demonstrated on CT as a peripheral lung opacity with a broad base and a truncated apex which has diminished enhancement and internal lucencies, a configuration that reflects the lung's dual blood supply [42]. When pulmonary infarction is present, a hemorrhagic effusion is often present and the clinical presentation includes pleuritic chest pain and hemoptysis. Chronic thromboembolic disease and pulmonary artery tumors can have overlapping presentations with acute pulmonary embolism and can be readily differentiated from acute pulmonary embolism on CT.

The negative predictive value of CT is excellent and similar to V/Q scans, in the 98–99% range (strong evidence) [43]. Even when a negative CT is technically limited, the recurrence rate of pulmonary embolism is very low with a negative predictive value similar to that of an adequate CT [44]. Advances in CT technology have led to an expectation of routine superb high-resolution images, which have resulted in depiction of isolated small subsegmental pulmonary emboli in a higher proportion of patients than with older CT technology [45]. Because the pulmonary capillary bed physiologically traps small clots and thus protects the systemic circulation, the clinical significance of these small pulmonary emboli is unclear [2, 46]. In fact, there is growing evidence that a proportion of the pulmonary emboli demonstrated on CT represent over diagnosis of clinically unimportant disease [47].

Supporting Evidence The PIOPED II study [43] prospectively evaluated 824 patients from multiple centers who had suspected pulmonary embolism and were evaluated with CT pulmonary angiography between 2001 and 2003. Each patient also underwent a clinical probability assessment with the Wells score. The CT results

were compared with a composite reference standard which required results of a V/Q scan, venous ultrasound, or digital subtraction angiography to ultimately determine the presence or absence of pulmonary embolism. The CT angiogram was technically adequate in 94% of patients in whom CT demonstrated a sensitivity of 83% and specificity of 96% for pulmonary embolism (strong evidence). However, when the clinical probability was discordant with the CT results, the performance of CT declined substantially. A positive CT in a patient with high clinical probability was 96% accurate, but the positive predictive value declined in 58% for those with a low clinical probability. Similarly, a negative CT in a patient with a low clinical probability of pulmonary embolism had a negative predictive value of 96%, which declined to 60% in patients who had a high clinical probability of disease [43].

Duplex Ultrasound of the Lower Extremity

Summary of Evidence Pulmonary embolism is a component of venous thromboembolic disease that includes deep vein thrombosis. In fact, a majority of pulmonary emboli originate from lower extremity deep vein thrombosis. Additionally, even in the absence of pulmonary symptoms, nearly half of patients with proximal deep vein thrombosis have pulmonary embolism [48]. As anticoagulation is the treatment for both deep vein thrombosis and pulmonary embolism, the diagnosis of deep vein thrombosis leads to the appropriate treatment of both diagnoses. Duplex ultrasound of the lower extremities is the modality of choice for evaluating the deep veins of the lower extremity for thrombi with equivalent diagnostic performance to conventional and CT venography [49]. Thrombi below the knee are uncommonly of clinical significance; therefore the popliteal vein is typically the most proximally examined vein. Lower extremity duplex ultrasound evaluations include the common femoral, femoral (formerly known as superficial femoral vein), and popliteal vein to the tibioperoneal trunk [50]. Duplication of the femoral vein occurs in about 10% of the population, and evaluation of

only one vein in a patient with duplication of the femoral venous system is a cause of false-negative results [51]. The ultrasound diagnosis of deep vein thrombosis relies on lack of compressibility of a thrombus-containing vein, with compression applied perpendicular to and along the entire course of each vein. Other signs of deep vein thrombosis include enlargement of the vein and abnormal spectral Doppler such as monophasic flow (or other patterns of loss of the normal respirophasic flow) and lack of augmentation with calf compression. Acute thrombus is often anechoic and cannot be directly visualized on ultrasound, but subacute and chronic thrombi demonstrate increasing echogenicity over time [52]. CT venography after CT pulmonary angiography has a similar performance to lower extremity ultrasound in demonstrating deep vein thrombosis and can also demonstrate iliac and inferior vena cava thrombosis. After much study, CT venography has not achieved widespread acceptance in clinical practice largely due to the risks of radiation exposure without substantive incremental benefit in patient outcomes compared with ultrasound, although it remains of value in some patients [53].

Supporting Evidence Duplex ultrasound of the lower extremity does not expose the patient to ionizing radiation and has demonstrated comparable diagnostic performance to conventional and CT venography of the lower extremities. Appelman et al. [52] in a level 2 evidence study prospectively evaluated the diagnostic performance of lower extremity ultrasound compared with conventional venography in 112 patients who were clinically diagnosed with deep vein thrombosis. With venography as the reference standard, 46% (52/112) were ultimately diagnosed with proximal deep vein thrombosis and vein compressibility on ultrasound which represents a sensitivity and specificity of 96% and 97%, respectively. Using data from PIOPED II, Goodman et al. [54] compared ultrasound of the lower extremity with CT venography for the 711 patients who had adequate imaging with both modalities. They found a 96% concordance between ultrasound and CT venography for the

presence or absence of deep vein thrombosis (moderate evidence).

Echocardiography

Summary of Evidence Although not a primary imaging modality in patients suspected of having pulmonary embolism, echocardiography does play a role in its diagnosis and has prognostic implications in a subset of patients. Echocardiography may be performed in patients with pulmonary embolism who have nonspecific clinical presentations. In that setting, the echocardiographic findings of right ventricular dilatation, which is present in about 25% of patients with pulmonary embolism, and other signs of right heart pressure overload and right heart failure including dilated right atrium and inferior vena cava, may suggest the correct diagnosis. A more specific echocardiographic sign of pulmonary embolism is the “McConnell sign” which describes decreased contractility of the right ventricular free wall compared to the apex in patients with pulmonary embolism. Rarely, an embolism in transit may be directly observed within the right atrium or right ventricle. In patients with acute hemodynamic instability, an echocardiogram that excludes right ventricular dysfunction will guide the work-up away from acute pulmonary embolism [55]. Echocardiography can also be used in risk stratification of patients who have been diagnosed with pulmonary embolism who are hemodynamically unstable; right ventricular dysfunction predicts short-term morbidity and mortality [56, 57]. However, in hemodynamically stable patients with pulmonary embolism, the imaging finding of right heart dysfunction on echocardiography has poor predictive value.

Supporting Evidence Kucher et al. [56] evaluated a management strategy that included early echocardiography for evaluating hemodynamically unstable patients with suspected pulmonary embolism. They found echocardiography to be valuable in a prospective series of 204 consecutive European patients with suspected pulmonary embolism who had a pulmonary embolism prevalence of 48% (98/204). Probability of disease was assessed using the Wells score. Heart rate

and blood pressure were measured and a shock index was derived by dividing the heart rate by the systolic blood pressure. A shock index ≥ 1 was considered a marker for hemodynamic instability. 10% (21/204) of patients were hemodynamically unstable with a high clinical probability of pulmonary embolism and were evaluated by echocardiography within 30 min. One-third (7/21) of the unstable patients had normal right ventricular function, and the diagnosis of pulmonary embolism as a cause of hemodynamic instability was excluded; this was confirmed with CT pulmonary angiography. Stable patients with low clinical probability underwent D-dimer testing; 139 of whom underwent subsequent CT pulmonary angiography. Hemodynamically stable patients with central pulmonary embolism underwent echocardiography. Echocardiographic signs of right heart dysfunction were present in 62% and this served as a trigger for reperfusion therapy in 66% (14/21) of unstable and 35% (9/26) of stable patients with a central clot. The 30-day pulmonary embolism mortality was 5% with all deaths attributed to right ventricular failure. Echocardiographic signs of right ventricular failure, however, were not associated with 3- or 6-month mortality (moderate evidence).

In a larger series of stable patients from the International Cooperative Pulmonary Embolism Registry (ICPR), Kucher et al. [57] evaluated 1035 patients with pulmonary embolism who underwent echocardiography within 24 h of diagnosis. Thirty-nine percent (405/1035) of patients had right ventricular hypokinesis on echocardiography, and this subset had a significantly lower 30-day survival than those without RV hypokinesis on echocardiography (84% vs. 91%, $p < 0.001$). RV hypokinesis as an independent predictor of early death remained significant even after multivariate adjustment (moderate evidence).

What Evaluation Is Appropriate for Pregnant Women with Suspected Pulmonary Embolism?

Summary of Evidence Pulmonary embolism is uncommon in pregnant women, but is a leading

cause of maternal mortality in the United States and generally in the developed world. Suspected pulmonary embolism in pregnancy requires particular attention because the risk-benefit analysis for any work-up and treatment must include both the mother and the fetus in the calculation. Additionally, the physiologic changes of pregnancy have some overlap with the symptoms of thromboembolic disease, thus increasing diagnostic uncertainty [39]. Clinical practice guidelines for evaluating pulmonary embolism in pregnant women were developed in 2012 by the American Thoracic Society along with the Society of Thoracic Radiology and endorsed by the American College of Obstetrics and Gynecology [58]. They created a practical diagnostic algorithm that gives weight to keeping maternal and fetal radiation exposure as low as possible in addition to yielding diagnostically useful information (Fig. 16.2). The fetus is well recognized to be vulnerable to the detrimental effects of ionizing radiation; it is less well recognized that maternal breast tissue is particularly vulnerable to ionizing radiation due to its physiologic proliferation during pregnancy. Therefore, in women with symptoms of deep vein thrombosis leg ultrasound, a nonionizing radiation test is recommended as the first choice imaging modality. For women without symptoms of deep vein thrombosis, the lower-dose combination of chest radiography and lung scintigraphy are given preference over CT pulmonary angiography for women whose chest radiographs are normal. Low-dose perfusion-only lung scintigraphy (low-dose Q scan) confers a substantially lower radiation dose to the mother and to the fetus and is a good choice for imaging pregnant women with suspected pulmonary embolism [59].

The seven specific recommendations of the joint society guidelines are summarized here [58]:

1. D-dimer testing is not recommended to exclude pulmonary embolism in pregnant women.
2. If clinical signs of deep vein thrombosis are present, then ultrasound of the lower extremities should be performed, which if positive,

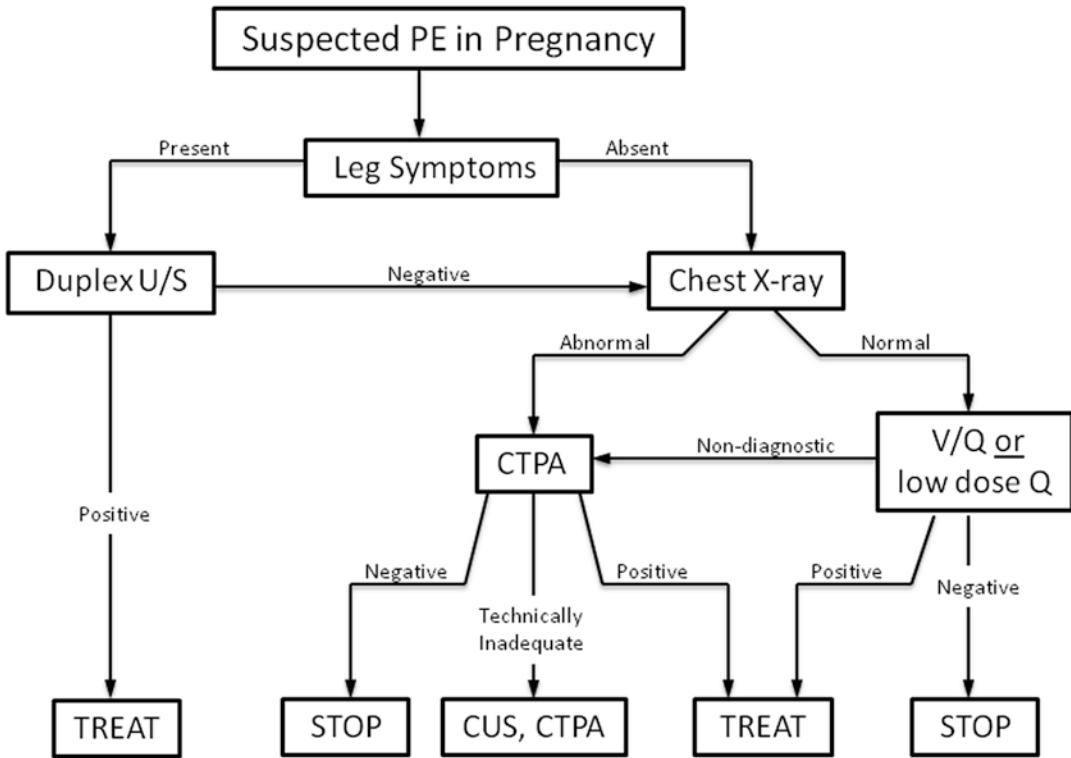


Fig. 16.2 Suggested algorithm for evaluation of pulmonary embolism in pregnancy. *U/S* ultrasound, *CTPA* computed tomographic pulmonary angiography, *V/Q* ventilation/perfusion study, *low-dose Q* low-dose perfusion-only lung scintigraphy. [Adapted with kind permission of the American Thoracic Society from Leung

AN, Bull TM, Jaeschke R, Lockwood CJ, Boiselle PM, Hurwitz LM, et al. An official American Thoracic Society/Society of Thoracic Radiology clinical practice guideline: evaluation of suspected pulmonary embolism in pregnancy. *American Journal of Respiratory and Critical Care Medicine*. 2012;184(10)]

treat with anticoagulation; if negative, continue with further evaluation.

3. If clinical signs of deep vein thrombosis are absent, further evaluation for deep vein thrombosis is not recommended, and the work-up should proceed to pulmonary vascular evaluation.
4. Chest radiography is the first recommended chest imaging examination and the first imaging test that exposes the patient to ionizing radiation, albeit a low dose.
5. Lung scintigraphy rather than CT pulmonary angiography is recommended for women whose chest radiograph is normal.
6. If scintigraphy is nondiagnostic and further testing is warranted, CT pulmonary angiography is recommended.

7. If the chest radiograph is abnormal, then CTPA is the next recommended imaging test.

Supporting Evidence The joint society guidelines can be quite useful diagnostically; however, the publication notes that there is a paucity of high-quality research on this important clinical problem, and therefore the level of evidence for all of the recommendations is insufficient. Astani et al. [60] retrospectively compared the radiation dose of CT pulmonary angiography, perfusion scintigraphy, and V/Q scanning in 53 pregnant women with suspected pulmonary embolism and found substantially lower maternal doses and slightly lower fetal doses for scintigraphy compared with nonoptimized clinical CT scans performed

between 2006 and 2012 (limited evidence). The effective dose, breast absorbed dose, and uterus/fetus absorbed doses were estimated. The effective mean doses for CT and perfusion scintigraphy were 21 and 1.04 mSv, breast absorbed doses were 44 and 0.28 mGy, and uterus absorbed/fetus absorbed doses were 0.46 and 0.25 mGy, respectively. When ventilation scintigraphy was added to the perfusion scan, the scintigraphic doses increased to an effective dose of 1.29 mSv, a breast absorbed dose of 0.37 mGy, and a fetal absorbed dose of 0.40 mGy.

Perisinakis et al. [61] calculated maternal and fetal doses for different maternal sizes and fetal gestational ages using a phantom and a 256 detector row CT scanner. They estimated the maternal effective dose to be 1 mSv and fetal/embryo effective dose to be 0.05 mGy, with maternal and fetal dose increasing with maternal size and fetal dose also increasing with gestational age. Compared with low-dose perfusion scanning, the maternal dose of CT was lower, and the fetal dose was higher. However, the authors conclude that low-dose perfusion scintigraphy is overall the more dose efficient imaging modality.

What Risk Factor Prediction Tools Are Available for Determining Which Pediatric Patients Need Imaging for Pulmonary Embolism and Which Do Not?

Summary of Evidence Based on moderate evidence (level 2), the five most important risk factors for predicting the probability of pulmonary embolism in pediatric patients are indwelling central venous catheter, immobilization, history of prior pulmonary embolism or deep venous thrombosis, hypercoagulable states, and excess estrogen states. If none of these factors are present, the probability of PE is 0.5%. With one or two risk factor(s), the probability increases to 8% and 62%, respectively. With any three or more risk factors, the probability is quite high at 89% [8].

Supporting Evidence In children, a risk factor for pulmonary embolism can be identified in 96–98% of cases with multiple prior studies and review articles discussing pediatric risk factors for pulmonary embolism [4–7, 62]. However, unlike adults where well-established risk stratification algorithms have been developed and widely used in clinical practice, pediatric risk factor stratification and prediction algorithms are just now coming to light. Two recent retrospective reviews have been published specifically evaluating pediatric thromboembolic risk factors and how they can be used to predict who is likely to have a pulmonary embolism and/or who should receive imaging evaluation [8, 63].

In the first study, the authors specifically targeted older children and young adults with their population having a mean age of 20.7 years [63]. Here, the authors retrospectively reviewed 116 pulmonary CTAs of which 16 (14%) were found to be positive for pulmonary embolism. The authors identified three risk factors significantly associated with pulmonary embolism on pulmonary CT angiography. These risk factors were cardiac disease ($p = 0.004$), history of previous PE and/or deep vein thrombosis ($p = 0.001$), and immobilization ($p < 0.001$). Using the presence of two or risk factors as a clinical threshold for imaging, the authors found a sensitivity for positive pulmonary embolism of 75% with a specificity of 99% [63].

In the second study, a retrospective review of 226 consecutive pulmonary CT angiographic studies was performed on a younger cohort than the above study [8]. All patients were in the pediatric age range with a mean age of 14.1 years (age range from 4 months to 18 years). Thirty-six cases (16%) were positive for pulmonary embolism. Here, five risk factors were found to be significantly associated with pulmonary embolism, including immobilization ($p < 0.001$), excess estrogen state ($p = 0.002$), indwelling central venous catheter ($p < 0.001$), hypercoagulable state ($p = 0.003$), and prior deep vein thrombosis and/or pulmonary embolism ($p < 0.001$). Interestingly, cardiac disease was not found to be

significantly associated with a positive diagnosis of a pulmonary embolism in this study. When none or only one risk factor was present, the probability of PE was 0.5% and 8%, respectively. The probability increased to 62% with two risk factors. With three or more risk factors, the probability of the child having a pulmonary CT angiography positive for pulmonary embolism was 89% (Fig. 16.1). Similar to the first study, using two or more risk factors as a threshold for imaging resulted in a sensitivity for a positive pulmonary embolism result of 89%, and a specificity of 94% [8].

What Are the Differences in Imaging Findings of PE in Pediatric Versus Adult Patients?

Summary of Evidence Although many of the imaging findings of pediatric pulmonary embolism are similar to those seen in adults, there is moderate evidence (level 2) to support the contention that lung parenchymal findings differ in children as compared to their adult. Most lung parenchymal findings are not significantly different in children with PE compared to those children without PE. One exception is wedge-shaped peripheral consolidation, which has been shown to be significantly associated with PE in a retrospective study of 22 pediatric patients diagnosed with PE by pulmonary CT angiography [64].

Supporting Evidence Many of the CT findings of pulmonary embolism span the age spectrum and have not been shown to be significantly different between children and adults. These findings include the presence of a partial or complete filling defect in a pulmonary artery on two consecutive images in the case of acute pulmonary embolism. With chronic pulmonary embolism, the filling defect may be eccentric and adherent to the vessel wall, there may be vessel wall thickening and vessel stenosis, and signs of recanalization of the pulmonary artery may be seen.

In terms of PE distribution, Kristaneepaiboon et al. found similar distribution in children as what is expected in adults with 37% affecting the

right lower lobe, 27% affecting the left lower lobe, 15% in the right upper lobe, 12% in the right middle lobe, and 12% in the left upper lobe. The authors also found PE at the level of the lobar pulmonary artery in 39%, the segmental pulmonary artery in 35%, the subsegmental pulmonary artery in 16%, and the main pulmonary artery in 10% [11].

In contrast to adults, Lee et al. demonstrated only wedge-shaped peripheral consolidation to be significantly associated with pulmonary embolism ($p = 0.03$). Other pleural and parenchymal abnormalities including atelectasis, linear opacities, ground-glass opacity, mosaic attenuation pattern, patchy increased attenuation, pleural effusions, and nodules/masses were not found to be significantly more likely in pediatric patients with PE compared to those without PE [64].

What New Advanced Computed Tomography Techniques Have Become Clinically Available for Imaging Pediatric Pulmonary Embolism?

Summary of Evidence Pulmonary CT angiography currently remains the imaging modality of choice for the evaluation of pediatric pulmonary embolism [65]. Despite its relatively high-radiation dose, pulmonary CT angiography has multiple advantages in that it is widely available, with sub-second scan times, and a high sensitivity and specificity for PE diagnosis. Additionally, it has the ability to give alternative diagnoses when no PE is demonstrated [66]. Recently, advanced pulmonary CT angiographic techniques have been described in an effort to further refine and perfect the CT diagnosis of PE. Dual-energy computed tomography is one such technique. However, it has undergone limited evaluation in the pediatric population. Dual-energy computed tomography perfusion imaging is attractive as it can provide both standard anatomic sequences, which can depict CT findings of acute and chronic embolism, and physiologic perfusion imaging demonstrating pulmonary

embolism-associated perfusion abnormalities. This additional information can be acquired without significantly increasing patient radiation dose. However, dual-energy CT angiography/CT perfusion can have many potential diagnostic pitfalls, leading to a false-positive diagnosis for pulmonary embolism. Thus, there is incomplete evidence to suggest that dual-energy computed tomography perfusion imaging should be routinely utilized in pediatric pulmonary embolism imaging.

Supporting Evidence Currently, no randomized, highly generalizable study has been performed evaluating standard pulmonary CT angiography with dual-energy CT angiography/CT perfusion. However, there are a number of recent review and technical innovation manuscripts expressing the benefits of dual-energy pulmonary CT angiography/CT perfusion in pediatric pulmonary embolism imaging [67–70]. Additionally, Zhang et al. recently evaluated 32 pediatric patients who received dual-energy CT angiography/CT perfusion of the pulmonary arteries. Nine (28.1%) were found to have a positive study for pulmonary embolism utilizing a comprehensive dual-energy CT angiographic evaluation including standard anatomic, perfusion, and vascular images. In comparison to standard anatomic imaging, this comprehensive scanning technique found significantly more segmental and subsegmental pulmonary emboli. However, despite these promising findings, clinical experience is currently limited, and further evidence is needed to support its incorporation into routine clinical practice.

Take-Home Tables and Figures

Table 16.1 summarizes the sensitivity and specificity of the various imaging modalities discussed above. The values in Table 16.1 are derived from studies with a wide range of evidence strength, and consequently comparison between imaging modalities must be done with caution.

Diagnostic algorithms for evaluation of suspected pulmonary embolism in adults (Fig. 16.1) and in pregnancy (Fig. 16.2) are presented.

Imaging Case Studies

Case 1

History

A 77-year-old woman presents with new onset right-sided chest pain, left leg pain and swelling, and shortness of breath.

Imaging

A portable chest radiograph was performed and compared with a radiograph from 6 weeks earlier (Fig. 16.3a, b). The new radiograph demonstrates a peripheral airspace opacity in the right lower lobe and a small right pleural effusion. The right hilum is prominent. A chest CT with contrast was performed for suspected pulmonary embolism and demonstrated pulmonary emboli in the right and left pulmonary arteries (Fig. 16.3c, d). There is a small pleural effusion and right lower lobe peripheral parenchymal opacities with a broad pleural base, a truncated apex, internal lucencies, and regions of diminished enhancement typical

Table 16.1 Summary of various imaging modalities in detection of pulmonary embolism

Modality	Sensitivity (%)	Specificity (%)	References
Chest radiography ^a	12%	82%	[33]
Ventilation-perfusion scintigraphy	82% ^b	97% ^c	[34]
CT pulmonary angiography	83%	96%	[43]
Echocardiography ^d	77%	94%	[55]

^aFor a normal radiograph

^bFor patients with high or intermediate probability V/Q scan result

^cFor patients with a high probability V/Q scan

^dFor McConnell sign—echocardiographic finding of normal wall motion at the apex of the heart and abnormal wall motion in the mid-free wall

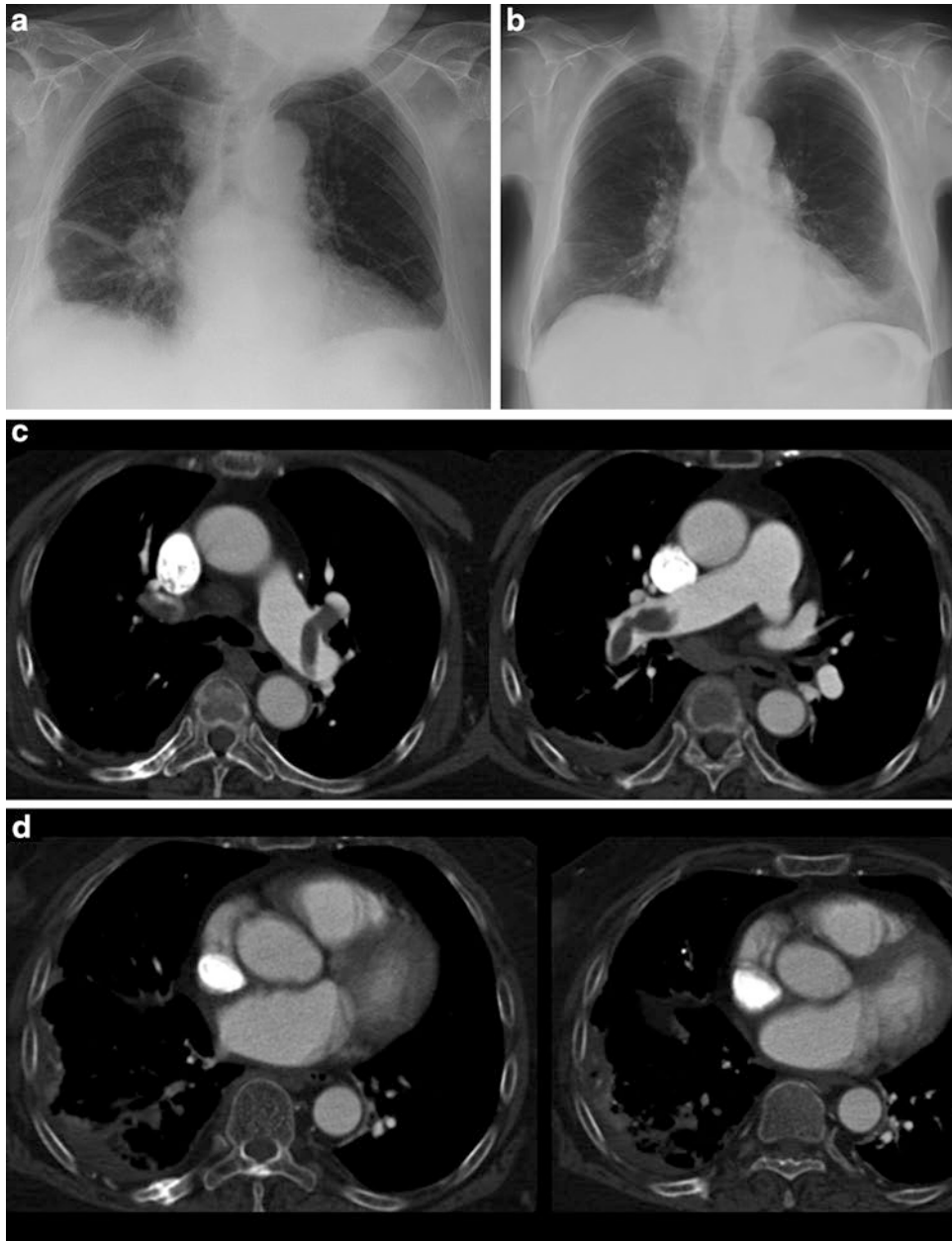


Fig. 16.3 (a–e) A 77-year-old woman presents with new onset right-sided chest pain, left leg pain and swelling, and shortness of breath. (a) Portable chest radiograph demonstrates a peripheral airspace opacity in the right lower lobe and a small right pleural effusion. The right hilum is prominent. (b) Normal chest radiograph 6 weeks prior to presentation. (c, d) A chest CT with contrast demonstrates pulmonary emboli in the right and left main pulmonary arteries and

occlusive emboli in the right lower lobe branch pulmonary arteries. There is a small pleural effusion and right lower lobe peripheral parenchymal opacities with a broad pleural base, a truncated apex, internal lucencies, and regions of diminished enhancement typical for pulmonary infarction. (e) Duplex ultrasound of the lower extremities demonstrates a noncompressible left femoral vein with absent venous flow and internal hypoechoic foci consistent with deep vein thrombosis

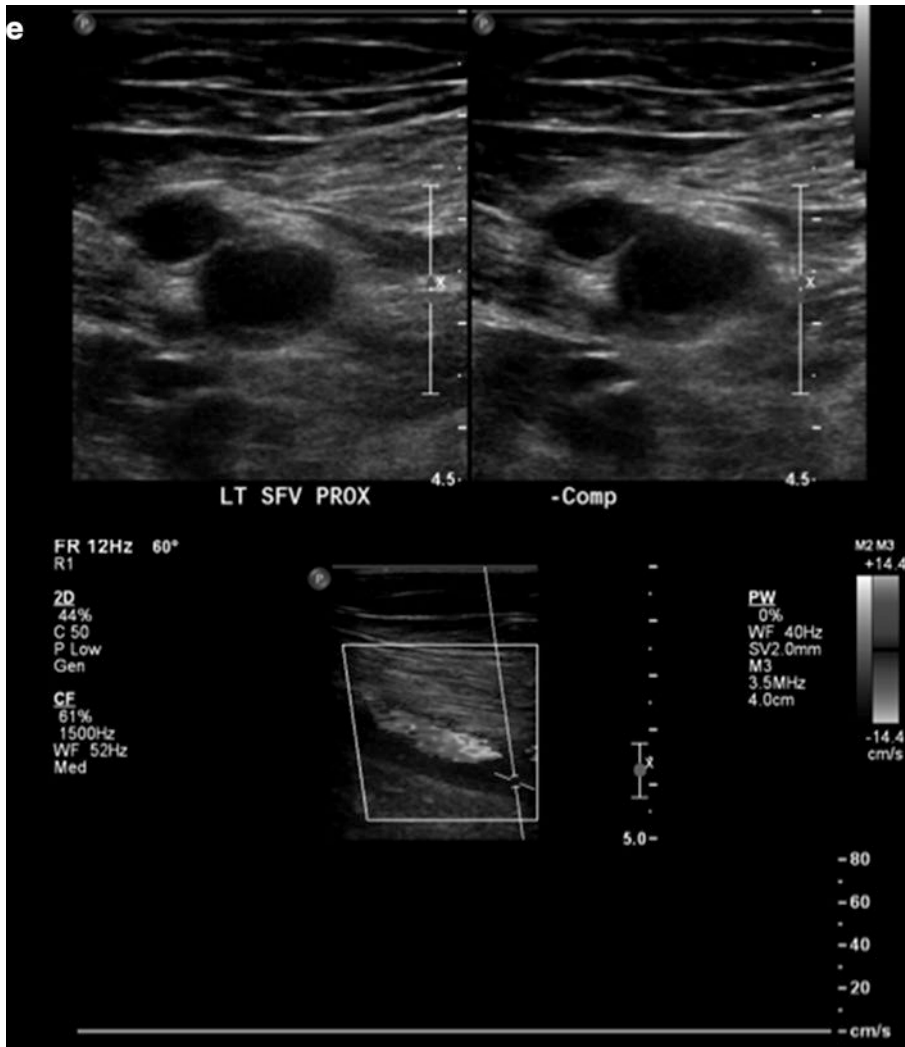


Fig. 16.3 (continued)

for pulmonary infarction. Duplex ultrasound of the lower extremities (Fig. 16.3e) demonstrated a noncompressible left femoral vein with absent venous flow and internal hypoechoic foci consistent with deep vein thrombosis.

Discussion

This case exemplifies the fact that thromboembolic disease including deep vein thrombosis and pulmonary embolism is a single disease process. The initial imaging test was a chest radiograph, which demonstrated abnormalities that are nonspecific, but typical for pulmonary

embolism with infarction. The choice of chest radiography as an initial imaging test is appropriate and most useful to triage patients with normal findings to further imaging with V/Q scan and those with abnormal radiographs to CT, as was done in this case. The CT scan then showed the presence and extent of pulmonary embolism, the pulmonary infarcts and pleural effusion as well as right heart strain. Because the patient had pain and swelling in her left leg, duplex ultrasound of the lower extremity was performed which demonstrated the deep vein thrombosis. Although treatment with anticoagu-

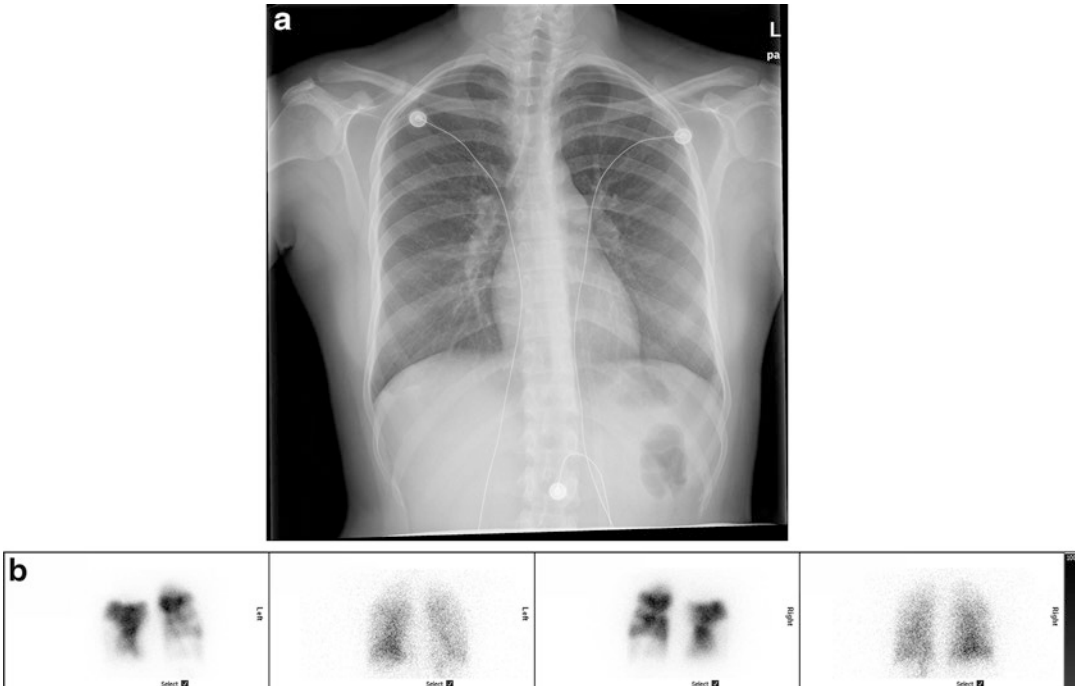


Fig. 16.4 (a, b) 18-year-old woman with antiphospholipid antibody syndrome and a right femoral deep vein thrombosis diagnosed as an outpatient and developed shortness of breath. (a) Posteroanterior chest radiograph is normal. (b) V/Q scan demonstrates lobar ventilation

perfusion mismatches in the right upper lobe, much of the right lower lobe (except for its medial basal segment) and in the apicoposterior segment of the left upper lobe, diagnostic of pulmonary embolism

lation was not altered by the additional diagnosis of deep vein thrombosis, post thrombotic syndrome is common, occurring in 15% to 50% of patients with deep vein thrombosis [71]. A definitive diagnosis of deep vein thrombosis in this elderly lady may provide insight in her follow-up care.

Case 2

History

An 18-year-old woman with antiphospholipid antibody syndrome and a right femoral deep vein thrombosis diagnosed as an outpatient, developed shortness of breath.

Imaging

A chest radiograph was performed and was normal (Fig. 16.4a). A V/Q scan (Fig. 16.4b) was then performed. It was positive for pulmonary

embolism and demonstrated lobar ventilation perfusion mismatches in the right upper lobe, much of the right lower lobe, except for its medial basal segment and in the apicoposterior segment of the left upper lobe.

Discussion

This young woman presented with symptoms of deep vein thrombosis and pulmonary embolism. Antiphospholipid syndrome is a hypercoagulable state and well-recognized risk factor for thromboembolic disease. Her young age and known hypercoagulable state suggest a high likelihood of recurrent disease and repeat imaging over her lifetime. Therefore particular attention should be paid to choosing imaging modalities that minimize exposure to ionizing radiation. Duplex of the lower extremity, which was performed as an outpatient, is an excellent choice. Because this was her initial presentation for pulmonary embolism, a decision was made to image her lungs. In

light of the normal chest radiograph, a V/Q scan, which confers a lower radiation dose, was an appropriate choice for diagnosing pulmonary embolism. Because of the increased risk of recurrent disease, the choice of a lower-dose imaging modality, to serve as a reference, will make it easier to follow her course using this lower-dose modality, should her symptoms recur in order to minimize her lifetime exposure to medical radiation.

Future Research

- Refine the diagnostic algorithms in various populations in order to guide the imaging of those who will benefit and obviate unnecessary imaging which may lead to excessive radiation exposure, intravenous contrast administration, and unnecessary treatment with anticoagulants and their attendant risks.
- Better understand the difference between small physiologic clots that are now demonstrable on CT in contrast to pulmonary thromboembolic disease with its associated short- and long-term morbidity, mortality, and risk of recurrent disease.
- To learn when it is safe to refrain from treating small pulmonary emboli in stable patients. We await results of an ongoing clinical trial [72].
- Technological development research to decrease radiation exposure for patients who warrant imaging.

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Blunt Injuries to the Thorax and Abdomen in Adults: Evidence-Based Emergency Imaging

17

Laura B. Eisenmenger, Booth Aldred,
and Marta E. Heilbrun

Key Points

- Conventional radiography is the appropriate initial screening evaluation of the chest in patients with major trauma. Computed tomography (CT) is appropriate for the definitive evaluation of abnormalities identified on initial radiography.
- Clinical evidence of hemodynamic instability or ongoing blood loss is the strongest indicator for operative intervention in the abdomen. Among patients with such indication of ongoing hemorrhage, transabdominal ultrasound can be used to identify intraperitoneal hemorrhage from solid organ injury with high specificity.
- CT has high sensitivity for surgically important injuries of the abdomen; however, sensitivity and specificity for detection of bowel and mesenteric injury remains somewhat limited.

Definition and Pathophysiology

Thoracic trauma is responsible for approximately 25% of trauma deaths in North America. Since death from thoracic trauma commonly occurs after presentation to the hospital, many of these deaths are presumed to be preventable with prompt and appropriate treatment. Important injuries leading to rapid death in trauma include aortic rupture, massive hemothorax, pericardial tamponade, and tension pneumothorax. Pulmonary contusion, myocardial contusion, tracheobronchial injury, and diaphragmatic rupture may also be fatal if not recognized and treated emergently. Fewer than 10% of chest injuries require thoracotomy for treatment [1].

Because of the large potential space of the peritoneum, large volumes of hemorrhage can occur without tamponade, and exsanguination may occur rapidly from arterial and large venous injuries in the organ parenchyma. The spleen and liver are the most frequently injured solid organs. Blunt trauma may result in compression or shear injury to the viscera, leading to hemorrhage and peritonitis. Mechanisms of injury include direct blows to the abdomen (motor vehicle accident, off-road vehicle accident, handlebars, kicks, etc.) and seatbelt injury, especially when associated with distraction-type spine injury.

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Epidemiology

Traumatic injuries are the leading cause of death of individuals between the ages of 1 and 44 in the USA [2]. In 2013, injuries were the fifth leading cause of death in the USA. Because trauma deaths tend to occur in younger individuals, there is a great burden on society in terms of years of life lost and lost lifetime earnings.

Motor vehicle accidents account for approximately half of unintentional injury deaths in the 5–24-year-old range, while falls dominate the 75+-year-old demographic. Injury death rates are higher in the elderly population (over age 75), as well as in individuals in their early 20s. Males also have higher death rates than females.

Overall Cost to Society

Corso et al. determined in the year 2000 the lifetime costs of injury in the USA at \$80 billion in direct costs and \$326 billion for lost productivity [3]. In 2004, the Agency for Healthcare Research and Quality determined that injuries were responsible for 1.9 million hospitalizations, accounting for 5% of all hospital stays [4]. These hospitalizations cost \$19.5 billion, accounting for 6.6% of total hospital care costs in the USA. An injury-related hospital stay costs approximately 37% more than a noninjury-related hospitalization [5]. Hospital stays for injuries also had a higher in-hospital mortality rate than all other conditions.

Goals of Imaging

The goals of imaging in chest and abdominal trauma are twofold. Initial imaging must allow for rapid identification of life-threatening injuries to enable treatment of the injuries in the initial hour after presentation of the patient to the hospital. Secondary imaging provides a detailed evaluation of all injuries potentially leading to morbidity and mortality.

Methodology

A search of the MEDLINE/PubMed (National Library of Medicine, Bethesda, MD) was performed using a single or combination of MeSH and free terms *wound, injury, blunt abdominal trauma or blunt thoracic trauma and diagnostic imaging, ultrasonography, tomography, X-ray computed tomography, multidetector computed tomography or radiography, and diagnosis, diagnostic accuracy, or sensitivity specificity*. The bibliographies of relevant articles were searched for other potentially relevant articles. No time limits were applied for the searches, which were repeated up to several times up to April 16, 2015. Limits included English language, abstracts, and human subjects.

Discussion Issues

What Imaging Is Appropriate for Adult Patients with Blunt Trauma to the Chest?

Summary of Evidence

- Portable chest radiography is an appropriate initial imaging test to evaluate blunt thoracic trauma, demonstrating high sensitivity for clinically important disease (moderate evidence) [5].
- CT or computed tomographic angiography (CTA) may be necessary to evaluate abnormalities identified on conventional radiography (moderate evidence).
- CT or CTA may also be used as initial imaging in cases of high-impact trauma where extensive intrathoracic and vascular injury is suspected (moderate evidence) [6].
- The National Emergency X-Radiography Utilization Study (NEXUS) Chest decision instrument criteria may be useful to risk stratify those patients who need additional imaging after radiography (moderate evidence).
- Patients with a normal CXR may not need a subsequent CT (limited evidence).

Supporting Evidence In the setting of blunt chest trauma, neither chest radiography (CXR) nor computed tomography (CT) reveals clinically important findings in the majority of patients. Despite this, chest imaging is the most frequently performed radiography during blunt trauma patient evaluation. The CXR is recommended for almost all blunt trauma victims by current Advanced Trauma Life Support (ATLS) guidelines [7, 8]. This approach exposes a disproportionately young population to ionizing radiation [9, 10]. Studies that do not identify actionable disease or otherwise dictate patient management create unwarranted cost and place a strain on healthcare systems related to the time and resources required to process and interpret uninformative studies [11].

If chest trauma is suspected, however, thoracic imaging is indicated. Many treatable chest injuries are associated with significant mortality. This was confirmed in by a recent systematic review performed in order to characterize the risk factors for mortality in blunt chest wall trauma patients. Combining the results of 29 studies, the analysis by Battle et al. found a combined odds ratio of 1.98 (1.86–2.11, 95% CI), 2.02 (1.89–2.15, 95% CI), 2.43 (1.03–5.72, 95% CI), and 5.24 (3.51–7.82) for mortality for blunt chest wall trauma patients aged 65 years or more, with three or more rib fractures, preexisting conditions, and pneumonia, respectively [12]. These rib fractures are best detected on radiography and/or CT [12]. The studies included in the analysis were of significant variability in quality, making it difficult to draw strong conclusions attributing the absolute risk conferred to a patient from rib fractures specifically.

In order to better determine in whom chest imaging is warranted and how much, a multi-institution trail (NEXUS Chest) was undertaken to determine if a clinical decision tool could be employed to reduce imaging without compromising clinical outcomes [13]. In the NEXUS Chest, trial criteria were established to indicate when it was appropriate to obtain chest imaging in blunt trauma. Thoracic injury seen on chest imaging (TICI) was defined as the presence of a pneumothorax, hemothorax, aortic or great vessel injury,

two or more rib fractures, ruptured diaphragm, sternal fracture, and pulmonary contusion or laceration seen on radiographs. Thoracic trauma was divided into thoracic trauma of major clinical significance, minor clinical significance, and no clinical significance [13]. Thoracic trauma of major clinical significance included aortic or great vessel injury, ruptured diaphragm, pneumothorax which received evacuation procedure, hemothorax which received drainage procedure, sternal fracture which received surgical intervention, multiple rib fractures which received surgical intervention or epidural nerve block, or pulmonary contusion which received mechanical ventilatory assistance of any type for management. Thoracic trauma of minor clinical significance included pneumothorax which received no evacuation procedure but observed as inpatient >24 h, hemothorax which received no drainage procedure but observed as inpatient for >24 h, sternal fracture which received no surgery but had in-hospital pain management or observed as inpatient >24 h, sternal fracture with no surgical intervention and no inpatient observation, multiple rib fractures which received in-hospital pain management or observation >24 h, multiple rib fractures with no surgical intervention and no inpatient observation, or pulmonary contusion or laceration requiring no mechanical ventilatory assistance but observed >24 h. Thoracic trauma of no clinical significance included hemothorax with no surgical intervention and no inpatient observation, pneumothorax with no surgical intervention and no inpatient observation, pneumomediastinum without pneumothorax requiring no inpatient observation, or pulmonary contusion or laceration requiring no mechanical ventilatory assistance, no surgical intervention, and no inpatient observation.

The NEXUS Chest decision instrument criteria were defined as involvement of the following: a patient older than 60 years, a rapid deceleration mechanism (defined as a fall >20 feet [>6.0 m] or motor vehicle crash >40 mph [>64 km/h]), the presence of chest pain, intoxication, abnormal alertness/mental status, distracting painful injury, and/or tenderness to chest wall palpation. Of 9905 enrolled patients in the NEXUS Chest trial

[13], thoracic injury was seen on chest imaging in 1478 (14.9%) patients with 363 (24.6%) of these having major clinical significance, 1079 (73.0%) minor clinical significance, and 36 (2.4%) no clinical significance. The most common diagnoses were multiple rib fractures, pulmonary contusion or laceration, and pneumothorax seen in 67.4%, 39.9%, and 35.7% of patients with TICI, respectively. The NEXUS Chest decision instrument had a sensitivity of 98.8% (95% CI, 98.1%–99.3%), an NPV of 98.5% (95% CI, 97.6%–99.1%), and a specificity of 13.3% (95% CI, 12.6%–14.1%) for the prediction of TICI. The sensitivity and NPV for clinically major TICI were 99.7% (95% CI, 98.2%–100.0%) and 99.9% (95% CI, 99.4%–100.0%), respectively, and the sensitivity and NPV for clinically major or minor TICI were 99.0% (95% CI, 98.2%–99.4%) and 98.7% (95% CI, 98.1%–99.3%), respectively. From these findings, it is suggested that if all of the NEXUS Chest decision instrument criteria are absent, there is very low risk for intrathoracic injury, and chest imaging is not indicated. If one or greater of the criteria are present, intrathoracic injury cannot be excluded and chest imaging may be indicated. With the low specificity of NEXUS Chest decision instrument, implementation will likely spare a low percentage of patients from imaging; however, given the high frequency of trauma-related chest imaging, this could translate into substantial resource savings and decreased radiation exposure.

A retrospective study after the original NEXUS Chest trial collected data from two large urban level 1 trauma centers on patients from July 2007 through March 2011 who presented with trauma in order to examine the question of whether thoracic CT is necessary after a negative CXR [14]. Of the 3639 participants, 2848 (78.3%) had CXR alone and 791 (21.7%) had CXR and chest CT. CT followed a normal CXR result in 589 patients. Of these, 82.0% (95% CI, 78.7–84.9%) had normal CT results and 18.0% (95% CI, 15.1%–21.3%) had CTs diagnosing injuries. These injuries included mostly rib fractures, pulmonary contusion, and incidental pneumothorax. Only 2.0% (95% CI, 1.2%–3.5%) had injuries classified as clinically major, 13.2%

(95% CI, 10.7%–16.2%) were clinically minor, and 2.7% (95% CI, 1.7%–4.4%) were clinically insignificant. Of 202 patients with CXRs suggesting injury, 87.6% (95% CI, 82.4%–91.5%) had chest CTs confirming injury, and 12.4% (95% CI, 8.5%–17.6%) had no injury on CT. These findings suggest that while a chest CT after a normal CXR result in patients with blunt trauma does detect injuries, most will not lead to significant changes in patient management.

Rodriguez et al. [15] performed a more recent multicenter NEXUS Chest CT trial from September 2011 to May 2014 prospectively enrolling blunt trauma patients over 14 years old. This trial sought to derive and validate two decision instruments (DIs) for selective chest CT in adult blunt trauma patients, similar to the prior NEXUS Chest CT trial. In this study, the investigators employed recursive partitioning to derive two DIs: Chest CT-All maximized sensitivity for all injuries and Chest CT-Major maximized sensitivity for only major thoracic injuries (while increasing specificity). They performed a validation phase employing similar methodology to prospectively test the performance of both DIs. 11,477 total patients were enrolled in this study with 6002 patients in the derivation phase and 5475 patients in the validation phase. The derived Chest CT-All DI consisted of (1) abnormal chest X-ray, (2) rapid deceleration mechanism, (3) distracting injury, (4) chest wall tenderness, (5) sternal tenderness, (6) thoracic spine tenderness, and (7) scapular tenderness. The Chest CT-Major DI had the same criteria without rapid deceleration mechanism. In the validation phase, Chest CT-All had a sensitivity of 99.2% (95% CI 95.4%–100%), a specificity of 20.8% (95% CI 19.2%–22.4%), and a negative predictive value (NPV) of 99.8% (95% CI 98.9%–100%) for major injury and a sensitivity of 95.4% (95% CI 93.6%–96.9%), a specificity of 25.5% (95% CI 23.5%–27.5%), and a NPV of 93.9% (95% CI 91.5%–95.8%) for either major or minor injury. Chest CT-Major had a sensitivity of 99.2% (95% CI 95.4%–100%), a specificity of 31.7% (95% CI 29.9%–33.5%), and a NPV of 99.9% (95% CI 99.3%–100%) for major injury and a sensitivity of 90.7% (95% CI 88.3%–92.8%), a specificity

of 37.9% (95% CI 35.8%–40.1%), and a NPV of 91.8% (95% CI 89.7%–93.6%) for either major or minor injury. From their findings, this group estimated that using these DIs would result in a safe reduction in chest CT utilization of approximately 25%–37%, without harm to patients.

What Imaging Is Appropriate for Patients with Blunt Trauma to the Abdomen?

Summary of Evidence

- Ultrasonography (FAST—focused assessment with sonography in trauma) is the first-line test to exclude injury that would require immediate surgery and, however, is of insufficient sensitivity to dictate management of intra-abdominal organ injury and hemoperitoneum (moderate evidence).
- CT is the imaging modality of choice for evaluation of the abdomen in trauma patients (moderate evidence).

Supporting Evidence Hemodynamic status and evidence of ongoing blood loss are the strongest indicators of the need for intervention in the blunt trauma patient. Thus, initial imaging is intended to immediately and accurately detect surgically treatable hemorrhage. Patients who do not require immediate laparotomy or intervention then undergo further diagnostic testing. In fact, missed abdominal injuries (especially of the bowel and pancreas) are a well-known cause of increased morbidity and mortality in patients who survive the initial phases of multiple trauma [16–18]. Trauma patients commonly have concomitant injuries (thereby diverting the responding physicians' attention) or an altered mental state from drug and/or alcohol intoxication.

A 2012 systematic review by Nisjima et al. [19] performed to assess the precision and accuracy of symptoms, signs, laboratory tests, and bedside imaging studies to identify intra-abdominal injuries in patients with blunt abdominal trauma found that signs and symptoms that predict intra-abdominal injury are heterogeneous.

Twelve studies on the diagnostic accuracy of clinical findings and 22 studies on bedside US diagnostic accuracy studies were included in their review. These studies compared at least one finding with a reference standard of CT, diagnostic peritoneal lavage, laparotomy, autopsy, and/or clinical course. In this review, the prevalence of intra-abdominal injury in adult emergency department patients with blunt abdominal trauma among all evidence level 1 and 2 studies was 13% (95% CI, 10%–17%), with 4.7% (95% CI, 2.5%–8.6%) being clinically significant as demonstrated by requiring surgery or angiographic embolization of injuries. The presence of a seat belt sign (likelihood ratio (LR) range, 5.6–9.9), rebound tenderness (LR, 6.5; 95% CI, 1.8–24), hypotension (LR, 5.2; 95% CI, 3.5–7.5), abdominal distention (LR, 3.8; 95% CI, 1.9–7.6), or guarding (LR, 3.7; 95% CI, 2.3–5.9) suggested an intra-abdominal injury. The absence of abdominal tenderness to palpation did not rule out an intra-abdominal injury (summary LR, 0.61; 95% CI, 0.46–0.80) [19].

The initial imaging exam most commonly performed in the setting of blunt trauma is the focused assessment with sonography for trauma (FAST) exam. As a noninvasive test, the FAST exam has replaced diagnostic peritoneal lavage for initial detection of the blood in the peritoneum [20, 21]. The Association for Medical Ultrasound, in conjunction with the American College of Emergency Physicians, has issued guidelines for the performance of the FAST exam [22]. These recommend that four-quadrant imaging of the abdomen be performed to evaluate the hepatorenal fossa, pouch of Douglas, left subphrenic space, right and left paracolic gutters, as well as a subxiphoid view to examine the pericardium. A meta-analysis by Stengel et al. [23] investigated the accuracy and positive and negative predictive value for the trauma ultrasound in 2001. This analysis ultimately found 19 studies that met inclusion criteria for the purpose of investigating the diagnostic value of emergency ultrasound for detection of free fluid. Of the 19 studies, 14 were IIb (exploratory cohort study with good reference standards, clinical decision rule after derivation, or validated only on split

sample or databases) and 5 were IIIb (nonconsecutive study or without consistently applied reference standards). These 19 studies contained data on 6492 patients. Negative predictive value ranged from 0.78 to 0.99. The authors concluded that ultrasound had relatively high specificity for intraperitoneal hemorrhage, indicating high reliability if free fluid was identified. However, the sensitivity of ultrasound for intraperitoneal fluid was relatively low, with a negative likelihood ratio of only 0.24. The more recent Nishima et al. review [19], pooling data from 22 studies, found that the presence of intraperitoneal fluid or organ injury on FAST exam was more accurate than any history and physical examination findings for intra-abdominal injury (adjusted summary LR, 30; 95% CI, 20–46). A normal FAST result decreases the chance of injury detection on the reference standard test (adjusted summary LR, 0.26; 95% CI, 0.19–0.34). Symptoms and signs may be most useful in combination, particularly in identification of patients who do not need further diagnostic workup [19].

The early diagnostic evaluation of patients with severe trauma is dependent on rapid and comprehensive imaging [24]. CT is now widely considered the reference standard for the detection of blunt trauma injuries [25, 26]. CT identifies the injuries that require intervention while also ruling out injury, so that the trauma team can focus on the critical care issues [27, 28]. Given the higher sensitivity and specificity of CT compared to other modalities, diagnosis of abdominal injuries in the stable patient now relies extensively on the accurate interpretation of findings from CT examinations. For example, in one study of 2912 patients with blunt trauma, of which 340 had blunt abdominal trauma and 30 had blunt hollow viscus injury, the sensitivity and specificity of CT were 86% and 88%, respectively, whereas the sensitivity and specificity of clinical exam were 53% and 69% [29]. In a study of initial imaging with whole-body CT (pan-scan), a total of 1756 injuries were detected in 982 patients scanned. Of these, 360 patients had an Injury Severity Score (ISS) greater than 15. The sensitivity of the initial pan-scan was 86.7% for thoracic injuries, 85.7% for abdominal injuries,

and 86.2% for pelvic injuries. Specificity was 98.9% for thoracic injuries, 97.5% for abdominal injuries, and 99.8% for pelvic injuries. In total, 62 patients had 70 missed injuries, indicating a residual risk of 6.3% (95% confidence interval 4.9%–8.0%) [25].

Imaging in evaluation of blunt abdominal trauma is taking a stepwise approach with bedside US (FAST) preceding CT. A retrospective study [30] of 19,940 consecutive, predominantly blunt (89.3%) trauma patients age 18 or older admitted to a level 1 trauma center after ED evaluation from 2002 through 2011 was performed to evaluate FAST scan and CT utilization after implementation of after a point-of-care emergency ultrasound program. The percentage of patients who received FAST as the sole imaging modality for the abdomen during their trauma evaluation went from 2.0% to 21.9% while the percentage of patients who only received abdominal CT dropped from 21.7% to 2.3% over the last decade. Use of FAST increased by an average of 2.3% (95% CI 2.1 to 2.5, $P < 0.01$), while abdominal CT use decreased by the same rate annually. Patients who underwent FAST were on average younger, more likely to be male, more likely to have higher median ISS, more likely to be admitted to the ICU, more likely to go to the OR, more likely to undergo abdominal CT, more likely to have a positive result on abdominal CT, and more likely to die when compared to patients who did not receive an FAST. FAST had a sensitivity of 20.0% (CI 16.7–23.6%), specificity of 98.3% (CI 97.6–98.7%), positive likelihood ratio of 11.5, negative likelihood ratio of 0.81, PPV of 0.73, and NPV of 0.84 for predicting intra-abdominal injuries diagnosed on abdominal CT. The increasing use of FAST scanning may decrease the utilization of CT, thereby reducing radiation doses to patients and decreasing health-care costs; however, given the low sensitivity of ultrasound for predicting intra-abdominal injuries, a negative FAST scan cannot exclude intra-abdominal injury [30].

In order to determine if additional imaging is necessary after a negative FAST, Sirlin et al. undertook a retrospective study [31]. In a trauma registry with 4000 patients, 3679 patients had a

negative FAST exam, and of those 99.9% ($n = 3641$) had no injuries (true-negative findings). Among the 3641 patients with true-negative findings, 93.6% ($n = 3407$) required no additional tests and 6.4% ($n = 234$) underwent CT or other tests. Thirty-eight patients had false-negative US findings for abdominal injury. The injuries that were missed in 24 patients were nonsurgical and 14 patients required surgical intervention. Cumulatively, 65 injuries were missed including retroperitoneal hematoma ($n = 13$) and injuries to the spleen ($n = 10$), liver ($n = 9$), kidney ($n = 8$), adrenal gland ($n = 8$), and small bowel ($n = 7$). Of the 38 patients 25 had no trace of hemoperitoneum. Mean diagnostic delay until recognition of missed injury was $16.8 \text{ h} \pm 4.3$ (standard error of the mean). The missed injury was identified within 12 h in 19 of the 38 patients and within 24 h in 34. Based on these results, the authors conclude that combination of negative US findings and negative clinical observation virtually excludes abdominal injury in patients who are admitted and observed for at least 12–24 h.

What Are the Optimum Protocols for Imaging Patients with Blunt Trauma?

Summary of Evidence

- CT of the thorax is indicated if the initial CXR is abnormal (moderate evidence).
- FAST exam is a good initial test to rule out clinically significant intra-abdominal injury (limited evidence).
- The evidence is evolving as to the impact of whole-body CT vs selective CT imaging on length of stay and patient outcomes (moderate evidence).
- Modifications of a routine CT protocol may have a role in further characterizing specific injuries (limited evidence).

Supporting Evidence If imaging is indicated in blunt chest trauma, radiography remains the most common initial imaging evaluation for blunt

trauma to the chest, even if CT is to be performed. Portable chest radiography can quickly identify those emergent conditions that require treatment prior to further evaluation by CT. This includes tension pneumothorax, large hemothorax, medical device malpositioning, and aortic injury. Radiography has high sensitivity for clinically important disease [8]. Additional imaging, usually with CT or computed tomographic angiography (CTA), is often necessary to adequately evaluate abnormalities identified on conventional radiography (moderate evidence). CT has also been shown to demonstrate significant disease in patients with initially normal chest radiographs changing management in up to 20% of cases [32, 33]. CT or CTA may also be used as initial imaging in cases of high-impact trauma where extensive intrathoracic and vascular injury is suspected (moderate evidence) [6].

The NEXUS Chest decision instrument criteria include an assessment of multiple clinical variables: a patient older than 60 years, a rapid deceleration mechanism (defined as a fall >20 feet or motor vehicle crash >40 mph), the presence of chest pain, intoxication, abnormal alertness/mental status, distracting painful injury, and/or tenderness to chest wall palpation. If all of the NEXUS Chest decision instrument criteria are absent, there is very low risk for intrathoracic injury, and chest imaging is not indicated. If one or greater of the criteria are present, intrathoracic injury cannot be excluded and chest imaging with CT or CTA may be indicated [13].

A 2013 Cochrane Review performed to assess the effects of trauma algorithms that include ultrasound examinations in patients with suspected blunt abdominal trauma found only four studies that met their strict enrollment criteria [34]. By the authors' assessment, the trials were of moderate methodological quality. Pooled mortality data from three trials involving 1254 patients found that the relative risk in favor of the US arm was 1.00 (95% CI 0.50 to 2.00). Ultrasound-based pathways did have a significant impact on the volume of CT scans performed (random effects RD -0.52 , 95% CI -0.83 to -0.21). However, the authors postulate that given

the low sensitivity of ultrasound, the reduction in CT scans may either translate to a number needed to treat or number needed to harm of two. As such, there is insufficient evidence from RCTs to justify promotion of ultrasound-based clinical pathways in diagnosing patients with suspected blunt abdominal trauma [34].

CT is superior to clinical evaluation, diagnostic peritoneal lavage, and FAST scans for diagnosing important abdominal injuries [21]. Studies have suggested that “pan-scan” or total body CT of the patient can lead to more accurate and faster diagnosis, reduce time in the ED, change treatment decisions, reduce ventilation, reduce ICU and hospital days, and reduce organ failure rates; however, there is no definite improved survival [35–38]. While most in the USA perform CT based on injury severity and selective imaging, whole-body CT has been standard in many European emergency departments since the late 2000s [24, 26, 36]. This practice is based on both retrospective studies demonstrating a statistically significant immediate survival benefit despite greater injuries [36] and prospective studies showing a reduction in 30-day mortality in patients who undergo whole-body versus selective CT [26]. However, the effect of whole-body CT imaging on mortality, change of treatment, hospital stay, and length of stay in patients with severe blunt trauma remains unclear when weighed against overutilization concerns [24, 26, 39]. Significant concerns persist regarding the impact and appropriateness of whole-body CT in patients with severe blunt trauma including (a) the proliferation of unnecessary imaging, (b) the risk of radiation exposure, (c) the added cost of the additional imaging, (d) added time of transport to and from the scanner, and (e) the expense of working up incidental findings [37, 40–42]. This protocol is currently being tested in a prospective randomized clinical trial in five institutions, four in Europe and one in the USA. The randomized study of early assessment by CT scanning in trauma patients (REACT)-2 trial should provide additional evidence to support or refute the routine use of whole-body CT in blunt trauma [43]. Preliminary

results from the REACT-2 trial, presented at RSNA 2015, suggest that the prospectively collected data analysis is leaning toward the conclusion that the whole-body CT imaging strategy does not translate to a significant difference in mortality rate but a significant decrease in trauma room LOS for patients [44].

The protocol for trauma patients undergoing a CT without known allergic reaction to contrast included a bolus of intravenous contrast material, typically 100–150 ml (350 mg of iodine per milliliter, total iodine load of 35–52.5 g) injected at a rate of 3–5 ml/s through an 18- or 20-gauge cannula located in a large peripheral vein. Use of a dual-syringe power injector allows the contrast material to be followed immediately by 30–70 ml of saline solution as a chasing bolus, also at a rate of 3–5 ml/s. Oral contrast material for evaluating patients is no longer administered at most large trauma centers in the setting of blunt trauma [45–47]. A typical trauma CT protocol includes portal venous phase images of the abdomen and pelvis 60–90 s after contrast administration. A delayed series obtained 5–10 min after contrast administration increases the sensitivity for detecting injuries of the urinary tract, as well as further characterizing solid visceral organ injuries that involve the vasculature [48–50]. Selective (rather than routine) acquisition of the delayed phase series is recommended to limit the amount of radiation delivered [45]. There is some evidence that supports the addition of an arterial phase series 25–30 s after contrast administration of the abdomen and/or pelvis in selected trauma patients such as those with severe mechanisms of injury and those who have a displaced fracture of the pelvic ring on the portable radiograph of the pelvis obtained at the time of admission [48, 51–54]. Arterial phase images facilitate detection of trauma to the major vessels and demonstrate vascular injuries of the solid organs that are not apparent on portal venous or delayed phase images. In the pelvis, arterial phase images help characterize foci of active extravasation as arterial in origin [48, 55]. With the speed of 64-detector scanners (and beyond), these CT angiograms can be readily integrated into comprehensive proto-

cols that use a single bolus of intravenous contrast material. In fact, a whole-body CT angiogram (circle of Willis to symphysis pubis or beyond) is possible and has been advocated for patients with severe polytrauma [56, 57].

The presence of gross or microscopic hematuria after abdominal trauma is a good predictor of the presence of a urinary tract injury [58]. CT cystography should be obtained in the case of pelvic fractures or gross hematuria to identify bladder rupture as well as distinguish between intraperitoneal and extraperitoneal bladder rupture [59, 60]. This distinction between an intraperitoneal and an extraperitoneal rupture is important and has direct therapeutic implications because intraperitoneal ruptures require surgical repair and extraperitoneal ruptures can typically be treated conservatively without surgery [61].

Take-Home Figures

Figures 17.1 and 17.2 are algorithms for blunt thoracic trauma and blunt abdominal trauma.

Imaging Case Studies

Case 1

Figure 17.3a–c presents a 32-year-old male with blunt chest trauma from a hand-gliding accident.

Case 2

Figure 17.4a–f shows a 46-year-old female pedestrian hit by a motor vehicle at approximately 55 miles per hour.

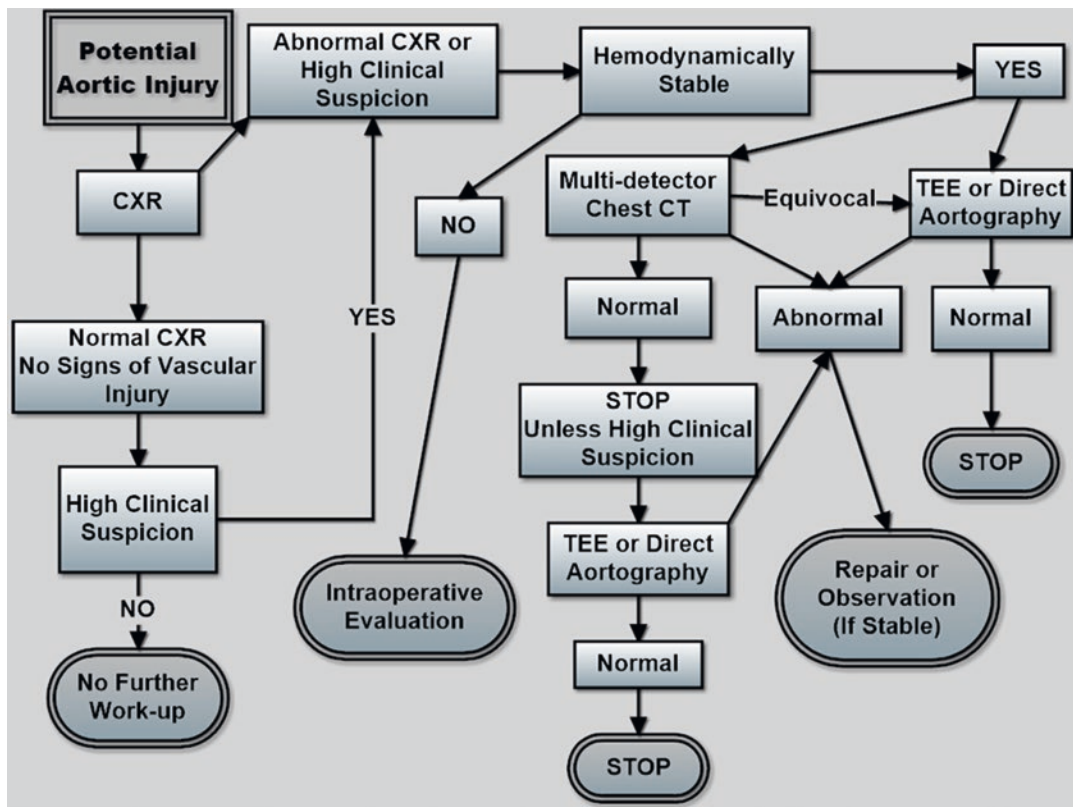


Fig. 17.1 Blunt thoracic trauma algorithm

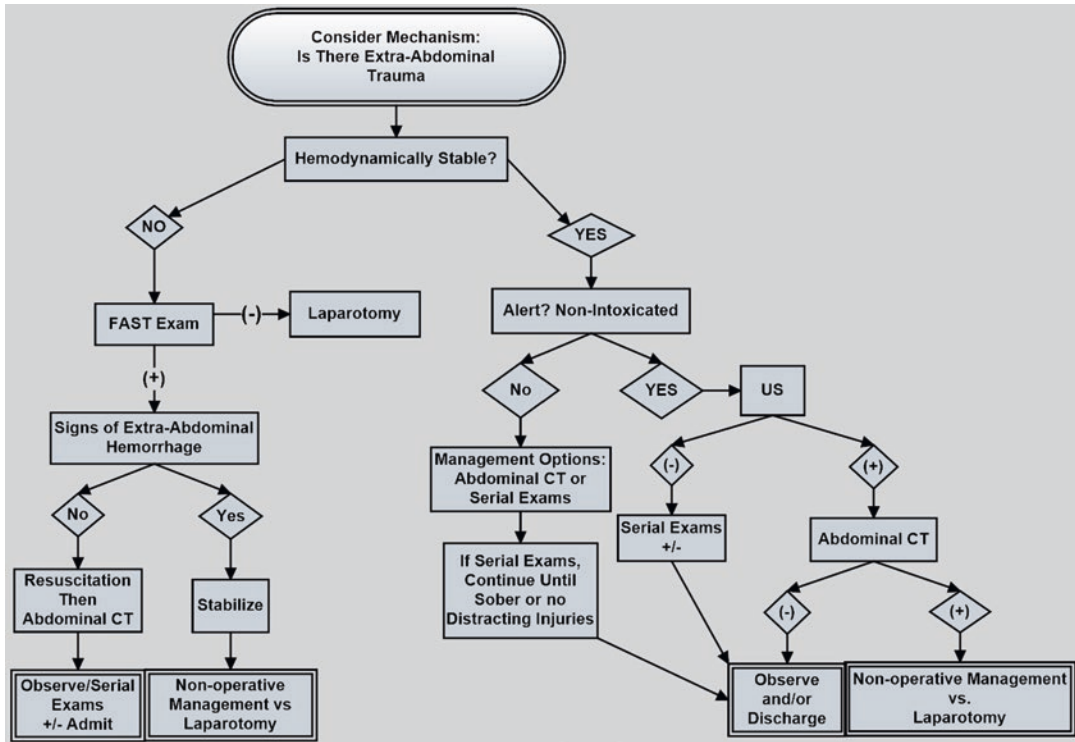


Fig. 17.2 Blunt abdominal trauma algorithm

Suggested Imaging Protocols

CTA chest trauma protocol for Siemens definition 128AS+	
Oral contrast	None
Intravenous contrast	115 ml of Isovue 370 at 4 ml/s with 50 ml of NS chase
Start	Top of lung species
End	Through adrenals
Gantry rotation time/Length	0.5 full
Slice thickness	0.6 mm
Pitch	0.9
KVP	Care KV
Auto mA (minimum/maximum)	Care Dose 4D Reference mAs of 350
DFOV	Optimized
SFOV	Large
Algorithm	I30f medium smooth
Window	Mediastinum and lung
Delay (from start of injection)	Bolus tracking
Recon thickness	3 mm
Recon spacing	3 mm
Direct MPRs	Sagittal 3X3 and Coronal Mediastinum

CT abdomen and pelvis trauma protocol for Siemens definition 128AS+

Oral contrast	None
Intravenous contrast	115 ml of Isovue 370 at 3 ml/s with 50 ml of NS chase
Start	Top of diaphragm
End	Through ischial tuberosity
Gantry rotation time/length	0.5 s
Detector coverage	
Slice thickness	0.6 mm
Interval	
Pitch	0.8
Speed	
KVP	Care KV
Auto mA (minimum/maximum)	Care dose 4D Reference mAs of 350
DFOV	Optimized
SFOV	Large
Algorithm	I30f medium smooth
Window	Abdomen
Delay (from start of injection)	70 s
Recon thickness	5 mm
Recon spacing	5 mm
Direct MPRs	Cor 3X3 body

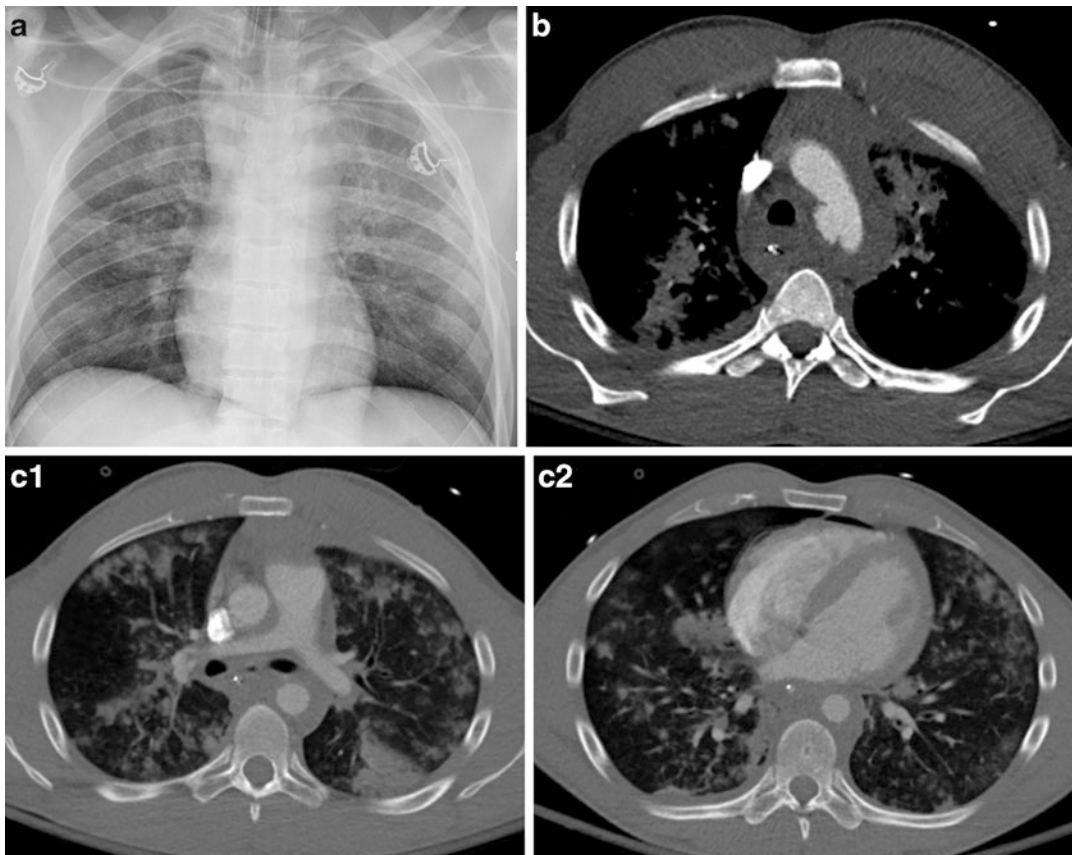


Fig. 17.3 (a–c) A 32-year-old male with blunt chest trauma from a hand-gliding accident. (a) AP chest radiograph. Mediastinal widening and patchy bilateral parenchymal opacities. (b) CT chest angiography. Axial slice through the level of the aortic arch with an aortic injury with surrounding periaortic hematoma. Patchy pulmonary parenchymal

opacities are present bilateral indicating pulmonary contusions. (c) CT chest angiography. Axial slice through the level of pulmonary arteries with patchy bilateral parenchymal opacities with areas of subpleural sparing typical of pulmonary contusions/hemorrhage. Note the small caliber of the pulmonary arteries in this hypovolemic state

Future Research

- Prospective studies regarding the effect of immediate “whole-body CT” on the severely injured trauma patient
- Prospective studies regarding the use of FAST in the setting of the severely injured trauma patient

Summary

- Conventional radiography is the appropriate initial screening evaluation of the chest in patients with major trauma. Computed

tomography (CT) is appropriate for the definitive evaluation of abnormalities identified on initial radiography.

- Clinical evidence of hemodynamic instability or ongoing blood loss is the strongest indicator for operative intervention in the abdomen. Among patients with such indication of ongoing hemorrhage, transabdominal ultrasound can be used to identify intraperitoneal hemorrhage from solid organ injury with high specificity.
- CT has high sensitivity for surgically important injuries of the abdomen; however, sensitivity and specificity for detection of bowel and mesenteric injury remains somewhat limited.



Fig. 17.4 (a–f) A 46-year-old female pedestrian hit by a motor vehicle at approximately 55 miles per hour. (a) AP chest radiograph. Patchy parenchymal opacities predominantly in the right lung base. (b) CT chest angiography. Axial image demonstrating pulmonary contusions in the right middle and lower lobes as well as pulmonary lacerations involving the right middle lobe with pneumohematoceles. A small pneumothorax is present along the posterior pleura. (c) CT abdomen, arterial phase. Coronal image through the kidneys demonstrating right renal fractures extending to the hilum with a perinephric fluid collection. Additional fluid is seen in the right paracolic gutter extending into the pelvic, corresponding to hemoperitoneum. (d) CT abdomen, portal venous phase. Coronal

image through the kidneys demonstrating right renal fractures with active contrast extravasation into the perinephric space. Additional contrast extravasation is seen in the right paracolic gutter from a hepatic source. (e) CT abdomen, arterial phase. Coronal image through the liver with a large, hypoattenuating hepatic laceration involving the hepatic dome with active contrast extravasation in the right hepatic lobe along the inferior margin of the laceration. (f) CT abdomen, arterial phase. Axial image through the liver with a large, hypoattenuating hepatic laceration involving much of the right hepatic lobe with active contrast extravasation along the anterior margin of the laceration. Retroperitoneal fluid is also present in the right perirenal space and surrounding the pancreas

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Acute Chest Infections in Adults and Children: Evidence-Based Emergency Imaging

18

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Key Points

- Obtaining a CXR is appropriate in older patients (>40 y/o) with acute respiratory illness (ARI) (moderate evidence).
- Obtaining a CXR is appropriate in patients with ARI and dementia (moderate evidence).
- A CXR is not necessary for patients with ARI who are younger than 40 and have normal vital signs and a normal physical exam, provided they can follow-up, and that the risks of delayed diagnosis of pneumonia are minimal (moderate evidence).
- A CXR is not necessary for patients with ARI, and a high pretest probability of community-acquired pneumonia (CAP) who will be treated for CAP regardless of CXR findings (moderate evidence).

- CXRs are sufficiently sensitive and highly specific for the diagnosis of CAP in children (moderate evidence).
- Imaging studies have a limited value with regard to differentiating between bacterial and viral lower respiratory tract infection in children (moderate evidence).
- Although CT is more sensitive than CXR for pneumonia, it is not indicated in immunocompetent adult or pediatric patients with suspected uncomplicated CAP (moderate evidence).
- CT does provide more information than radiographs with regard to complicated pulmonary infections with bronchopleural fistula, empyema, or pleural effusion (moderate evidence).
- In immunocompromised patients, CT is more sensitive and specific for pneumonia and should be performed in adult and pediatric cases where pneumonia is suspected, but the CXR is normal, equivocal, or nonspecific (strong evidence).
- Ultrasound does have an advantage over CT in identifying and characterizing complicated effusions in children by being more cost-effective and not employing ionizing radiation (moderate evidence).

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Definitions and Pathophysiology

Acute respiratory illness (ARI) is defined as one or more of the following: cough, sputum production, chest pain, or dyspnea (with or without fever) (Table 18.1). Most cases of ARI are caused by infection, and the most commonly encountered forms of acute infection in the chest are bronchitis and pneumonia. The distinction between acute bronchitis and pneumonia is an important one as ~90% of cases of acute bronchitis are viral in etiology and are self-limited. Pneumonia can be caused by bacterial, mycobacterial, viral, and fungal organisms and can be life-threatening; often requiring antimicrobial therapy [1]. As shown in Table 18.1, incidence of specific pathogens differs by age.

Acute bronchitis is inflammation of the airways. There are typically few if any findings on chest imaging. Pneumonia is inflammation of the pulmonary parenchyma primarily affecting the alveoli; the small sacs within the lung where gas exchange takes place, also called the “airspaces.” The primary imaging manifestations of pneumonia are those of “airspace/alveolar disease,” namely, partial alveolar filling (ground glass) and complete alveolar filling (consolidation) (Fig. 18.1a, b). “Tree-in-bud” is another common manifestation of infectious pneumonia and represents spread of infection through the terminal airways and into the central aspect of the airspaces (Fig. 18.1a, b) [2].

Some of the major risk factors for pneumonia include recent viral respiratory tract infection, smoking, a variety of chronic lung diseases, young (<1 y/o) or old (>65 y/o) age, conditions that predispose to aspiration, and immunocompromised state [3].

Immunocompromised is defined as being in a state where the immune system is weakened or absent, some commonly encountered causes include acquired immunodeficiency syndrome (AIDS), chemotherapy, or other immunosuppressive drugs. Immunocompromised patients are susceptible to infection by “opportunistic” organisms. Also, they are more likely to develop widely disseminated infections. For example, in patients

with AIDS, their CD4 count helps predict what types of pneumonias they are most at risk of developing (Table 18.2) [4].

Epidemiology

Pneumonia is a global health issue. Of the 156 million children estimated by the world health organization (WHO) to have pneumonia in 2008, 151 million cases occurred in developing nations, accounting for 1.6 million deaths that year, 28–34% of all deaths in those under 5 years of age [5, 6]. Pneumonia is the leading cause of death among children in low-income nations [5, 7]. The WHO estimates that one in three newborn infant deaths is due to pneumonia [8].

Pneumonia and influenza are the most common infectious causes of death in the US. In 2010, pneumonia and influenza combined was the ninth leading cause of death, accounting for approximately 50,000 deaths with an age-adjusted death rate of 15.1 per 100,000 people [9]. Pneumonia and influenza are more deadly among the elderly; death rates for those aged 65 and older in 2010 was 106.3 per 100,000 people [9]. Given the aging population, the burden of pneumonia is expected to increase, a common trend in most developed nations.

Overall Cost to Society

In 2005, the total cost to the US economy of influenza and pneumonia was estimated at \$40.2 billion when including all direct and indirect costs [10]. Pneumonia was one of the top ten most expensive conditions seen during inpatient hospitalizations in the US in 2011, with an aggregate cost of nearly \$10.6 billion for 1.1 million hospital stays [11]. CAP results in 10 million doctor visits and 64 million days of restricted activity annually [12]. Childhood pneumonias are a frequent cause of doctor visits, antibiotics prescriptions, loss of work days of parents, and reduction of quality of life [13].

Table 18.1 Causes of pulmonary infection by age, listed in order of prevalence

0-4 weeks	4-8 weeks	8-12 weeks	12 weeks-4 years	Childhood (5-18 years)	Adult (18-64 years)	Elderly (≥65 years)
Group B <i>Streptococcus</i> Gram-negative enteric bacteria <i>Listeria</i> <i>monocytogenes</i>	<i>Chlamydia</i> <i>trachomatis</i> Viruses (RSV, parainfluenza) <i>Streptococcus</i> <i>pneumonia</i> <i>Bordetella pertussis</i> Group B <i>Streptococcus</i> Gram-negative enteric bacteria <i>Listeria</i> <i>monocytogenes</i>	<i>Chlamydia</i> <i>trachomatis</i> Viruses (RSV, parainfluenza) <i>Streptococcus</i> <i>pneumonia</i> <i>Bordetella pertussis</i>	Viruses (RSV, parainfluenza, influenza, adenovirus, rhinovirus) <i>Streptococcus</i> <i>pneumoniae</i> <i>Haemophilus influenzae</i> (non-type B) <i>Moraxella catarrhalis</i> Group A <i>Streptococcus</i> <i>Mycoplasma</i> <i>pneumoniae</i> <i>Mycobacterium</i> <i>tuberculosis</i>	<i>Mycoplasma</i> <i>pneumoniae</i> <i>Chlamydia</i> <i>pneumoniae</i> <i>Streptococcus</i> <i>pneumoniae</i> Viruses (RSV, parainfluenza, rhinovirus) <i>Mycobacterium</i> <i>tuberculosis</i>	<i>Streptococcus pneumoniae</i> Viruses (influenza, parainfluenza, adenovirus) <i>Mycobacterium</i> <i>tuberculosis</i> Methicillin-resistant <i>Staphylococcus aureus</i>	<i>Streptococcus</i> <i>pneumoniae</i> Viruses (influenza, parainfluenza, adenovirus) <i>Haemophilus</i> <i>Influenzae</i> <i>Moraxella catarrhalis</i> <i>Legionella pneumoniae</i> <i>Mycobacterium</i> <i>tuberculosis</i> Gram-negative bacilli

Modified from Lichenstein R, Suggs AH, Campbell J. Pediatric Pneumonia. Emerg Med Clin North Am. 2003; 21: 437-451 and from Stupka JE, Mortensen EM, Anzueto A, et al. Community-acquired pneumonia in elderly patients. *Aging Health* 2009; 5(6): 763-74

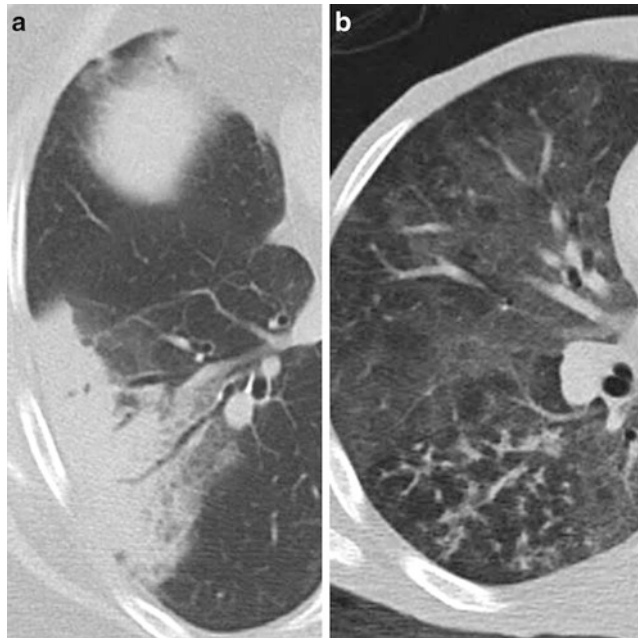


Fig. 18.1 (a, b) Axial image from a non-contrast CT of a patient with community acquired pneumonia (CAP) (a) demonstrating airspace disease primarily manifesting as consolidation, aka complete alveolar filling. Note the air bronchogram and how the pulmonary vessels are not visible where they traverse the consolidation. CT image from a different patient with CMV pneumonia (b) demonstrates

widespread ground glass, aka partial alveolar filling. Note how the pulmonary vessels are still visible as they traverse the ground-glass opacity. This patient also has some focal tree-in-bud nodularity in the dependent right lung representing endobronchial spread of infection. This pattern of mixed ground glass and nodules is common in CMV and can be very subtle on CXRs

Table 18.2 CD4 count and risk of opportunistic infection in HIV/AIDS

CD4 <400	CD4 <200	CD4 <100
Recurrent bacterial pneumonia	<i>Pneumocystis jiroveci</i> pneumonia	<i>Mycobacterium avium</i> complex
<i>Mycobacterium tuberculosis</i>	Disseminated <i>Mycobacterium tuberculosis</i>	Cytomegalovirus

Modified from Allen CM, Al-Jahdali HH, Irion KL, et al. Imaging lung manifestations of HIV/AIDS. *Ann Thorac Med* 2010; 5(4):201–16

Goals of Imaging

The main goal of imaging acute pulmonary infections in the emergency department is diagnosis. Early diagnosis will support adequate and early treatment; it could also prevent potential costs and complications. This is particularly important in patients with a weak immune system such as young children, the elderly, or the immunocompromised.

Methodology

A review of the current diagnostic imaging literature was performed utilizing PubMed,

MEDLINE, and Google Scholar search databases covering January 1, 1980 through May 1, 2015. Searches were performed using various combinations of the following key terms:

Infection terms diagnosis, acute respiratory illness, acute bronchitis, lower respiratory tract infection, pneumonia, community-acquired pneumonia, opportunistic, HIV, AIDS, pleural effusion, parapneumonic effusion, empyema

Imaging terms imaging, radiology, radiography, chest, chest X-ray, chest radiography, computed tomography, CT, CAT scan, ultrasound

Population terms pediatric, child, children, adults, immunocompetent, immunocompromised

Other imaging terms cost, direct, indirect, epidemiology, impact, evidence based, appropriate, indication, indicated, guidelines

Searches were limited to English-language articles and human studies. Abstracts were reviewed and selected based on relevance, recency, and methodology. Additional relevant articles were selected from the references of reviewed articles and from published guidelines. We excluded case reports, animal studies, and basic science articles.

Discussion of Issues

When Is a Chest Radiograph (CXR) Indicated for Workup of Suspected Chest Infection in Adults?

Summary of Evidence

- Obtaining a CXR is appropriate in older patients (>40 years of age) with acute respiratory illness (ARI) (moderate evidence).
- Obtaining a CXR is appropriate in patients with ARI and dementia (moderate evidence).
- A CXR is not necessary for patients with ARI who are younger than 40 and have normal vital signs and a normal physical exam, provided they can follow-up, and that the risks of delayed diagnosis of pneumonia are minimal (moderate evidence).
- A CXR is not necessary for patients with ARI and a high pretest probability of community-acquired pneumonia (CAP) who will be treated for CAP regardless of CXR findings (moderate evidence).

Supporting Evidence

Radiographs have been used in medical imaging for over 100 years, and the chest radiograph (CXR) is as relevant for diagnosis of cardiothoracic disease now as it was in the early days of radiography. The relatively low dose of ionizing radiation combined with excellent spatial resolution, low cost, and high availability make the CXR an excellent first step in the diagnostic work-up of patients with suspected chest infec-

tion. That being said, radiography, like any diagnostic tool, should be used judiciously.

Community-Acquired Pneumonia (CAP)

The major indication for obtaining a CXR in patients with ARI in the emergent setting is to confirm the diagnosis of community acquired pneumonia (CAP) when suspected based on history and physical exam. Airspace opacification, particularly consolidation (the classic finding of CAP), stands out against adjacent aerated lung and “silhouettes out” adjacent soft tissue structures resulting in a perceptible finding on CXR (Fig. 18.2a–d). Despite the fact that ARI is commonly encountered in the emergency setting, there is a paucity of large randomized controlled trials evaluating the utility of CXR in this setting. There are some data regarding when to utilize a CXR in suspected cases of CAP [14–22]. There are many societal guidelines concerning when to use a CXR in this setting. However, some of these guidelines are conflicting [23–25].

One of the larger prospective studies to address the use of radiography in the evaluation of ARI is Benacerraf et al. from 1981 [14]. One thousand one hundred two consecutive patients were evaluated with the goal of identifying selective indications for CXR based on age, symptoms, and physical exam findings. Put briefly, the study showed that for patients younger than 40 years with ARI symptoms but normal physical exam findings and absence of hemoptysis, the yield of CXR was exceedingly low. A study by Heckerling reviewing 464 patients confirmed that CXRs were nearly always negative in the absence of physical exam findings [15]. Patients with dementia were an exception and had a very high incidence of pneumonia on CXR (75.8%) whereas only two of the 106 patients presenting with acute asthma (1.9%) had pneumonia.

Several more recent studies have been published which evaluate when a CXR is appropriate in suspected CAP [16–19]. O’Brien et al. examined a series of 350 patients with ARI and a positive CXR with an equal number of age-matched patients with ARI and a negative CXR [16]. Their

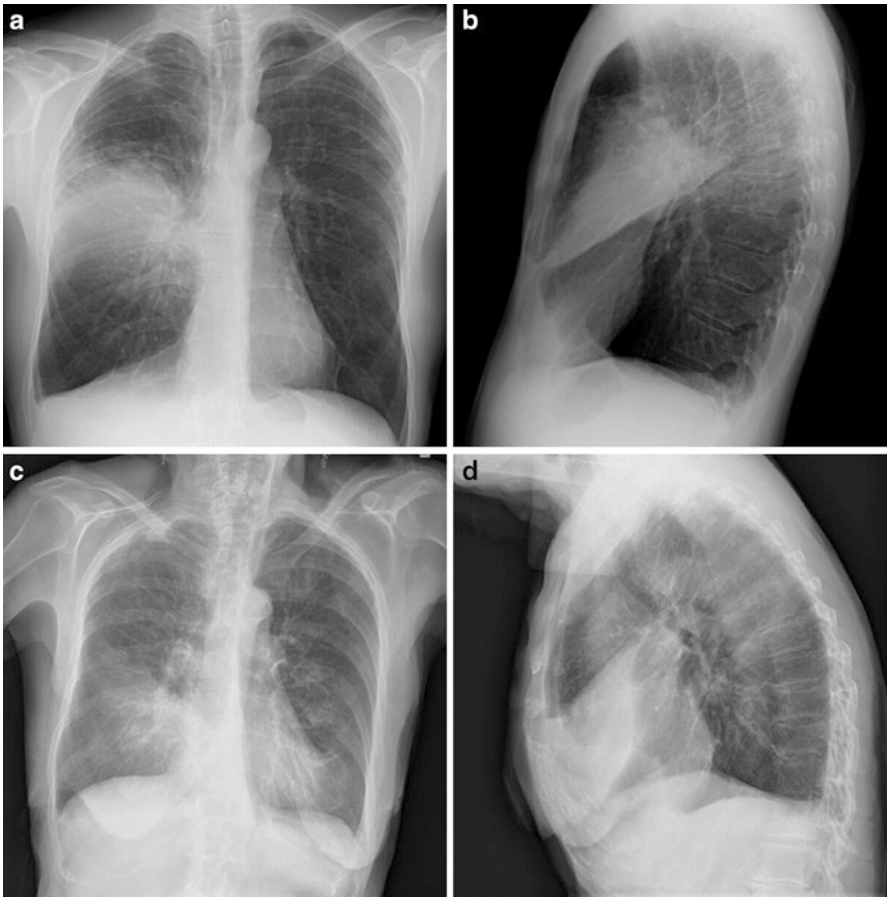


Fig. 18.2 (a–d) Frontal (a) and lateral (b) CXRs from a patient with obvious CAP. Note the dense consolidation in the right upper lobe. On the lateral view the well-defined margin of the consolidation represents where it abuts the minor fissure. Frontal (c) and lateral (d) CXRs from a different patient demonstrate a slightly less obvious case of

CAP in the right middle lobe. On the frontal view, there is indistinct increased density which hides the right heart border, a “silhouette sign.” On the lateral view, the consolidation is contained by the minor and major fissures resulting in well-defined margins

findings confirm earlier work, re-demonstrating the fact that CXRs are rarely positive in patients with ARI and a normal physical exam or normal vital signs. Only 5% of the cases of CAP occurred in this group of patients. Other studies, including a more recent Iranian study with a nearly identical design as O’Brien et al. had similar findings [18]. A random chart review by Nolt et al. identified vital sign abnormalities and age greater than 50 as independent predictors of CAP [19]. The data suggest that for most patients with ARI and an otherwise normal exam CXR is unnecessary. The authors did include exceptions for patients with unreliable follow-up or moderate to high

likelihood of morbidity if CAP is not diagnosed promptly [16, 18].

A review of 2706 patients admitted to the hospital with a diagnosis of CAP by Basi et al. found that approximately one third of these patients had a negative initial CXR and only a small percentage developed radiographic evidence of pneumonia while in the hospital [20]. Other studies have shown similar findings [21, 22]. Studies such as these call into question the sensitivity of CXR for CAP in situations where there is a high pretest probability of pneumonia. In patients with a high probability of CAP based on symptoms, physical exam findings, and vital signs, the management

plan is unlikely to change based on CXR findings making the exam unnecessary. Indeed, a study by Aagaard et al. showed that in clinical practice CXRs were only obtained in 61% of patients with a clinical diagnosis of pneumonia [21].

There are a variety of societal guidelines concerning the role of the CXR in the diagnostic work-up of CAP. Some of the most promulgated guidelines are those of the Infectious Diseases Society of America in conjunction with the American Thoracic Society (IDSA/ATS) [23], the American Association of Family Physicians (AAFP) [24], and the British Thoracic Society (BTS) [25]. According to the IDSA/ATS guidelines, chest radiography should be obtained whenever CAP is suspected in adults to establish the diagnosis and to aid in differentiating CAP from other common causes of ARI, such as acute bronchitis. The guidelines also state that CXRs are sometimes useful for suggesting the etiologic agent, prognosis, alternative diagnoses, and associated conditions. When the initial CXR is clear, but pneumonia is highly suspected, it may be reasonable to treat their condition presumptively with antibiotics and repeat the imaging in 24–48 h.

The AAFP also recommends CXR in the initial workup of suspected CAP to confirm the diagnosis, but gives more specific guidelines as to when a CXR is indicated for diagnosing CAP in the setting of ARI [26]:

CXR should be performed in:

- Any patient with at least one of the following abnormal vital signs:
 - Temperature > 100° F (37.8° C)
 - Heart rate > 100 beats per minute
 - Respiratory rate > 20 breaths per minute
- Any patient with at least two of the following clinical findings:
 - Decreased breath sounds
 - Crackles (rales)
 - Absence of asthma

The BTS guidelines are different from the American guidelines. They state that it is not necessary to perform a CXR in patients with suspected CAP *unless*:

- The diagnosis is in doubt, and a chest radiograph will help in differential diagnosis and management of the acute illness.
- Progress following treatment for suspected CAP is not satisfactory at review.
- The patient is considered at risk of underlying lung pathology such as lung cancer.

This less aggressive approach toward CXR in the setting of suspected CAP could, at least in part, be related to the fact that medical imaging is a limited resource in the UK due to their nationalized healthcare system, the National Health Service (NHS). These recommendations may also reflect an attempt at cost containment by the NHS. There is no strong data concerning the cost-effectiveness of obtaining a CXR in suspected CAP to either confirm or refute these guidelines.

When Is a CXR Indicated for Workup of Suspected Chest Infection in Children?

Summary of Evidence

Chest radiographs are sufficiently sensitive and highly specific for the diagnosis of CAP in children (moderate evidence).

- Imaging studies have limited value in the differentiation between viral and bacterial lower respiratory tract infection in children (moderate evidence).

Supporting Evidence

Community-Acquired Pneumonia

Despite their limitations, there is moderate evidence to suggest that chest radiographs are sufficiently sensitive and highly specific for the diagnosis of community-acquired pneumonia (CAP) in children. Table 18.3 summarizes the test characteristics of the only three studies in which complete sensitivity and specificity data of chest radiography are available: reported sensitivities range between 71 and 87% and specificities from

Table 18.3 Diagnostic performance of chest radiography in detection of pneumonia in immunocompetent patients

Author	Year	Study size	Sensitivity	Specificity	PPV	NPV
Rigsby et al. [27]	2004	240	85%	98%	n/a	n/a
Lamme et al. [28]	1986	179	81–87%	95–96%	n/a	n/a
Patenaude et al. [29]	1995	373	71%	90%	n/a	n/a
Graffelman et al. [30]	2007	129	n/a	n/a	75%	57%

Summary: reported sensitivities range between 71 and 87%, and specificities between 90 and 98% [2–4]

(Used with permission of Springer Science from Choy G, Yager PH, Noviski N, Westra SJ. Imaging of Chest Infections in Children. In Medina LS, et al., eds: Evidence-Based Imaging in Pediatrics: Improving the Quality of Imaging in Patient Care. New York: Springer Science; 2010.)

90 to 98% [27–29]. In a few more limited studies, sensitivity and specificity values were not directly specified, but accuracy was reported to range between 58 and 77% [30, 31]. Of note, a large randomized clinical trial of children less than 5 years of age presenting in an ambulatory care setting with uncomplicated pneumonias failed to demonstrate any evidence that the routine performance of chest radiography improves clinical outcomes [32, 33].

When viral causes of ARI such as bronchiolitis are suspected, CXRs are not needed in uncomplicated cases. In a retrospective study of 298 patients in an urban children's hospital at the University of Colorado by Roback et al., clinicians did not typically obtain CXRs in first-time wheezing episodes. The yield of radiography is greater when there is a high temperature, absence of a family history of asthma, and localized wheezing on physical exam [31]. Perlstein et al. developed a publication of a set of evidence-based guidelines as implemented at the Children's Hospital of Cincinnati that demonstrated 20% decrease in number of CXRs ordered [34].

Therefore, recently published evidence-based practice recommendations by the Infectious Disease Society of America (IDSA) [35] and the British Thoracic Society (BTS) [36] recommend against the routine use of chest radiography in children with suspected community-acquired pneumonia who do not require hospitalization. Prior to the institution of these guidelines, CXRs were ordered in 83% of pediatric ambulatory

emergency room visits, frequently inappropriately so [37]. Follow up CXRs after 4–6 weeks are only recommended for children with recurrent pneumonia involving the same lobe, to look for underlying anatomic causes [35].

In summary, accepted indications for chest radiography are severe disease necessitating hospitalization, confirmation of diagnosis when there is an atypical clinical presentation, initial assessment of complications, and exclusion of other thoracic causes of respiratory distress [33, 38].

Differentiation of Bacterial and Viral Pneumonia

In a study of 72 adult patients by Graffelman et al. in the primary care setting, limited value was found using chest radiography in predicting the etiology of viral versus bacterial lower respiratory infections. The positive predictive value and the negative predictive value for bacterial infection were 75% and 57%, respectively [39]. In young children, the classic segmental or lobar airspace consolidation as a radiographic hallmark of bacterial pneumonia is present in only a minority of cases, and this radiographic presentation is nearly absent in neonates. Bilateral interstitial opacities with peribronchial thickening and hyperinflation, thought to represent viral small airways disease (bronchiolitis, Fig. 18.3a, b), is in fact a nonspecific finding, that is indicative of a lower respiratory tract infection of any cause in young children [40]. The fixed hyperinflation, being the most

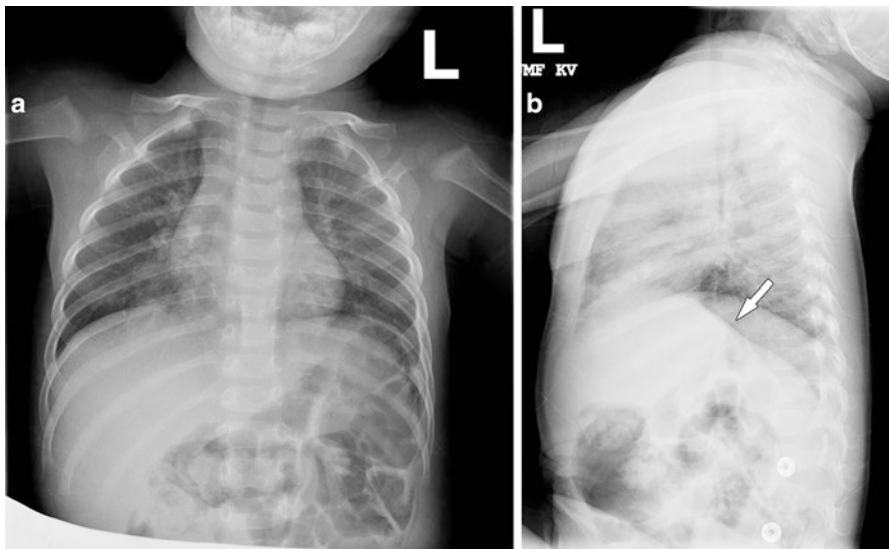


Fig. 18.3 (a, b) An 18-month-old boy with respiratory syncytial virus pneumonia. (a) Frontal CXR shows perihilar streaky lung opacities and peribronchial thickening, typical of viral infections, with more focal opacity medially in the right lung base, from superimposed atelectasis. This was mistaken for alveolar consolidation indicative of

bacterial pneumonia, and for this reason antibiotic treatment with Amoxicillin was given unnecessarily. (b) Lateral CXR better demonstrates air trapping in the right lung base, with flattening of the right hemidiaphragm (arrow)

important radiographic feature of pneumonia in infancy, is due to air trapping in the alveoli resulting from degrees of mucosal swelling in the relatively small-caliber terminal airways of infants that would not compromise air exchange in older individuals. In addition, the collateral pathways of ventilation via the channels of Kohn and Lambert are yet underdeveloped in small children, and finally there is more hypersecretion in the inflamed airways in children as compared to adults. This latter effect also contributes to mucous plugging of the airways, which frequently leads to (sub-)segmental atelectases, mimicking alveolar consolidations, which are frequently misinterpreted to represent bacterial pneumonia [40].

A streptococcal pneumonia may initially have a strikingly round appearance in children younger than 8 years [40], thereby simulating an intrapulmonary mass or abscess, until it spreads further to reach a normal anatomic boundary such as a fissure (Fig. 18.4a, b). Staphylococcal pneumonias are frequently acquired after viral infections,

such as influenza, and the virulence of this organism can cause complications such as lung necrosis (leading to post-infectious pseudocysts or pneumatoceles) or empyema. Mycoplasmal pneumonias seen predominantly in older children, although caused by a bacterium susceptible to specific antibiotics, have a radiographic appearance that frequently mimics that of a viral infection [40]. The contrary situation, a viral infection mimicking a bacterial infection, is much more common [40–42], and this is reflected in the low 30% positive predictive value of radiographic criteria to predict bacterial pneumonia [43]. Radiographic criteria alone overestimate the presence of bacterial pneumonia [40], potentially leading to overprescription of antibiotics. On the other hand, the main utility of CXRs in the ambulatory care setting may be that the high 92% negative predictive value of radiographic criteria for bacterial pneumonia [43] allows clinicians to withhold antibiotics in symptomatic children with a negative CXR [40].

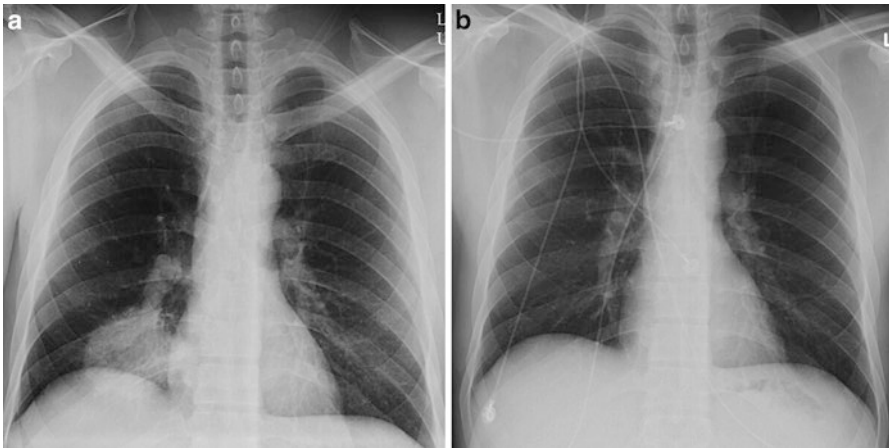


Fig. 18.4 (a, b) Frontal CXR (a) in a 37-year-old woman with HIV demonstrates round mass-like consolidation in the right lower lobe. The finding resolved several weeks later and after a course of antibiotics (b) consistent with round pneumonia. The non-segmental distribution of round pneumonia is thought to be related to exudative

fluid tracking through interalveolar channels. Round pneumonia is more common in younger patients, is usually caused by *Streptococcus pneumoniae*, and is often mistaken for a tumor or an atypical infection, such as a fungal infection

Viral and bacterial infections frequently coexist, and radiographic criteria alone do not reliably distinguish between them [35, 43, 44]. This is compounded by a reported high interobserver variability for interpretation of CXRs [45–48]. The overlap in clinical and radiographic manifestations of viral and bacterial infections of the lung in children frequently leads to communication problems between radiologists and referring physicians, due to use of inexact and poorly defined terminology in radiology reports [49]: the terms “peripheral airways disease,” “(focal) airspace consolidation,” or “(focal) infiltrate” are ambiguous, as they are interpreted in a nonuniform way by referring physicians. The only reliable finding was found to be the presence of an “alveolar infiltrate,” whereas the presence of an “interstitial infiltrate” was found to be unreliably diagnosed by pediatric radiologists [50]. As a result of this, referring physicians agree with radiologists’ interpretations in only 78% of cases, and antibiotics are frequently prescribed even when no bacterial agent can be proven [49, 51, 52]. It is, therefore, important not to overcall pediatric CXRs for the presence of a bacterial infection, which is the most common interpretation error made by radiologists unfamiliar with pediatric imaging [53, 54].

In What Situations Does Computed Tomography (CT) Add Value for Workup of Suspected Chest Infection?

Summary of Evidence

- Although CT is more sensitive than CXR for pneumonia, it is not indicated in immunocompetent patients with suspected uncomplicated CAP (moderate evidence).
- For complicated pulmonary infections with bronchopleural fistula, empyema, or pleural effusion, CT provides more information than plain radiographs (moderate evidence).
- In the immunocompromised patient, CT is more sensitive and specific for pneumonia and should be performed in cases where pneumonia is suspected but the CXR is normal, equivocal, or nonspecific (strong evidence).

Supporting Evidence

Computed tomography is a 3D imaging technique with high contrast resolution. By its very nature, it will be more sensitive than CXR, which is 2D and has low contrast resolution. The increased sensitivity of CT comes with a cost. In addition to being much more expensive and less available, the dose of radiation from a chest CT is

on the order of 100's of times that of a CXR. As such, usage of CT is typically limited to situations where the examination has a high probability of changing patient management.

Community-Acquired Pneumonia

There have been a few studies evaluating the sensitivity of CT for CAP relative to CXR. Although no randomized controlled trials have been performed, there are a few retrospective reviews as well as one prospective study by Syrjala et al. which evaluated the use of CT for diagnosis of CAP by assessing 47 patients who had clinically suspected CAP and simultaneous CXR and CT [55]. CT identified all 18 cases diagnosed with CXR and an additional 8 cases which were radiographically occult. CXR "missed" 31% of the cases of pneumonia. One of the larger reviews by Hayden et al. identified 97 of 1057 ED patients with a diagnosis of pneumonia who had both CXR and CT [56]. Within this selected group, there were 26 patients (27%) who had pneumonia which was not visible on CXR. A recent observational cross-sectional study including 3423 patients by Self et al. examined CXR test characteristics for detection of pulmonary opacities relative to CT [57]. Chest radiographs showed poor sensitivity and positive predictive value (43.5% and 26.9%, respectively). A retrospective analysis of quality improvement data on adult ED patients admitted with pneumonia over 21 months in Rhode Island showed that 49/428 (11%) of the cases of pneumonia were diagnosed by CT in the setting of a negative CXR [58].

The available data clearly show that CT is more sensitive than CXR for the diagnosis of CAP. What is less clear is whether this increase in sensitivity justifies the added cost and risk of performing CT in what would prove to be a large number of patients with suspected CAP and a negative CXR. It is also not clear whether performing CT in this subset of patients would improve patient outcomes.

The IDSA/ATS consensus guidelines briefly address the use of CT in patients with suspected CAP and a negative CXR. They consider CT a reasonable alternative to empiric treatment with antibiotics and follow-up CXR when there is high

clinical suspicion of CAP [23]. It would make sense to utilize CT in situations where it has the greatest change of adding value to the management of the patients. Intuitively, this would include critically ill patients in whom a timely diagnosis would reduce the morbidity and mortality associated with delayed diagnosis. The BTS guidelines state that CT scanning currently has no routine role in the investigation of CAP [25].

Complicated Pneumonia

A variety of complications, including parapneumonic effusions, empyema, cavitation, and bronchopleural fistula are possible with severe cases of pneumonia. Typically, these patients are ill and are often already hospitalized; however, complicated cases of pneumonia do occasionally present to the ED.

There have been a few studies examining the value CT adds to the workup of complicated pneumonia. Baber et al. demonstrate that CT adds value by detecting/characterizing complications in ill patients, helping to guide further management [59]. CT also helps to detect alternative diagnoses as demonstrated by Banker et al. [60]. This retrospective review sought to assess the impact of CT on clinical decision making in immunocompetent ED patients with CXR findings of pneumonia. The patients in the CT arm had more extensive clinical management, greater chance of having antibiotic regimen changed, longer hospital stay, and 16% of the CT patients had an alternative/additional diagnosis identified by CT (pulmonary embolism, lung cancer, hypersensitivity pneumonitis, multiple myeloma, renal cell carcinoma, small bowel obstruction, lung nodule, and endobronchial mass).

There are several studies in the pediatric literature which evaluate the role of CT in the management of complicated pneumonia. Donnelly et al. looked at 56 patients with complicated pneumonia who were not responding to treatment [61]. Chest CT was compared to a CXR performed earlier on the same day. All 56 CT scans demonstrated at least one finding (cavitary necrosis, abscess, bronchopleural fistula, cavitation, loculated pleural effusions, malpositioned chest tube, pericardial effusion, or bronchial

obstruction) that were not seen on CXRs. A total of 110 findings were seen on CT and not on CXR, with an average of approximately of two findings per CT scan. In another retrospective analysis of 17 children who underwent both CT scanning and CXR, evidence of cavity necrosis is often seen on CT before or in the absence of findings on CXR [62].

In a case series of 42 immunocompetent children, CXR was suboptimal in detecting abscesses, bronchopleural fistulae, fluid loculations, and parenchymal involvement, when compared to CT [63]. Chest radiograph accuracy rates were reported as follows: fluid loculations (42%), abscess formation (40%), bronchopleural fistulae (33%), and parenchymal involvement (84%). A limitation of this study is the lack of reported sensitivity and specificity values. Despite these studies confirming the expected higher sensitivity of CT, it is unclear whether the value added by CT in these situations actually contributes to better patient outcomes.

Immunocompromised Patients with Acute Respiratory Illness (ARI) and a Negative Chest Radiograph

The number of immunocompromised patients is increasing driven primarily by increasing use of immunosuppressive drugs for organ transplantation, treating cancer, autoimmune conditions, and the continued presence of the human immunodeficiency virus (HIV) [64]. Pulmonary complications are common in immunocompromised patients, often initially manifesting with symptoms of ARI. Of all pulmonary complications, pulmonary infections comprise nearly 75%, many of which progress rapidly if left untreated [64, 65].

Immunocompromised patients with ARI warrant special consideration for a variety of reasons. First and foremost, the consequences of a delayed diagnosis of pneumonia are often dire. Second, immunocompromised patients are at risk for infection with a variety of opportunistic organisms which may require a unique treatment regimen. Identifying any findings which can help narrow the diagnosis to a specific organism is of great value. Also, some of these opportunistic

infections can be quite subtle on CXR. This is exacerbated by the fact that these patients can have trouble mounting an effective inflammatory response to infection, necessitating a more sensitive imaging exam [66].

CT is more sensitive than CXR for pneumonia in immunocompetent patients [55–58]; studies show that this is true to an even greater extent for immunocompromised patients [64, 67–69]. Although CXR remains the initial imaging examination of choice due to its availability and low cost, when an immunocompromised patient with ARI and suspected pneumonia has a negative CXR, a CT scan should be performed. An observational study of immunosuppressed bone marrow transplant patients with suspected pneumonia showed sensitivities ranging between 39% and 59% using CT as the reference [64]. In a study of 49 patients with HIV and a diagnosis of CAP who received both CXR and CT at admission, CT identified all of the cases of CAP diagnosed on CXR, 9 cases. CT also identified lesions not visualized on CXR in the remaining 40 patients (82%). Some of these lesions included pleural effusions ($n = 14$), ground-glass opacification ($n = 20$), pericardial effusions ($n = 8$), cavitation ($n = 4$), cysts ($n = 4$), bullae ($n = 4$), abscess ($n = 1$), and pneumothorax ($n = 1$). In 20 of 23 cases, hilar lymphadenopathy identified on CT, was not recognized on CXR [67].

The pediatric literature also supports lowering the threshold for CT in immunocompromised patients [70–73] (Fig. 18.5a, b). In these high-risk groups, it is absolutely critical to have a high sensitivity, as failure to detect results in failure to treat and subsequent high mortality [72]. CT has been shown to have higher accuracy than plain radiography for early detection of pneumonia in immunocompromised and hospitalized patients [72, 74–76]. For example, in a series of 48 patients (median age of 11 years and range of 2–19 years), CXRs and CT were rated independently by three experienced radiologists and subsequently correlated with biopsy or bronchoscopic washing results [72]. CT was shown to identify more true-positive cases of bacterial and fungal pneumonia than radiography (91% versus 85%). Unfortunately, no detailed numbers of sensitivity

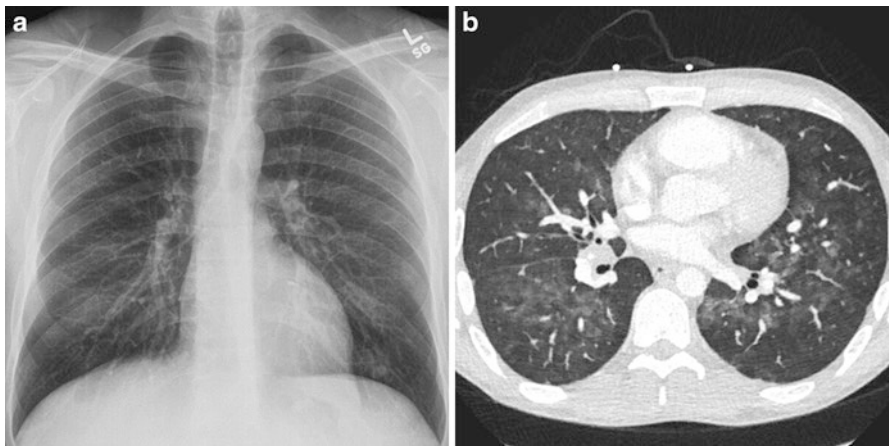


Fig. 18.5 (a, b) Frontal CXR (a) from a patient with HIV, fever, and dyspnea. The patient was not on therapy for her HIV and had a CD4 count below 200. The study was read as normal, but due to the high index of suspicion for an opportunistic infection a follow-up CT was performed (b). Note the subtle patchy ground-glass opacity, a finding

that is easily missed on CXR. The patient was presumptively diagnosed with *Pneumocystis jiroveci* pneumonia (PJP) which was confirmed with sputum testing. This case illustrates the importance of CT in the setting of an immunocompromised patient with a high index of suspicion for pneumonia and a negative CXR

and specificity were cited. In 87 adult patients with febrile neutropenia (median age 47, range 18–80 years), CT detected pneumonia 5 days on average earlier than chest radiographs and was more sensitive in the detection of poorly defined opacities, ill-defined nodules, consolidation, ground-glass opacities, pleural effusions, cavitations, and bullae [69].

Identifying Infectious Etiology in Immunocompromised Patients

In addition to increased sensitivity relative to CXR, CT also has increased specificity and is able to identify a variety of patterns of lung disease. Certain opportunistic infections have relatively characteristic patterns of pulmonary involvement which can be identified on CT with a higher degree of confidence relative to CXR [64]. Examples include *Pneumocystis jiroveci* pneumonia (PJP), invasive pulmonary aspergillosis, and cytomegalovirus (CMV) [77–81] (Fig. 18.6a–d). Recognizing these patterns and raising concerns for a particular organism based on imaging findings allows for early initiation of empiric therapy; microbiologic data may not be available for days or weeks in these cases [64, 82, 83].

For the evaluation of children who are severely ill or immunocompromised, CT can add value in cases of fungal infection or PJP. Janzen et al., in a retrospective review of 45 children who underwent both CT and CXR, found that the first choice diagnosis was correct in 44% on chest CT and correct in 30% on CXR [70]. Equivocal or normal chest radiographs are common, reported in up to 39% of patients with PJP infection and in up to 10% of patients with other known pulmonary disease [84]. In adult AIDS patients, the high negative predictive value of high-resolution CT allows one to withhold empiric treatment for PJP pneumonia when the CT scan is negative [85].

CT can aid in the detection of fungal infections via identification of nodules, cavitation, ground-glass opacities, and halo effect [71, 72, 75]. CT can play an important role in evaluating pulmonary aspergillosis and candidal pneumonias [72]. In a study to evaluate if CT adds information to CXR, 33 cases were reviewed retrospectively [86]. It was found that in 16 cases CT added no additional useful information, but in 17 cases CT added confidence and changed management (biopsy, changing antibiotics, bronchoscopy).

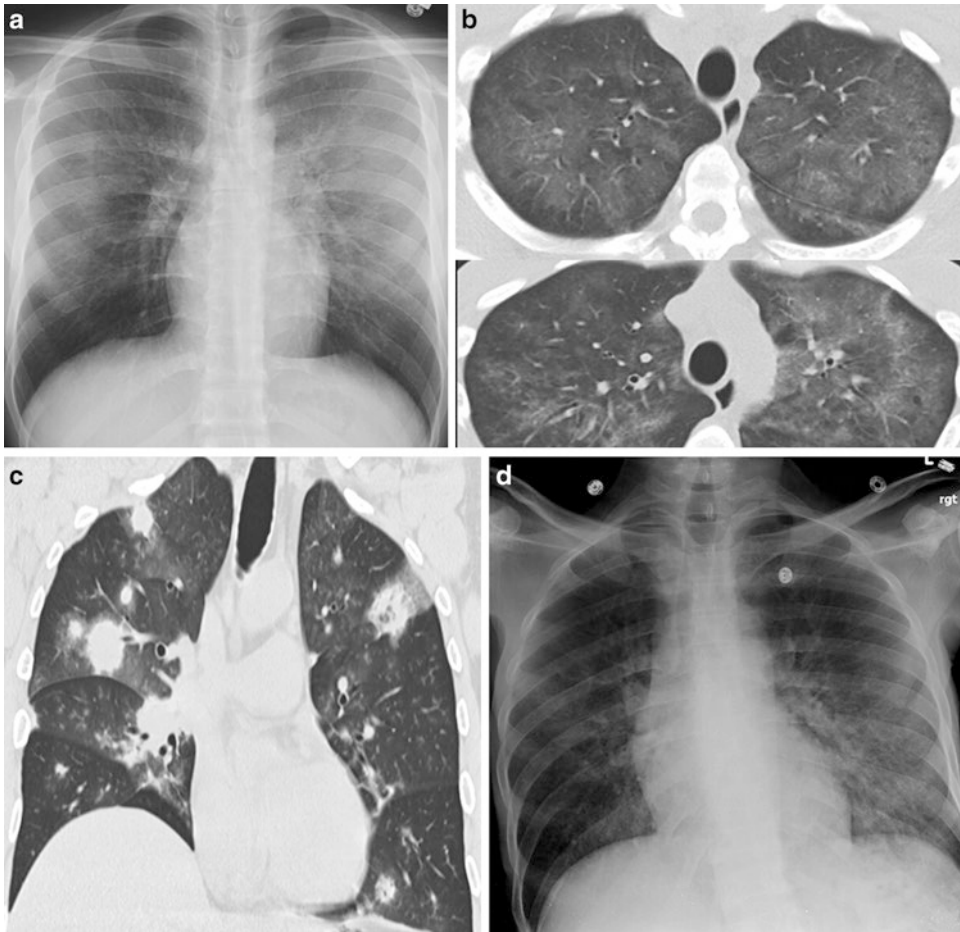


Fig. 18.6 (a–d) Cases showing the characteristic imaging patterns seen in PJP, angioinvasive aspergillus, and CMV pneumonia. A frontal CXR (a) and CT (b) from a patient with HIV, low CD4 count, and PJP demonstrate the classic findings of ground-glass opacity with peripheral sparing. Also note the lack of lymph node enlargement and pleural effusions. A coronal reconstruction from a chest CT (c) from a patient with neutropenic fever demonstrates several nodular areas of consolidation with surrounding ground-glass halos representing hemorrhage. This is the classic imaging manifestation of angioinvasive

aspergillus infection. Frontal CXR (d) and CT (e) images from a 41 y/o man with weakness, chills, and a CD4 count of 17 demonstrate the classic findings of CMV pneumonia. Note the widespread ground-glass opacity with superimposed areas of centrilobular nodularity. These cases illustrate the added specificity of CT over CXR. Although many infections have nonspecific findings on imaging, often there are findings which can help narrow the differential or even suggest a particular organism, as is the case with these examples. This allows for prompt empiric therapy and hopefully a better outcome for the patient

In What Situations Does Ultrasound (US) Add Value for Workup of Suspected Chest Infection in Children?

Summary of Evidence

- Ultrasound maintains an advantage over CT in identifying and characterizing complicated effusions, by its greater cost-effectiveness and

because it does not employ ionizing radiation (moderate evidence).

Supporting Evidence

Complications of pneumonia in children are broadly due to accumulation of pleural fluid that may become infected and organize over time. Parapneumonic pleural effusions are almost exclusively seen in bacterial infections, and not

in uncomplicated viral pneumonias [40]. However, fluid overload may also cause pleural effusions in hospitalized patients, making this distinction less clear in this group.

Ultrasound is the best test to further characterize these effusions and guide further treatment [87]. Based on appearance on imaging tests and response to treatment, pleural fluid collections may be classified as stage I (early exudative phase), stage II (intermediate fibrino-purulent phase), and stage III (late organizing phase). Reactive uncomplicated parapneumonic pleural effusions (stage I) are typically sonolucent and move with a change in patient position, whereas complicated (infected) pleural collections (stage II) exhibit an echo-complex pattern: echogenic debris, septations, and lack of movement with patient positioning [87, 88] (Fig. 18.7a–c). CT is poor in detecting these septations. CT can help to diagnose empyemas by virtue of demonstrating their mass effect on the underlying lung tissue, but published CT criteria to differentiate empyemas from uncomplicated reactive pleural effusion have been shown to be less reliable than sonographic evaluation [89].

There are several studies evaluating the prognostic implications of the use of ultrasound versus CT and the implications for treatment decisions [87, 90–92]. Ultrasound can be helpful in both prognosis and treatment decisions. It is a low-cost test, widely available, portable, does not

use ionizing radiation, and rarely requires sedation. This has to be contrasted to CT, which has a relatively high radiation dose, in the order of 100 times that of a CXR. Ultrasound is effective in demonstrating “high-grade” effusions containing septations, fronds, loculations, and debris. Ultrasound depiction of the thickness and number of these septations predict the success of chest tube drainage [87]. Kearney et al. demonstrated in a retrospective review of 50 patients who underwent both US and CT, that although both US and CT have effective roles, neither technique reliably identified the stage of pleural effusions or predicted whether patients would require surgical intervention [91]. The preponderance of evidence suggests that ultrasound is the most effective initial cross-sectional modality when pleural complications are suspected [87, 90, 92], whereas CT is the preferred modality to diagnose parenchymal complications [87, 89, 91, 93–95] (Fig. 18.7a–c).

Take Home Tables

Table 18.1 summarizes causes of pulmonary infection by age, and Table 18.2 covers CD4 count and risk of opportunistic infection in HIV/AIDS. Table 18.3 presents the diagnostic performance of chest radiography in detecting pneumonia in immunocompetent patients.

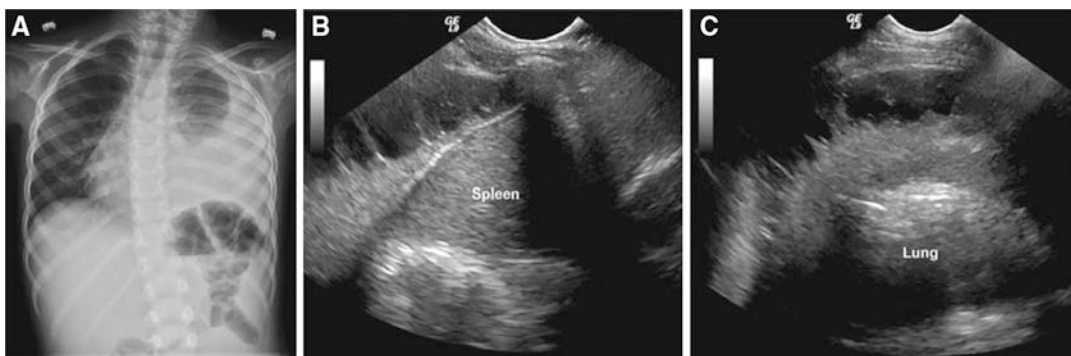


Fig. 18.7 (a–c) Empyema, role of ultrasound. Chest radiograph shows left-sided pleural collection. Ultrasound images demonstrate this collection to be complex (grade 2), with loculations, echogenic fluid, and fibrous adhesions. (Used with permission of Springer Science from

Choy G, Yager PH, Noviski N, Westra SJ. Imaging of Chest Infections in Children. In Medina LS, et al., eds: Evidence-Based Imaging in Pediatrics: Improving the Quality of Imaging in Patient Care. New York: Springer Science; 2010.)

Imaging Case Studies

Case 1

Figure 18.1a, b addresses a patient with community acquired pneumonia.

Case 2

Figure 18.2a–d addresses a patient with obvious CAP.

Case 3

In Fig. 18.3a, b, an 18-month-old boy with respiratory syncytial virus pneumonia is presented.

Case 4

Figure 18.4a, b presents a 37-year-old woman with HIV with round, mass-like consolidation in the right lower lobe.

Case 5

In Fig. 18.5a, b, a patient with HIV, fever, and dyspnea is presented.

Case 6

Figure 18.6a–d presents cases demonstrating characteristic imaging patterns seen in PJP, angioinvasive asperillosis, and CMV pneumonia.

Case 7

Figure 18.7a–c demonstrates the role of ultrasound in empyema.

Suggested Imaging Protocols

- Radiography: Lateral and posterior-Anterior (PA) views are optimal. Anterior-Posterior (AP) views can be useful. Decubitus views can be helpful in distinguishing free-flowing pleural fluid versus loculated fluid collections when effusions are suspected. With extensive pulmonary parenchymal consolidation, however, the value of decubitus films for the identification of loculated versus free pleural fluid is known to be limited.
- Chest CT: In chest infections, use of intravenous contrast is best tailored for the clinical question. Pulmonary parenchymal findings are usually easily characterized on non-contrast examinations, whereas mediastinal and pleural findings are often better characterized with contrast. Lower mA techniques (and kVp reduction in small children) can be used in the chest due to the high intrinsic contrast of air-filled lung parenchyma. Three-dimensional renditions (virtual bronchoscopy) and coronal reformats can be helpful tools to use before moving on to bronchoscopy or surgery.
- Ultrasound: Screening includes the whole pleural space and not only the lung bases. For more overview through inter- and subcostal scanning, lower frequency (3.5–7 MHz) sector transducers are used at first; subsequently, higher frequency (10–12.5 MHz) linear transducers can be useful in uncovering more detail in the near field before marking for needle placement [96].

Future Research

Future research should focus on the following:

- Cost-effectiveness research, for example: what is the cost-effectiveness of CXR and CT in suspected CAP?
- How can non-ionizing imaging modalities such as ultrasound and magnetic resonance be

utilized in the evaluation of pulmonary infection and its complications?

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Part IV

Abdominal and Pelvic Imaging



Appendicitis in Adults and Children: Evidence-Based Emergency Imaging

Booth Aldred, Laura B. Eisenmenger,
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Key Points

- CT demonstrates superior sensitivity and specificity for appendicitis compared to ultrasound in the adult population, with less variability, and is the imaging modality of choice in nonpregnant patients (strong evidence).
- MRI shows similar specificity and sensitivity to CT for the diagnosis of acute appendicitis in the nonpregnant adult and pediatric population (moderate evidence).
- In the pediatric population, CT has higher sensitivity than ultrasound, but similar specificity, with a trade-off of exposure to ionizing radiation (strong evidence).
- Limiting exposure to ionizing radiation warrants the use of US followed by CT for negative or equivocal cases in (nonobese)

pediatric patients (moderate evidence). The presence of an elevated absolute neutrophil count, nausea, or maximal tenderness in the right lower quadrant shows high sensitivity, but poor specificity in identifying pediatric patients with appendicitis (moderate evidence). Thus, these patients may benefit from imaging.

- Intravenous contrast enhanced CT is adequate for the diagnosis of acute appendicitis and obviates the need for enteral contrast (moderate evidence).
- There has been a decrease in the rate of negative appendectomy with use of preoperative imaging (moderate evidence).
- MRI is useful in pregnant women with suspected appendicitis, particularly beyond the first trimester (moderate evidence).

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Definition and Pathophysiology

Appendicitis, defined as inflammation of the vermiform appendix, is a prevalent disease whose etiology is not entirely understood [1, 2]. The common mechanism begins with obstruction, either by fecalith or lymphoid hyperplasia, with progressive increase in intraluminal pressure leading to compromised venous outflow, mucosal wall

breakdown, and bacterial overgrowth [2, 3]. The most common pathogens involved are *Escherichia Coli* and *Bacteroides fragilis* [1]. Wall ischemia can lead to hemorrhagic ulceration and gangrenous necrosis extending to the serosa that can lead to perforation [3]. Demonstrable obstruction is commonly absent in appendicitis on imaging and likewise, visible obstruction does not necessarily imply an acute infection [1, 4]. Delayed diagnosis can result in serious complications leading to abscess formation, peritonitis, wound infection, sepsis, infertility, adhesions, bowel obstruction, and rarely death with a mortality rate of 0.08%, increasing to 0.5% when perforated [1, 5, 6].

Epidemiology

Acute appendicitis is a common condition, with an estimated lifetime incidence of 8.6% in males and 6.7% in females and a male to female ratio of 1.1 to 1 [7]. Appendicitis is most common between the ages of 10 and 19 years with more recent epidemiological studies confirming this but showing an increase within the 30- to 69-year-old range secondary to aging demographics [7, 8]. Acute appendicitis is the most common reason for abdominal surgery in pediatric patients [5, 9], with 70,000–100,000 pediatric cases each year, and is diagnosed in 1–8% of children presenting with abdominal pain to the emergency department [9, 10]. Appendiceal rupture is most common in the pediatric and elderly populations with an overall rate of 10–35.5% and increases in likelihood with prolonged symptoms [11, 12].

Overall Cost to Society

Comprehensive societal cost data for patients with suspected acute appendicitis is lacking. An analysis of the Nationwide Inpatient Sample of the Health Care Utilization Project estimated that there were 292,297 hospitalizations in 2010 due to suspected acute appendicitis [13]. Recent data from the CDC estimated approximately 264,882 appendectomies in 2012 [14]. These admissions accrued an average hospital charge of between

\$9206 and \$10,584 per case, yielding an estimated national total of \$2.44 to \$2.76 billion dollars in hospital charges alone [14, 15]. Flum and Koepsell estimated the national cost of negative appendectomy at \$741.5 million dollars [15].

For pediatric patients, appendectomy is the most common surgical procedure performed in the hospital for non-neonatal- or nonpregnancy-related conditions [13]. Nationwide, an average of 238 pediatric appendectomies are performed daily. Annually, appendicitis accounts for approximately 87,000 pediatric hospital stays in the USA, representing 4.2% of all hospital stays for pediatric illness [13]. Appendicitis is the second most common reason for hospitalization for children and adolescents 6–17 years old. The aggregate total charges related to care of pediatric patients with appendicitis nationwide sum to over \$800 million annually [13]. At an institutional level, a retrospective chart review by Garcia Pena et al. showed that 308 pediatric patients who were observed for possible appendicitis collectively accumulated 487 inpatient observation days, with per patient cost of \$5831 [16].

Goals of Imaging

Imaging goals for suspected acute appendicitis are to determine if the patient has appendicitis, aid in earlier diagnosis, and identify complications, such as perforation or abscess, which may alter surgical management.

Methodology

Previously, data were primarily obtained from the meta-analyses of Terasawa [17] and Doria [18] and their colleagues. This edition adds the meta-analysis and sensitivity analysis by Parker et al. [19], a reanalysis of the prospective work performed by Mittal et al. [20], and a systematic review of the role of MRI in children [21]. These studies were identified via an updated PubMed search of English language articles through May 2015 using a combination of MeSH and free terms *appendicitis* or *appendix* and *diagnostic imaging*,

ultrasonography, X-ray computed tomography, CT, and magnetic resonance imaging or MRI. The bibliographies of relevant articles were searched for other potentially relevant articles. Studies were included if they were either prospective or retrospective evaluations of CT, graded compression ultrasound, or MRI with outcomes measured by surgical, pathological, or clinical follow-up.

Discussion of Issues

What Is the Accuracy of Imaging for Diagnosing Acute Appendicitis in Adults?

Summary of Evidence

- Computed tomography examination of adult patients has high sensitivity and specificity for acute appendicitis and is superior to graded compression ultrasound (moderate evidence).
- MRI has high sensitivity and specificity for diagnosis of appendicitis and is superior to graded compression ultrasound but less available (limited evidence).
- MRI appears to have moderately high diagnostic accuracy for appendicitis in pregnant patients after equivocal US (moderate evidence).

Supporting Evidence The meta-analysis by Parker et al. evaluated 74 studies published between 1999 and 2009 with data on appendicitis evaluating CT, US, or both for diagnosis [19]. Articles were included if sensitivity, specificity, NPV, and PPV were reported or calculable. Evaluation with US includes 8483 patients demonstrating a combined sensitivity of 87.5% (95% CI, 86.5–88.5%), a combined specificity of 92.7% (95% CI, 92.0–93.4%), a PPV of 91% (range 90.3–91.7), and a NPV of 89.8% (range 89.2–90.4). For the CT evaluation of appendicitis, there were 11,930 patients included demonstrating a combined sensitivity of 93.4% (95% CI, 92.7–94.1%), a combined specificity of 95.3% (95% CI, 94.8–95.8%), a PPV of 92.5% (range 91.9–93.1%), and a NPV of 95.9% (range 95.6–96.2%).

Sensitivities and specificities for the CT diagnosis of appendicitis were similar to those found

previously by Terasawa et al., at 95% and 94%, respectively [17]. Both analyses showed that the diagnostic accuracy for the US diagnosis of appendicitis is more heterogeneous than CT. The sensitivity and specificity of US calculated by Terasawa were 86% and 81%, respectively. A 2013 review of the literature performed by Pinto et al. demonstrated large variability in diagnostic accuracy of appendicitis by US with sensitivities ranging from 44% to 100%, and specificities ranging from 47% to 99% [22]. The authors ascribe this variability to operator dependency and patient factors including obesity, anatomic variants, and varying patterns of bowel gas. See Tables 19.1 and 19.2.

As MRI cost and scan time have decreased and become more available, the utilization of MRI for acute appendicitis has increased. Most evidence describes the use of MRI for appendicitis in the pregnant patient. A 2011 meta-analysis by Blumenfeld et al. included five retrospective studies evaluating the accuracy of MRI for appendicitis in the pregnant patient [26]. Summary sensitivity, specificity, PPV, and NPV were 90.5%, 98.6%, 86.3%, and 99.0%, respectively. The 2010 meta-analysis by Barger and colleagues reviewed ten retrospective studies on the performance of MRI for appendicitis in adults, of which 266 were pregnant patients [27]. This study included eight articles that compared MRI with pathology or clinical follow-up as the reference standard. The absolute number of true-positive (TP), true-negative (TN), false-positive, and false-negative results or sufficient data to calculate these values was required for inclusion by the authors. MRI demonstrated a combined sensitivity of 97% (CI: 92–99%) and combined specificity of 97% (CI: 94–99%), with a LR+ of 16.3 (CI: 9.1–29.1) and a LR- of 0.09 (CI: 0.04–0.197). Overall diagnostic odds ratio was 299.8 (CI: 97.5–921.6). More recent work has assessed the impact of MRI on clinical outcomes in the nonpregnant patient. Two recent prospective studies included a total of 275 adults undergoing MRI for acute appendicitis and demonstrated a sensitivity of 97% and a specificity of 93% and 97% for the diagnosis of acute appendicitis [28, 29].

A prospective study by Fonseca et al. including 79 pregnant patients evaluated for appendicitis by MRI

Table 19.1 Sensitivity and specificity of imaging in patients with suspected acute appendicitis

	Sensitivity (%)	Specificity (%)	Positive predictive value ^a (%)	Negative predictive value ^a (%)
Adults ^a				
Ultrasound	92.7	87.5	91.0	89.8
CT	93.4	95.3	92.5	95.9
Pediatric ^b				
Ultrasound	88	94	87	95
CT	94	95	95	97
Ultrasound followed by CT ^c	95	93	86	98

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^aFrom Parker et al. [19]

^bFrom Doria et al. [18]

^cTeo et al. [23], Garcia Pena et al. [24], and Kaiser et al. [25]

Table 19.2 Diagnostic performance of MRI in patients with suspected acute appendicitis

	Sensitivity (%)	Specificity (%)	Positive predictive value ^a (%)	Negative predictive value ^a (%)
Adults				
MRI (pregnant patients) ^a	90.5	98.6	86.3	99.0
MRI (pregnant patients) ^b	97	97	–	–
MRI (women) ^c	97	93	–	–
Pediatric ^d				
MRI	96.5	96.1	92.0	98.3

^aFrom Blumfield et al. [26]. Meta-analysis

^bFrom Barger et al. [27]. Systematic review

^cFrom [28, 29]. Prospective studies (total N = 275)

^dFrom Moore et al. [21]. Systematic review

showed higher discharge from the emergency department and an overall shorter length of stay compared to patients that did not undergo MRI [30]. The sensitivity and specificity of MRI were both 100%, with a positive likelihood ratio of 20. In a study by Rapp and colleagues, the conditional use of MRI following equivocal US in pregnant patients suspected of having appendicitis decreased the negative appendectomy rate (NAR) from 55% to 29% without any significant increase in perforation [31]. They found an overall sensitivity, specificity, PPV, and NPV of 89%, 97%, 74%, and 99%, respectively.

While the evidence related to MRI utilization and accuracy is increasing, most studies are small and single institution. Currently, the only consistent evidence demonstrating the value of

MRI for appendicitis is conditional use in pregnant patients. As radiation exposure concerns remain a powerful driver in modality choice, the evidence in support of MRI may increase.

What Is the Accuracy of Diagnostic Imaging in Pediatric Patients?

Summary of Evidence

- CT is more sensitive than ultrasound with similar specificity (Tables 19.1 and 19.2) (moderate evidence).
- A protocol of US followed by CT in negative or equivocal subjects may achieve similar sensitivity and specificity to CT alone, with less

radiation exposure and increased cost effectiveness (moderate evidence).

- A protocol of US followed by MRI in negative or equivocal subjects may achieve similar sensitivity and specificity to US compared with conditional CT use and eliminates ionizing radiation (moderate evidence).

Supporting Evidence Cross-sectional imaging is also the mainstay of diagnosis of acute appendicitis in the pediatric patient. A meta-analysis by Doria et al. [18] found 26 prospective and retrospective trials of graded compression US and/or CT in pediatric patients with suspected acute appendicitis (mean age range of 7–12 years). The eight studies included in the analysis described results from ultrasound only, CT only, or combined ultrasound and CT in 6850, 598, and 1908 patients, respectively. The mean sample prevalence of appendicitis from these trials was 31% for both US and CT (range, 15–75%). The weighted perforation rate in positive appendicitis cases was 26.5% [18]. For CT, the pooled sensitivity was 94% (95% CI, 92–97%), specificity was 95% (95% CI, 94–97%), and the summary diagnostic odds ratio was 239 (95% CI, 118–487). For the extracted data, the positive and negative likelihood ratios were 18.8 and 0.06, respectively. When these test specifications were applied to a population with the mean prevalence of appendicitis found in the trials examined by Doria et al. (31%), the positive predictive value was 89% and the negative predictive value was 97% (Tables 19.1 and 19.2) [18].

There were 23 studies of graded compression ultrasound that met inclusion criteria in the Doria et al. study. With one outlier removed, the pooled sensitivity of ultrasound in pediatric populations was 88% (95% CI, 86–90%), the pooled specificity was 94% (95% CI, 92–95%), and the summary diagnostic odds ratio was 202 (95% CI, 159–258). The positive and negative likelihood ratios were 14.7 and 0.13, respectively [18]. The positive predictive value of graded compression ultrasound was 87%, and the negative predictive value was 95%, using the mean prevalence of 31% for calculations (Tables 19.1 and 19.2) [18].

Thus, in patients with suspected acute appendicitis in whom evaluation with imaging is desired, the Doria et al. article demonstrated that there is a significant difference in the weighted pooled sensitivities for CT, with no significant difference in specificity of CT compared to ultrasound. However, as the authors noted, pediatric patients in general demonstrate greater sensitivity to ionizing radiation. This radiation exposure from CT should be included as a factor when weighing the risk of excess false-negative cases when US is the diagnostic modality.

In a secondary analysis of a 10-center prospective observational study of children presenting to emergency departments with abdominal pain, 965 pediatric patients were assessed with US to evaluate for appendicitis [20]. US demonstrated an overall sensitivity of 72% (CI 95%: 58.8%–86.3%) and an overall specificity of 97% (CI 95%: 96.2% to 97.9%). However, there was significant sensitivity variation dependent on how often US was utilized at each of the 10 tertiary pediatric care centers. At three sites that utilized US in 90% of cases, the sensitivity was 77.7%. At a single site that utilized US in 50% of cases, the sensitivity was 51.6%. At the four remaining sites combined, the sensitivity was 35% when US was utilized only 9% of the time. The conclusion is that the sensitivity of US for the diagnosis of acute appendicitis is confounded by the utilization rate of US in a given center [20].

Limitations in the pediatric appendicitis imaging literature include verification and selection bias, as in adults. Additional difficulties in analysis included lack of randomization of patients to imaging groups in many studies. Generalizability may also be an issue as CT has been more commonly studied in North America whereas ultrasound is more prevalently used in Europe and Asia. In addition, relatively few children under the age of 5 years were included in many of the studies, so that the results may not hold true for all children.

Ideally, an imaging protocol would combine the sensitivity of CT with the lack of ionizing radiation afforded by US in order to maximize diagnostic accuracy and minimize patient risk. Two prospective studies were identified in the

literature search that examined the combination of graded compression US as the initial imaging, followed by CT study if the appendix was not visualized or if the US was inconclusive for the diagnosis of appendicitis [23, 24]. Together, these trials enrolled 585 patients with a prevalence of appendicitis ranging from 23 to 43% with a pooled prevalence of 39%. The overall sensitivity varied from 77 to 97%, with a pooled sensitivity of 95% (95% CI, 83–100%). The range of specificity was 89–99%, with a pooled result of 93% (95% CI, 97–97%). These series demonstrated a greater sensitivity and lower specificity when the combined US followed by CT results were considered, as compared to cases when the US data was considered alone, with an associated increase in the negative predictive value of the testing algorithm. Another randomized trial of 600 patients compared results of CT and US versus US alone in a pediatric population [32]. This study demonstrated similar results to the two aforementioned series, with the combined CT and US protocol demonstrating a sensitivity of 99% and specificity of 89%, while US alone showed a sensitivity of 86% and specificity of 95% [32]. Subsequent pediatric studies have not shown such high sensitivity as the Doria paper, such as a recent one by Trout that reported 67% sensitivity at a high volume Children's Hospital, suggesting that there continues to be wide variation in sonographic performance [33].

An additional consideration in deciding on the use of US versus CT is patient body habitus. An elevated body mass index (BMI) can limit visualization of the appendix with ultrasound, with non-visualization of the appendix in 79% of overweight children compared to 33% in normal weight and 25% in underweight children [34]. Two prospective studies and one retrospective study concluded that there was a trend of decreasing sensitivity with increasing BMI, but no statistical significance [35–37]. Obese children had similar length of stay, perforations, and complications compared to children with normal BMI. However, obese children were three times more likely to undergo CT [36]. A retrospective study by Grayson et al. found that increased intraperitoneal fat was correlated with a signifi-

cantly increased likelihood of visualizing a normal appendix on CT of pediatric patients [38].

A formal cost-effectiveness analysis compared a protocol based on US followed by CT if negative to use of CT and US alone. The Markov decision analytic model indicated that the incremental cost-effectiveness ratio (ICER) of the US followed by CT protocol was below \$10,000 in both male and female pediatric patients [39]. This cost falls well below the threshold for societal willingness to pay of \$50,000. Thus, the protocol of US followed by CT was found to be a cost-effective imaging strategy (moderate evidence).

The utilization of MRI alone or conditionally subsequent to equivocal or negative US was prospectively evaluated in two small trials demonstrating sensitivity and specificity ranges of 93.3%–100% and 98%–100%, respectively, for both conditional MRI and MRI alone [40, 41]. In a larger retrospective study, Aspelund et al. demonstrated that US selectively followed by MRI was comparable to CT with no difference in length of stay, negative appendectomy rate, perforation, or complications [42]. There were 662 patients included in the study divided into a CT cohort and US with conditional use of MRI, with 142 patients receiving MRI. Sensitivity, specificity, PPV, and NPV of the US with conditional MRI group were 100%, 98%, 98%, and 100%, which were equivalent to the CT cohort, suggesting a highly accurate non-ionizing pathway [42].

A recent systematic review of MRI by Moore et al. summarized the results from 11 studies comprising 1698 children [21]. Two of these studies reported outcomes including negative appendectomy rates of 1.4–3.1% [21, 42]. Importantly, the MR protocol most commonly used was limited to 4–5 sequences and did not require gadolinium contrast or oral contrast. Since the imaging time was short, the need for sedation was minimized. The key pulse sequence is the single-shot fast spin echo performed in both axial and coronal planes. Moore et al. suggest that four sequences have shown adequate accuracy for this diagnosis, by using T2w SSFSE without and with fat saturation inversion recovery (SPAIR) in axial and coronal planes. They note that in general, children under age five will need sedation.

Which Subjects Suspected of Having Appendicitis Should Undergo Imaging?

Summary of Evidence

- A pediatric clinical prediction rule that relies on signs and symptoms in conjunction with basic laboratory values may be useful in identifying subjects who do not need imaging (Table 19.3). This prediction rule has been revalidated and refined at multiple institutions (moderate evidence).
- The Alvarado score could be used to stratify patients who should undergo CT (limited evidence).
- Limited data and modeling studies suggest that CT is most useful when the clinical probability of acute appendicitis is intermediate to high, as a confirmatory test in subjects for whom surgery is considered (limited evidence).

Supporting Evidence Clinical exam and serum laboratory testing remains the standard initial method of determining which patients may have appendicitis. However, given the historical rates of both missed diagnosis and unnecessary laparotomy, a number of investigators have attempted to formalize the clinical exam into a valid scoring tool or decision rule for deciding which subjects are at risk of appendicitis. In 1986, Alvarado

Table 19.3 Clinical decision rule for determination of pediatric patients at low risk for acute appendicitis

Presence of either prediction rule has a sensitivity of 98.1% and a NPV of 95.3% in identifying pediatric patients at low risk

1. Absolute neutrophil count (ANC) $< 6.75 \times 10^3/\mu\text{L}$ and no maximal tenderness in the RLQ
2. Absolute neutrophil count (ANC) $< 6.75 \times 10^3/\mu\text{L}$ and maximal tenderness in the RLQ but no abdominal pain with walking/jumping or coughing

Data from Kharbanda et al. [43]

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introduced a tool termed the MANTRELS criteria for scoring of appendicitis risk in adults. However, diagnostic accuracy is low, with significant inter-provider variability in the application of these criteria [44].

Multiple recent studies suggest that the Alvarado score may be used for stratification of patients who should undergo CT. A recent meta-analysis of 29 studies evaluating the use of the Alvarado score found that children with a pretest probability of acute appendicitis of either 60% or 40% with Alvarado scores of 4 and 5, respectively, were negative by imaging. In adults with a pretest probability of either 60% or 40% and Alvarado scores of 8 and 9, respectively, ruled in the diagnosis [45]. Tan et al. conducted a retrospective study evaluating 358 subjects with suspected appendicitis and concluded that patients with an Alvarado score between 4 and 8 would benefit from CT [46]. Very recently, the same author conducted a small prospective study that found CT is beneficial mainly in patients with an Alvarado score of 6 and below in males and 8 and below in females [47].

Efforts have focused on using clinical and laboratory examination as a triage tool in pediatric subjects to determine children who are at sufficiently low risk for appendicitis such that imaging may be avoided. Kharbanda et al. developed, revalidated, and refined a clinical prediction rule resulting in a model that identified patients at low risk with [1] an absolute neutrophil count of $6.7 \times 10^3/\mu\text{L}$ or less and no maximal tenderness in the right lower quadrant or [2] an absolute neutrophil count of $6.75 \times 10^3/\mu\text{L}$ or less with maximal tenderness in the right lower quadrant but no abdominal pain with walking/jumping or coughing. This refined rule had a sensitivity of 98.1% (95% CI, 97.0%–98.9%), specificity of 23.7% (21.7%–25.9%), and negative predictive value of 95.3% (92.3%–97.0%) (Table 19.2). Application of this rule could allow for a reduction in use of CT by 20% [43]. Limitations in this study include the potential for enrollment bias and interobserver variability.

Garcia Pena et al. also performed recursive partitioning analysis of a retrospective cohort of 958 children with equivocal acute appendicitis, who were risk stratified into three groups based

on clinical signs and symptoms and laboratory values [24]. Three different management guidelines with subsequent modeling of outcomes were developed. Outcomes included the number of negative appendectomies and missed or delayed diagnoses of appendicitis. The authors showed that management guidelines with more selective use of imaging could reduce the number of imaging exams with minimal increase in the negative appendectomy rate and the number of missed diagnoses of appendicitis. However, these guidelines have not yet been validated, so the effectiveness in clinical practice is uncertain.

There is only limited evidence as to which subjects at risk for appendicitis should undergo imaging. Recent investigations by Nathan et al. [48] and Kim et al. [49] suggest that imaging is more likely to be of value for clinical decision-making when performed in subjects determined clinically to be of high probability for acute appendicitis. In a study of community emergency physicians, Nathan et al. found that when the emergency physicians determined that appendicitis was unlikely, the diagnostic yield from CT was extremely low. However, neither emergency physicians nor consulting surgeons were able to define when appendicitis was certain. Kim et al. found that CT would substantially decrease the rate of negative laparotomy in subjects with clinically evident appendicitis [49]. In addition, modeling demonstrates the potential adverse effect of false-positive diagnoses if CT is used to screen a more low-risk population [50]. These results would suggest that the most appropriate use of CT is in subjects of intermediate risk as well as in subjects at high pretest probability for appendicitis. In effect, confirmatory CT should be performed in all subjects prior to being taken to the operating room (OR) for suspected appendicitis, but if it is unlikely that a patient is going to the OR, CT should be avoided [48].

What Is the Effect of Imaging on Negative Appendectomy Rate?

Summary of Evidence

- The negative appendectomy rate decreases with increasing use of preoperative imaging, in particular CT, in adults (strong evidence).

- The negative appendectomy rate decreases with increasing use of preoperative imaging in the pediatric population (moderate evidence).

Supporting Evidence The Krajewski et al. meta-analysis published in 2011 which compared the CT era to the pre-CT era included 10 studies with 4485 adult patients evaluated during the pre-CT era and 1629 patients during the CT era. Utilization of CT imaging saw a negative appendectomy rate (NAR) of 21.5% decrease to 10%. The cumulative pooled odds ratio for the NAR after CT was 0.57 (95% CI 0.45–0.72) demonstrating the benefit of CT [51]. The limitation of this analysis is primarily related to the fact that the studies included were retrospective, resulting in selection bias. However, since a selection bias would be expected to result in a smaller difference in the NAR, it is likely that the results represent valid conclusions.

The results from the meta-analysis are now supported with results from newer prospective studies. For example, a quality improvement effort in Washington State, the prospective Surgical Care and Outcomes Assessment Program (SCOAP) included 53 hospitals in Washington State, and reported a significantly lower NAR after imaging when describing the experience since 2006. The study included 19,327 patients (age >15) who underwent urgent appendectomy, with a NAR of 15.4% in subjects without imaging, 10.4% in subjects who underwent US, and 4.1% in those who underwent CT [52]. An 18-year retrospective study at a single institution saw a pre-imaging NAR of 23% decrease to 1.7% after routine CT [53].

The data in pediatric patients is relatively consistent. A large retrospective study performed by Bachur et al. included 55,227 children with appendicitis, demonstrating an overall NAR of 3.6%. The patient-level NARs among boys stratified by age were 16.9% (age >5 years), 1.3% (5–10 years), and 1.1% (>10 years). Among girls, the rates were 13.3% (age <5 years), 1.8% (5–10 years), and 5.5% (>10 years). US and/or CT imaging decreases the NAR in all children except those younger than 5 years [54]. Many smaller studies have found the same results [55–57]. The strongest study arguing

against the liberal use of CT scans for NAR reduction is the study published in 2004 by Martin et al. [58]. This retrospective single-institution study reviewed results from 720 children undergoing appendicitis evaluation between 1998 and 2001 with US and/or CT. Although, during this period, the use of US decreased from 20.0% to 7.0% and the use of CT increased from 17.6% to 51.3%, no significant reduction of NARs observed.

Take Home Tables

Tables 19.1 and 19.2 cover the specificity and sensitivity of imaging for suspected acute appendicitis and the performance of MRI in detecting suspected acute appendicitis, respectively. Table 19.3 summarizes the clinical decision rule for determining pediatric patients at low risk for acute appendicitis.

Imaging Case Studies

Case 1

In Fig. 19.1, an 11-year-old male presented to the emergency department complaining of right lower quadrant (RLQ) abdominal pain, nausea, and emesis for less than 24 h.

Case 2

In Fig. 19.2, a 21-year-old male presents to the emergency department complaining of RLQ abdominal pain and nausea for 24 h.

Case 3

In Fig. 19.3, a 23-year-old pregnant female presents to the emergency department complaining of right lower and right upper quadrant abdominal pain and nausea for 24 h.

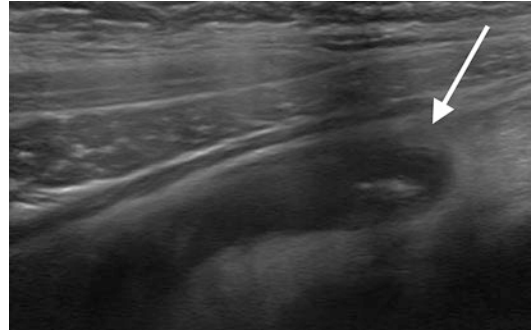


Fig. 19.1 Eleven-year-old male presented to the emergency department complaining of right lower quadrant (RLQ) abdominal pain, nausea, and emesis for less than 24 h. On physical exam, he was febrile and demonstrated right lower quadrant tenderness with guarding. Laboratory evaluation revealed a mildly elevated white blood cell count of 12,500 cells/mm³. An ultrasound was obtained, demonstrating a blind-ending, noncompressible tubular structure in the right lower quadrant compatible with a dilated appendix, measuring 13 mm in diameter and containing an echogenic, shadowing fecalith. On appendectomy, gross and histological findings established the presence of a nonperforated but friable, suppurative appendix



Fig. 19.2 Twenty-one-year-old male presents to the emergency department complaining of RLQ abdominal pain and nausea for 24 h. On physical exam, he was afebrile and demonstrated right lower quadrant tenderness with rebound pain. White blood cell count was elevated at 15,200 cells/mm³. CT demonstrated a dilated, 12 mm appendix with mural thickening and inflammatory changes in the periappendiceal fat. Gross examination of the appendix after appendectomy revealed dilated, necrotic appendix

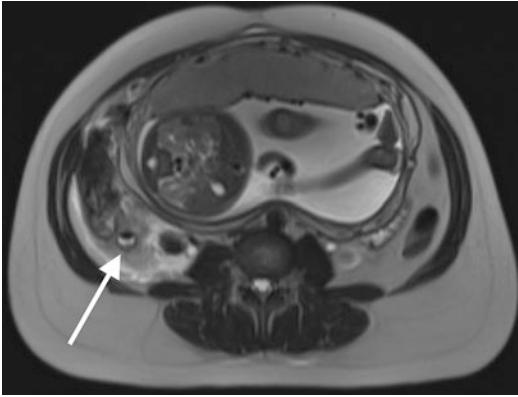


Fig. 19.3 Twenty-three-year-old pregnant female presents to the emergency department complaining of right lower and right upper quadrant abdominal pain and nausea for 24 h. On physical exam, she was febrile and demonstrated right lower quadrant tenderness with rebound pain. White blood cell count was elevated at 19,900 cells/mm³. MRI demonstrated a dilated appendix with mural thickening and a fluid level. Gross examination of the appendix found that the mid portion of the appendix was gangrenous and perforated with fecal matter present within the encased cavity

CT Protocols for Suspected Appendicitis

There is no consensus in the literature as to the ideal CT protocol with respect to use of intravenous contrast, oral contrast, rectal contrast, or non-contrast technique; indeed, there are varying reports of the efficacy of these protocols [5, 59–63]. There is also significant variability in terms of recommendations regarding focused imaging of the appendiceal region versus complete scan of the abdomen and pelvis, with trade-offs between radiation dose and more complete exam [64, 65]. In general, CT protocols are institutionally dependent, and the best technique for a given patient may vary depending on [1] the ability to tolerate administration of oral or rectal contrast and [2] any contraindications to intravenous contrast. Use of radiation dose reduction techniques is critical particularly given the relatively young age of most subjects with clinically suspected appendicitis (peak age 10–30 years). There is, however, a trend in the use of IV contrast alone without enteric contrast for emergency department patients to improve the throughput of

patients [61]. A large prospective study derived from the SCOAP trial that included 8089 patients found no improvement in the diagnosis of appendicitis following concomitant use of IV and enteral contrast [66]. Laituri and colleagues conducted a retrospective review demonstrating that contrast material does not reach the point of interest in 30% of patients receiving oral contrast for the CT evaluation of appendicitis. This is at the detriment of delayed diagnosis, emesis, and nasogastric tube placement [67].

ACR Appropriateness Criteria® Guidelines

Current ACR guidelines recommend that adults and adolescents with both classic and atypical signs and symptoms of appendicitis be imaged with enhanced CT of the abdomen and pelvis, with a rating of 8. Given discrepancy within the literature regarding the need for contrast, a non-enhanced CT abdomen and pelvis is a suitable alternative in suspected cases of appendicitis when the adult/adolescent patient presents with classic or atypical symptoms with ratings of 7 and 6, respectively. Abdominal US maintains a moderate rating of 6, although it is rarely utilized as a first line imaging modality in the United States despite its heavy utilization in Europe. Radiography maintains a role when the patient presents with atypical symptoms with a rating of 6. But when the patient presents with classic symptoms, radiography carries a lower recommendation of 4 [68].

The pregnant patient suspected of appendicitis is approached differently given the concern of ionizing radiation to the fetus. Abdominal US carries the highest recommendation with a rating of 8, followed by MRI and pelvic US with ratings of 7 and 6, respectively. CT abdomen and pelvis with contrast carries a moderate recommendation, with a rating of 5 and is often avoided unless absolutely necessary [68].

As with the pregnant patient, the pediatric patient (<14 years of age) requires a conservative approach to imaging. Abdominal US is widely accepted and remains first line imaging for the

pediatric population with a rating of 8. CT abdomen and pelvis with contrast carries a high rating of 7 and is still very useful when US is equivocal or the pediatric patient is obese. Radiography carries a moderate rating of 6 and is commonly used in the pediatric population when atypical symptoms are present [68].

Future Research

- Multicenter validation of proposed clinical decision rules aimed at determining when imaging is indicated in patients with suspected appendicitis.
- Determination of the overall cost and cost-effectiveness of imaging in patients with suspected acute appendicitis.
- Potential paradigm shift towards antibiotic conservative management for the treatment of acute appendicitis may influence the role of emergent abdominal imaging. Ongoing research continues to question the need for surgical management and further studies are needed.

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Evidence-Based Emergency Imaging for Non-appendiceal Acute Abdominal Pain in Adults: Pancreatitis and Diverticulitis

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Key Points

- The diagnosis of acute pancreatitis is based on analysis of the serum amylase and lipase levels, when combined with typical clinical signs and symptoms, and does not usually require imaging unless complications are suspected.
- CT has established indications and time frames for staging severity of pancreati-

tis in the acute phase. It is also commonly used to assess complications related to pancreatitis in the subacute and chronic phases.

- The role of MRI has been increasing in pancreatitis with improved technology, faster scanning times, and excellent contrast resolution.
- MRI permits the identification of calculi in the common bile duct (CBD) with a high degree of accuracy and permits accurate assessment of the pancreatic ductal system.
- Sonography is not routinely used for the diagnosis and evaluation of pancreatitis, due to intrinsic limitations in the technique, but has a role for revealing causes of pancreatitis, particularly CBD calculi. It can also be used for image-guided therapies, such as drainage of pseudocysts (moderate evidence).
- CT has a high accuracy for the depiction of colonic diverticulitis (moderate evidence), but its effect on outcome and patient management has not been well established to our knowledge (limited evidence).

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Definitions and Pathophysiology

The phrase “acute abdomen” is a broad term which refers to multiple clinical conditions characterized by severe abdominal pain and tenderness which develops over the span of a few hours [1]. Patients often present with a nonspecific clinical picture, even with a thorough history, physical examination, and laboratory analysis (which is often difficult or lacking in the emergency evaluation setting), making expeditious diagnosis a challenging task. Imaging examinations, particularly cross-sectional imaging with computed tomography (CT) and ultrasound (US) and occasionally but increasingly magnetic resonance imaging (MRI), are requested to help clinicians narrow their differential diagnosis and to triage patients, identifying those who will potentially benefit from surgical versus conservative treatment. Although there are innumerable causes of an acute abdomen (and pelvis), this chapter will focus on two common entities which manifest as an “acute abdomen”: acute pancreatitis and acute colonic diverticulitis.

Acute pancreatitis refers to acute inflammation of the pancreas [2]. Pancreatitis frequently involves and affects surrounding tissues and may also affect more distant organs. The most common causes of pancreatitis in North America are gallstones (38%) and alcohol abuse (36%) [2]. Acute pancreatitis can also be caused by a long list of other, much less common causes, including medications, metabolic factors, trauma, tumors, and anatomic variants leading to obstruction of exocrine pancreatic fluids [3]. Most patients have a mild or relatively mild and self-limited disease course. However, up to 10 to 20 % develop progressive inflammation associated with severe morbidity and even potential mortality and a prolonged length of hospital stay [3]. The mortality rate in mild pancreatitis is lower than 1%, whereas the reported mortality in severe pancreatitis reaches 30% [4]. The most common cause of death from acute pancreatitis is multi-organ failure.

Colonic diverticula are herniations of the mucosa through the colonic wall [5]. The presence of uninflamed diverticula is called diverticu-

losis. Decreased consumption of unprocessed cereals and grains and increased consumption of sugar and meat in Western diets are associated with the development of diverticula, particularly in the distal descending colon and in the proximal and mid-sigmoid colon [6]. Less commonly, diverticulosis can affect other portions of the colon, such as the right and transverse colon, or may be diffuse. Acute diverticulitis is a common, extraluminal pericolic infectious and inflammatory process caused by the perforation of colonic diverticula [5]. The location(s) of diverticulitis reflect the most common sites of underlying diverticulosis.

Hinchey et al. described a practical classification system for the staging of diverticulitis. Stage 1 is a pericolic or mesenteric abscess, stage 2 is a walled-off pelvic abscess, stage 3 is a generalized purulent peritonitis, and stage 4 is a generalized fecal peritonitis [7].

Epidemiology

Every year in the United States, over seven million people with acute abdominal pain present to an emergency department (ED), comprising up to 6.5% of the ED census [8]. Twenty-one percent of these patients will be diagnosed with nonspecific/undifferentiated abdominal pain [8]. The vast majority of patients discharged with undifferentiated abdominal pain have a benign course and will improve within several days [9]. Nevertheless, up to 28% will experience recurrent abdominal pain and will usually require repeated diagnostic imaging and other examinations. A substantial minority of patients with recurrent pain (13%) will undergo a therapeutic surgical intervention [10].

The National Hospital Discharge Survey estimated that 235,000 hospital discharges in the United States in 2007 had a primary diagnosis of acute pancreatitis [11]. The average length of stay for patients with pancreatitis was 6.1 days. This discharge data reflects a bimodal distribution of the disease, with alcohol-related pancreatitis occurring at an average age of 40 years, compared to gallstone pancreatitis which

typically presents around 70 years of age [2]. The latter etiology is more common in women, while the former is more common in men.

The presence of colonic diverticula in Western society is very high and is reported to affect almost 80% of the population over 85 years of age [12]. However, symptomatic acute diverticulitis will develop in only 20% of patients with colonic diverticula [12]. Approximately 25% of patients with acute diverticulitis will require surgery [13]. There were 276,000 patient hospital discharges with the primary diagnosis “diverticula of intestine” in 2007, according to the US National Hospital Discharge Survey [11]. The average length of stay was 4.8 days. Only 50% of admitted patients with diverticula and their complications were 65 years or older. This number highlights the importance of considering acute diverticulitis in the gamut of the differential diagnosis of acute abdominal and pelvic pain in younger patients. Relatively recently, a subset of younger patients has been identified with diverticulosis and diverticulitis, especially in obese individuals. Zaidi et al. reported a cohort of patients with acute diverticulitis [14] and found that 21.2% of patients were 40 years old or younger. Obesity was present in 85 of 104 (81.7%) patients in their study group.

Overall Cost to Society

There is limited available data, to our knowledge, to assess the potential or actual costs to society of patients presenting to the emergency department (ED) with acute abdominal pain. This limitation also pertains to patients with acute pancreatitis and acute colonic diverticulitis, as well as their complications. However, in general, abdominal pain was the most common presenting symptom in patients whose insurance claims had been disputed after a visit to an emergency department in the United States [15]. The average cost of services per patient in these disputes was US\$1107. Patients with acute abdominal pain have a significant impact on healthcare costs, especially when taking into account the more than seven million

annual ED visits due to various causes of abdominal pain [8].

The literature regarding costs of acute pancreatitis generally focuses on, and is limited to, the costs of hospitalization, and rarely includes data about indirect costs, to our knowledge. In 2003, the estimated total cost for acute pancreatitis admissions was \$2.2 billion in the United States [16]. The mean cost of hospitalization for an individual patient with acute pancreatitis was estimated at \$12,446.48 in 2010, with 288,597 admissions annually [17], with a calculated cost of over \$3.5 billion dollars.

In comparison, diverticulitis results in an estimated \$2.4 billion of direct healthcare costs per year in the United States [18]. One study assessed 148,874 patients who underwent segmental colectomy for diverticulitis from 1998 to 2010 [18]. The mean length of stay was 9.7 days, and the mean total hospital charges were \$59,561 for patients requiring operative management of their diverticulitis.

Goals of Imaging

The main goal of imaging in patients with acute abdominal (and/or pelvic) pain is to identify the etiology of pain and to exclude life-threatening conditions. The secondary goal is to determine which patients will benefit from surgical intervention versus conservative management. Additional goals include the staging of disease and the identification of complications.

Imaging of Pancreatitis

Methodology

A literature search was performed of English language articles from January 2005 to January 2015, using the MEDLINE database as well as EMBASE and the Cochrane Library. Search terms included the MeSH terms “diagnostic imaging” and “pancreatitis,” as well as the MeSH terms “computed tomography,” “CT,” “ultrasound,” “sonography/

ultrasonography,” “MRI,” “MRCP,” and “magnetic resonance imaging.” Inclusion criteria incorporated systematic reviews, meta-analyses, prospective studies, and retrospective studies related to pancreatitis. Review article and imaging and clinical society position papers related to staging systems for acute pancreatitis were also sought.

Discussion of Issues

What Is the Accuracy of Imaging for Staging Pancreatitis?

Summary of Evidence CT is the most studied imaging modality in the imaging of the acute abdomen and has demonstrated utility in staging acute pancreatitis 72–96 h after onset of symptoms, based on several developed and modified CT scoring protocols. CT is also an accurate and specific imaging modality for identifying complications of pancreatitis, including pseudocyst formation, hemorrhage, as well as development of a pseudoaneurysm, and necrotizing pancreatitis. Ultrasound is neither sensitive nor specific for the diagnosis of, nor for the staging of, acute pancreatitis due to intrinsic limitations of the technique and retroperitoneal location of the pancreas but has a role in the identification of gallstones and of common bile duct (CBD) calculi (i.e., choledocholithiasis) which are often associated with acute pancreatitis. MRI is less well studied compared to CT but has excellent contrast resolution, allowing visualization of the CBD and the pancreatic duct, as well as staging of acute pancreatitis, and the differentiation of hemorrhagic from necrotizing pancreatitis. MRI as a cross-sectional imaging modality requires further study of its accuracy in staging acute pancreatitis, with or without the use of IV gadolinium, although currently available literature suggests that it does have utility. MR can be employed for follow-up, to reduce radiation dose exposure, particularly in younger patients who would otherwise potentially receive multiple CT examinations in cases of complicated pancreatitis or recurrent episodes of pancreatitis. MR cholangiopancreatography (MRCP) is the noninvasive cross-sectional

imaging examination of choice for the identification of common bile duct calculi when ultrasound is inconclusive. MRI was given a score of 4 out of 9 in the ACR Appropriateness Criteria for imaging acute pancreatitis [19, 20].

How Is the Diagnosis of Acute Pancreatitis Established?

Summary of Evidence The diagnosis of acute pancreatitis is usually based on analysis of the serum amylase and lipase levels, combined with typical clinical symptoms, which if present, as per the revised criteria of the Atlanta classification system, does not require imaging unless complications are suspected [21]. However, imaging plays a substantial role in staging the severity of pancreatitis, assessing complications of pancreatitis, and revealing the underlying cause. Also, as per the revised Atlanta classification system, cross-sectional imaging can be used to identify pancreatitis in a patient with nonspecific abdominal pain who is not initially clinically suspected of having pancreatitis. Currently, cross-sectional imaging, particularly CT, is one of the three main criteria for establishing the diagnosis of acute pancreatitis, as per this revised classification system [21]. Benefits of CT include high spatial resolution, relatively easy access, relatively low cost, and fast scan times.

Supporting Evidence In North America, as noted above, acute pancreatitis is most commonly caused by gallstones and alcohol abuse, although other less common causes include hypertriglyceridemia, infectious causes, medications, trauma, sphincter of Oddi dysfunction, endoscopic retrograde cholangiopancreatography (ERCP) and other procedures, and congenital abnormalities, including pancreas divisum, annular pancreas, and choledochoceles [4].

There are several scoring systems which are employed in current practice to identify and stratify the severity of acute pancreatitis. Most of these systems rely primarily on the results of laboratory testing as well as on the clinical findings. These include the Ranson criteria, the

revised Atlanta classification, and the APACHE II (acute physiology and chronic health evaluation II) scoring systems [22–26]. These systems take into consideration patient age, as well as various blood tests including the white cell count and the creatinine level. The various scoring systems differ in the incorporation of other blood tests, vital signs, blood gases, and the timing of when to assess these indicators.

Over time, in addition to clinical assessment, cross-sectional imaging has become increasingly important in staging and triaging management of patients with known or suspected acute pancreatitis. CT is considered the imaging reference standard for assessing morphological complications from pancreatitis, including pseudocyst formation, splenic vein thrombosis, hemorrhagic pancreatitis, pseudoaneurysm formation, and pancreatic and peripancreatic necrosis [27]. CT is also helpful to diagnose or exclude the occasional patient with an underlying pancreatic mass leading to pancreatitis, particularly pancreatic adenocarcinoma and intraductal papillary mucinous neoplasm (IPMN) [20, 28, 29].

Several grading and scoring systems have been developed to examine the morphologic changes related to acute pancreatitis. The CT severity index was introduced by Balthazar in 1994 [30]. This index was based on scoring the presence and degree of pancreatic inflammation as well as necrosis on IV contrast-enhanced CT. It allowed differentiation of mild from severe pancreatitis and also numerically correlated with the patient's prognosis. In 2004, Mortele et al. introduced a modified CT severity index [31]. The modified CT severity index had a similar interobserver variability compared to the original CT severity index but correlated more closely with patient outcomes, especially with the length of the hospital stay and the development of organ failure.

In 2012, a study by Bollen et al. compared several CT scoring systems for pancreatitis including the Balthazar CTSI (CT severity index), the EP (extrapancreatic score), the EPIC (extrapancreatic inflammation on CT score), the MCTSI (modified CT severity index) (Table 20.1), the MOP (mesenteric edema and

Table 20.1 Modified CT severity index for assessing acute pancreatitis

Prognostic indicator	Score
Pancreatic inflammation	
Normal pancreas	0
Intrinsic pancreatic abnormalities with peripancreatic inflammatory changes	2
Pancreatic or peripancreatic fluid collection or peripancreatic fat necrosis	4
Pancreatic necrosis	
None	0
<30%	2
>30%	4
Extrapancreatic complications	
Pleural effusion, ascites, vascular complication (venous thrombosis, arterial hemorrhage, pseudoaneurysm), parenchymal complication (infarction, hemorrhage, subcapsular fluid collection), GI involvement (inflammation, perforation, intraluminal fluid collection)	2

Based on this scoring system, the severity of pancreatitis for a patient can be categorized as either mild (0–2 points), moderate (4–6 points), or severe (8–10 points). For extrapancreatic complications, either 0 (no complications) or 2 points are assigned, regardless of how many complications are present

Adapted with permission from Mortele KJ, Wiesner W, Intriere L, et al. Modified CT severity index for evaluating acute pancreatitis: improved correlation with patient outcome. *AJR* 2004;183:1261–1265

peritoneal fluid score), and the PSI (pancreatic size index) [32]. For the purpose of this study, the authors compared sensitivity, specificity, PPV, and NPV of the various scoring systems in predicting clinical severity and patient outcomes. They found no statistically significant differences between the various CT scoring systems [32] (Table 20.2).

The best known scoring system and associated lexicography is the Atlanta classification for acute pancreatitis. In 1992, the Atlanta Symposium divided acute pancreatitis into mild and severe forms, based on clinical and laboratory findings. In 2008, the revised Acute Pancreatitis Classification Working Group developed a morphological classification including interstitial edematous pancreatitis and necrotizing pancreatitis, which was finally published in 2012 [21]. 70–80% of patients fit into the mild or interstitial edematous type of pancreatitis, while

Table 20.2 Comparison of selected major radiological scoring systems for predicting the clinical severity and mortality of pancreatitis

Scoring system	Sensitivity % Severity/mortality	Specificity % Severity/mortality	PPV % Severity/mortality	NPV % Severity/mortality
Balthazar	66/78	85/79	50/18	92/98
EPIC	86/89	62/56	34/11	95/99
CTSI	87/86	83/74	53/16	97/99
MCTSI	78/86	81/50	46/9	95/98

CT severity index (CTSI), modified CT severity index (MCTSI), extrapancreatic inflammation on computed tomography (EPIC)

Modified with permission from Bollen TL, Singh VK, Maurer R, et al. A comparative evaluation of radiologic and clinical scoring systems in the early prediction of severity in acute pancreatitis. *Am J Gastroenterol* 2012;107:612–619

the other 20–30% are classified as severe. In 2009, Vege et al. proposed another subgroup of “moderately severe acute pancreatitis,” to describe and categorize patients with transient organ dysfunction [33]. According to the revised Atlanta criteria, with respect to determining patient outcome and severity of pancreatitis, in the first week only clinical parameters are important for treatment planning. However, subsequently, morphologic criteria defined on the basis of CT findings are combined with clinical parameters to help classify patients, identify complications, and determine optimal patient care.

According to the summary of recommendations by the International Association of Pancreatology and the American Pancreatic Association (IAP/APA), which were published in 2013, the indication for initial CT assessment in acute pancreatitis can be either for diagnostic uncertainty, for confirmation of severity of pancreatitis based on clinical predictors, or for the evaluation of patients with failure to respond to conservative treatment [34]. According to the systematic literature review performed by this group to answer imaging-related questions for pancreatitis, the consensus statement indicated that optimal timing for initial CT assessment should be at least 72–96 h after onset of symptoms. This was given a grade of 1C by the committee, indicating that there was strong agreement with regard to the recommendation, but the quality of the evidence was fairly low (level C) [34].

The statement from the IAP/APA regarding follow-up imaging of acute pancreatitis included the use of either CT or MR. Imaging was

suggested to be performed in patients in whom there is a lack of clinical improvement or frank deterioration and if invasive intervention is being considered. This was given a grade of 1C, which indicated strong agreement but fairly low evidence [34].

The American College of Radiology (ACR) Appropriateness Criteria recommend the use of CT with intravenous contrast to assess critically ill patients with known or suspected pancreatitis, those with the systemic inflammatory response syndrome (SIRS), and those with severe pancreatitis as scored by one of the main clinical scoring systems. Imaging with CT is given a rating of 8 out of 9 and is recommended after 48–72 h, similar to the IAP/APA recommendations [19]. CT is not recommended for imaging of patients less than 48 h from onset of symptoms. According to the British Society of Gastroenterology, in the hyperacute phase, assessment of pancreatitis should include clinical evaluation, focusing on cardiovascular, respiratory, and renal compromise. They also recommend calculation of body mass index, performing chest radiography, and applying the APACHE II scoring system [35]. CT for staging has not shown to affect the management of patients with acute pancreatitis early on, so it was not recommended, similar to other society guidelines/assessments [30]. In addition, early CT may lead to underestimation of the final severity of the disease and affect available radiology scoring systems. If the diagnosis is unclear or is not suspected to represent pancreatitis, then CT may provide findings to support or establish the diagnosis of pancreatitis.

If patients continue to be ill, more than 7–21 days after onset of symptoms, the ACR Appropriateness Criteria also recommend CT with intravenous contrast (rating of 9/9) to assess for complications of pancreatitis.

What Is the Role of Sonography in the Diagnosis of Acute Pancreatitis?

Summary of Evidence Sonography (US) plays an important role for the identification of gallstones and, in cases of acute pancreatitis, for the identification of common bile duct calculi which can obstruct the pancreatic duct at the ampulla, a leading cause of pancreatitis as noted above [27]. Sonography is recommended by the ACR Appropriateness Criteria as the first imaging modality to perform <48 h from onset of symptoms, to identify choledocholithiasis. This has been given a rating of 9 out of 9, although it has its limitations compared with MRI.

MRCP has a major role when US does not show a CBD stone and one is suspected to be present. However, CT and MRI are both currently given a rating of 4 out of 9 in this scenario, with CT reserved for patients who are obese or have overlying bowel gas. MRCP has been recommended as the second imaging modality by ACR Appropriateness Criteria if ultrasound is nondiagnostic [19].

For the staging of acute pancreatitis, ultrasound has little role, due to its technical limitations, other than in pregnant or pediatric patients [36]. However, ultrasound-guided interventions, including endoscopic ultrasound biopsy of solid lesions to differentiate malignancy from focal pancreatitis, are of value in selected patients in the subacute setting [36, 37]. Percutaneous or trans-gastric endoscopic ultrasound guidance for drainage of pseudocysts or infected pancreatic and peripancreatic fluid collections is performed at many centers and practices as well.

What Is the Role of MRI in the Diagnosis and Evaluation of Acute Pancreatitis?

Summary of Evidence ACR Appropriateness Criteria support the use of MRI in acutely ill patients 48–72 h after the onset of symptoms for evaluation of extent of complications. This was given a score of 7 out of 9. For patients with atypical signs and symptoms of pancreatitis and various other differential diagnoses under consideration, MRI was given an appropriateness score of 6 out of 9, compared to CT, which received a score of 7 out of 9 [19].

Supporting Evidence MRI has emerged as an important modality for the diagnosis of acute pancreatitis, particularly in patients with iodine allergy or with renal dysfunction [20, 29]. It is a modality which does not expose patients to ionizing radiation and has increasingly been advocated for imaging follow-up of complicated pancreatitis [38]. MRI with MRCP also has the added advantage of revealing CBD calculi as well as depicting the anatomy of the pancreatic ductal system, demonstrating variants including pancreas divisum and annular pancreas, which may predispose individuals to pancreatitis [38, 39]. MRCP after IV secretin stimulation has been demonstrated to improve delineation of the anatomy of the pancreatic ductal system and to help determine integrity of the ducts but is associated with slightly higher cost and is not available at many practices [40].

Additional benefits of MRI include high-contrast resolution and excellent depiction of the pancreatic ductal anatomy and of the biliary tract. MRI permits identification of calculi in the CBD with a high degree of accuracy and permits accurate assessment of the pancreatic ductal system (for anatomic variants as noted, as well as for strictures, obstruction, and underlying neoplasm) [20, 29]. MRI is effective in demonstrating hemorrhagic changes and/or necrosis, as well as the presence and size of fluid collections. According

to a study by Arvanitakis et al., IV gadolinium-enhanced images were as effective as CT in depicting the extent of pancreatic necrosis [38]. Even if intravenous contrast agents cannot be administered due to renal dysfunction, allergy, or other contraindication, non-contrast MR is considered superior to non-contrast CT. Vascular complications can still be identified, hemorrhage is seen, and although not as ideal as gadolinium-enhanced MR, the extent of necrosis can still be estimated [19].

A study by Viremouneix et al. prospectively compared non-enhanced MRI to contrast-enhanced CT (CECT) for assessing acute pancreatitis [41]. The authors found that MRI was a reliable method for the identification of pancreatitis and staging the severity when applying MRI findings to Balthazar's CT-based grading system. Diffusion-weighted imaging (DWI) has been shown to be a useful imaging sequence for the identification of acute pancreatitis without the need for intravenous contrast agents, although only a few small studies have been published on this specific topic to date to our knowledge [42, 43]. In the study by Yencilek et al., the authors found that DWI with calculation of apparent diffusion coefficient (ADC) values on MRI was helpful for diagnosing acute pancreatitis. Subgroup analysis of the 50 patients included in the study also demonstrated that the more severe the pancreatitis, the lower the ADC values [43].

What Is the Role of ERCP Versus MRCP in the Evaluation of Acute Pancreatitis?

Summary of Evidence According to the IAP/APA evidence-based guidelines [34], MRCP may reduce the need for ERCP in a proportion of patients with suspected CBD calculus as a cause of their pancreatitis, as long as the patients do not have symptoms of ascending cholangitis. In cases of suspected ascending cholangitis, ERCP is necessary for therapeutic intervention. MRCP is noninvasive and less operator dependent com-

pared to endoscopic ultrasound and is more widely available. This consensus statement gave MRCP a grade of 2C (weak evidence, from observational studies, unsystematic clinical experience, or from randomized, controlled trials with serious flaws) in this scenario.

What Is the Role of Imaging in Chronic Pancreatitis?

Summary of Evidence There are no specific criteria related to appropriateness for imaging of patients with chronic pancreatitis to our knowledge with CT, MRI, or ultrasound. However, patients may present with symptoms of acute onset chronic pancreatitis, in which case imaging may be requested.

Supporting Evidence Chronic pancreatitis is a progressive, irreversible inflammatory and fibrosing disease of the pancreas, with clinical manifestations including chronic abdominal pain, weight loss, and permanent pancreatic exocrine and endocrine insufficiency. Histologically, the disease is characterized by parenchymal fibrosis, ductal strictures and dilatation with calcifications, and atrophy of acinar and islet tissue [44]. On CT, dilatation of the pancreatic duct and its branches is the most common finding, which can be seen in 68% of patients, while overall parenchymal atrophy is seen in 54% of patients [45]. On sonography, the pancreatic parenchymal calcification and pancreatic duct calculi are often identifiable, but the degree of pancreatic parenchymal atrophy is difficult to quantify. MRI is not sensitive for the depiction of calcifications in the pancreatic parenchyma and is associated with longer scanning time and is more prone to various artifacts [46].

Take-Home Tables

Tables 20.1 and 20.2 highlight key information regarding pancreatitis imaging.

Imaging Case Study

Case 1

Figure 20.1a, b discusses a 70-year-old man with acute onset of pancreatitis 3 days earlier.

Suggested Imaging Protocols

CT

Imaging protocols can vary depending on the institution and the specific indication related to the pancreatitis. Evaluation of the pancreatic glandular enhancement with CT requires moderately rapid (3 mL/s) intravenous bolus administration of contrast material, as well as the use of narrow collimation for improved resolution. Although dual-phase scanning, using arterial and portal venous phase acquisitions, has been advocated by some authors for optimized pancreatic imaging, including of pancreatitis, a dual-phase CT is not necessary for the diagnosis of acute pancreatitis in most patients in our opinion.

If hemorrhage or hemorrhagic pancreatitis is clinically suspected, initial non-contrast CT

should be considered in addition to the IV contrast-enhanced phase, because visualization of hemorrhagic fluid can be more difficult following the injection of contrast material.

Use of multidetector rows at CT imaging will reduce scan times and motion artifact and increase anatomic coverage during a single breath hold. Thinner collimation allows increased spatial resolution and lesion detection but also creates increased image noise. The use of low-density oral contrast material such as Volumen (barium sulfate 0.1% w/v) may be helpful.

MRI

See Table 20.3. Image quality is important in MRI, especially since the examination takes longer to perform and may be challenging in patients who are unwell, are unable to cooperate, or who have multiple lines and tubes. Higher field strength magnets, multiphased-array body coils, improved fat suppression techniques, and faster scanning protocols, including use of spoiled gradient-recalled echo sequences, have been developed which allow for high-quality imaging in a relatively short period of time. However, overall imaging time for MR is longer than for

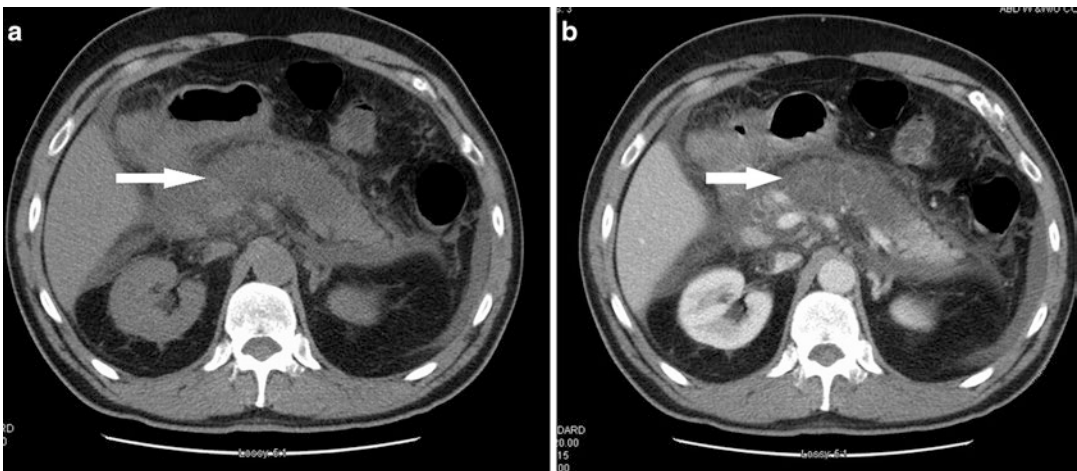


Fig. 20.1 (a, b) 70-year-old man with acute onset of pancreatitis 3 days earlier. Clinically, the patient was deteriorating, so a CT scan was performed with and without intravenous contrast. There is a large area of absent

enhancement in the pancreatic body, representing necrotic pancreatitis (*arrows*). The pancreatic tail demonstrates residual enhancement

Table 20.3 Example of MRI protocol for imaging pancreatitis

Exam	Series description	Coronal single-shot fast spin-echo T2	Axial dual in phase/opposed phase	Axial T2 fat saturated	Axial diffusion weighted image	Pre/Post axial T1 gradient echo (e-Thrive*)
Patient Position	Patient position	Supine	Supine	Supine	Supine	Supine
Position	Landmark					
	Coil type	Body coil	Body coil	Body coil	Body coil	Body coil
	Slice orientation	Coronal	Axial	Axial	Axial	Axial
Geometry	Field of view	FH 420	RL 340	RL 410	RL 400	RL 360
		RL 455	AP 300	AP 2.95	AP 378	AP 300
		AP 184	FH 120	FH 2.76	FH 209	FH 140
	Voxel size	FH 1.52	RL 1.5	RL 1.5	RL 3	RL 2
		RL 2.95	AP 2	AP 1.89	AP 3	AP 2
						FH 2
	Slice thickness/gap	6 mm/default	6 mm/default	6 mm/default	6 mm/1	2 mm
	Reconstruction matrix	320	256	560	288	384
	SENSE factor	1.7	1.6			1.5
	#Slices/locations	28	20	46	30	70
	Fold-over direction	Right to left	Anterior to posterior (A/P)	A/P	A/P	A/P
Contrast						
	Technique	Spin echo (SE)	Fast field echo (FFE)	SE	SE	Gadolinium
	Fast imaging mode	Turbo spin echo (TSE)		TSE	Echo planar imaging (EPI)	FFE
	TSE factor	SS				Turbo field echo (TFE)
	TE	275	2.3/4.6			Shortest
	TR	Shortest	185	1500	Shortest	Shortest
	Flip angle	90	70	90	90	10
	Fat saturation			Yes	Yes	Yes
	b-value				0, 500, 800	
Motion	Flow comp					
	NSA	1	1	4	5	1
Scan time	Scan duration	Breath hold	Breath hold	7:00	5:12	Breath hold
Coverage		Abdomen and pelvis	Abdomen	Abdomen	Abdomen	Abdomen

*e-THRIVE T1W high-resolution isotropic volume examination

CT, even with an efficient MR protocol using current equipment.

Contraindications may be present for MRI, including ocular implants, cochlear implants, many cardiac and extra-cardiac pacemakers, and significant claustrophobia. Adequate creatinine clearance in these acute ill patients must also be taken into consideration, as IV gadolinium ideally should be administered if possible, to assess for pancreatic necrosis. However, MRI of acute pancreatitis may be performed without IV gadolinium when creatinine clearance is substantially reduced [47].

Future Research

- Systematic reviews comparing MRI/MRCP to CT for imaging staging of pancreatitis
- Development of faster MRI protocols, including ones which can be performed quickly in patients who cannot hold their breath

Summary

- Acute pancreatitis is a relatively common cause of patient presentation to an emergency department with acute abdominal pain.
- CT is widely available and reproducible for staging of acute pancreatitis between 72 and 96 h after onset of symptoms, has utility earlier on when the diagnosis not clear by clinical and laboratory criteria, and is the imaging modality of choice for assessing complications.
- MRI is an alternative imaging modality for imaging in pancreatitis, due to its high-contrast resolution and excellent depiction of the pancreatic ductal system as well as of the CBD, and for the identification and characterization of fluid collections and edema in and around the pancreas.
- MRI has utility for reducing ionizing radiation exposure if repeated examinations are indicated in the acute and subacute setting, in patients with multiple episodes of pancreatitis requiring imaging, and in pregnancy.

Acute Colonic Diverticulitis

Methodology

A literature search was performed of English language articles from January 2005 to January 2015, using the MEDLINE database as well as EMBASE and the Cochrane Library. Search terms included the MeSH terms “diagnostic imaging” and “diverticulitis,” as well as the MeSH terms “computed tomography,” “CT,” “ultrasound,” “sonography/ultrasonography,” “MRI,” and “magnetic resonance imaging.” Inclusion criteria incorporated systematic reviews, meta-analyses, prospective studies, and retrospective studies related to pancreatitis. Review article and society position papers related to staging systems for acute pancreatitis were also sought.

Introduction

The vast majority of colonic diverticula are acquired “false” diverticula which do not contain all three layers of the bowel wall. These acquired diverticula result from increased intraluminal pressure, causing the mucosa to protrude through the bowel wall at points of weakness in the circular muscle where mucosal vasculature or vasa recta penetrate the muscular wall. In the Western population, colonic diverticula are more prevalent in the descending and sigmoid colon and are more frequently found in older male patients, occurring in >70% of those over 80 years [48, 49]. The incidence of right-sided diverticular disease, involving the cecum or ascending colon, is significantly higher in the Asian population, where a right-sided distribution is found in 20% of patients with diverticulosis and in up to 75% of cases of acute diverticulitis [50]. This discrepancy is assumed to be secondary to dietary and genetic factors. In comparison with patients with left-sided diverticular disease, patients with right colonic diverticular disease are younger at presentation, with a mean age of 35 to 45 years and with an equal gender distribution [51]. When right-sided diverticula are solitary, they are usually congenital and true

diverticula; when multiple, they are typically acquired and false diverticula [52].

Acute colonic diverticulitis (ACD) occurs when one or more of these diverticula become obstructed at the neck, resulting in stasis, inflammation, infection, and perforation. Typical presentations include symptoms and signs of lower abdominal pain and tenderness, altered bowel habits, and raised inflammatory markers. Imaging findings include segmental or focal colonic wall thickening in the presence of diverticulosis. Observed inflammatory change in the mesenteric fat is typically disproportionate to the degree of segmental colonic wall thickening where the offending diverticulum is located [53, 54]. Associated findings may include abscess formation (present in 10–20%), localized or contained perforation, and free peritoneal perforation. Another consequence of diverticulitis includes development of a fistula to adjacent pelvic structures including the gynecological tract, adjacent small bowel loops, the skin, and the urinary tract, particularly the bladder. Classification of the severity of ACD has important management implications, and a number of scales exist.

Discussion of Issues

Is Imaging Required to Diagnose Acute Colonic Diverticulitis?

Summary of Evidence Consensus guidelines from the surgical literature, including reviews by the American Society of Colon and Rectal Surgeons (ASCRS) 2006 [55], the Association of Coloproctology of Great Britain and Ireland (ACPGBI) 2011 [56], the Association of Surgeons of the Netherlands (ASN) 2012 [57], the Danish Surgical Society (DSS) 2011 [58], the European Association for Endoscopic Surgery (EAES) 2011 [59], and the World Society for Emergency Surgery (WSES) 2013 [60], were systematically reviewed by Vennix et al. [61]. All guidelines recommended radiological evidence to support the diagnosis of diverticulitis.

What Is the Modality of Choice for Imaging Suspected Acute Colonic Diverticulitis?

Summary of Evidence According to the American College of Radiology Appropriateness Criteria, CT is recommended as the first-line imaging in patients with left lower quadrant and suspected diverticulitis. This is given a score of 9 out of 9. The criteria indicate that this patient population may require intervention such as surgery to deal with associated complications including abscess and fistula formation, as well as obstruction and perforation. Thus, earlier characterization of the severity of diverticulitis and the detection of complications are recommended in order to allow more efficient triage and management of this patient population [62].

CT is proven to have a superior sensitivity and specificity over clinical diagnosis, contrast-enhanced enema, and ultrasound for the detection of inflamed diverticula and also is likely to have superior sensitivity for the detection of important associated findings, particularly perforation and small pericolic abscesses. CT Acute colonic diverticulitis (ACD):CT protocol is now nearly universally used as the imaging modality of choice given its widespread availability in the emergent setting, its reproducibility, and most importantly its ability to reveal other causes of abdominal and pelvic pain [62].

Supporting Evidence In a recently published meta-analysis, Andeweg et al. identified eight full-text studies which satisfactorily evaluated the accuracy of diagnostic imaging in patients with suspected ACD [63]. Summary sensitivity estimates for CT were 95% (95% CI: 91–97%), with a summary specificity estimate of 96% (95% CI: 90–100%).

Graded compression sonography for diverticulitis is a technique that is highly operator dependent and which requires a high level of expertise. The corresponding diagnostic yield is dependent on patient body habitus. The meta-analysis by Andeweg and colleagues summarizes the encouraging results for

graded compression ultrasound in 3 trials encompassing a total of 382 patients with a clinical suspicion for ACD [64–66]. Summary sensitivity estimates for US were 90% (95% CI: 76–98%), with a summary specificity estimate of 90% (95% CI: 86–94%). However, this meta-analysis did not include results from one comparison study which examined the diagnostic performance of ultrasound using CT as the reference standard [67]. This study found that the sensitivity of CT for the detection of diverticulitis was significantly higher than that of US: 81% versus 61% ($P = 0.048$), with fewer cases missed using CT than with US. Another advantage of CT is that it is more likely than US to reveal alternative diagnoses for left lower quadrant pain, with a sensitivity for alternate diagnoses ranging between 33% and 78% for US and between 50% and 100% for CT [68]. Transvaginal sonography remains of particular value in young female patients where gynecologic processes such as ectopic pregnancy and pelvic inflammatory disease are also important diagnostic considerations.

The diagnostic accuracy of MRI in suspected acute diverticulitis has a reported sensitivity of 86%–94% and a specificity of 88%–92% [69–72]. MRI is sensitive to motion artifacts which may obscure potentially important findings in the colon or between loops of bowel, and extraluminal gas may be difficult to visualize using MRI [71]. Although the incidence of ACD is reportedly not increased in pregnancy, MRI may be particularly valuable in this setting. Another potential role for MRI is for radiation dose reduction, when imaging patients less than 35 years of age with recurrent episodes of known or suspected diverticulitis or when multiple imaging examinations are required for a complicated episode of diverticulitis [62]

What Are the Key Imaging Findings Which Guide Subsequent Management in Patients with Acute Colonic Diverticulitis?

Summary of Evidence Beyond initial diagnosis, CT also allows the radiologist to rapidly and accurately classify the severity of ACD. Detection

of extraluminal complications provides the basis for important management decisions.

Clinical guidelines uniformly recommend a sigmoid colonic resection if ACD is complicated by luminal perforation. Laparoscopic lavage may be a safe approach for selected patients with Hinchey III perforated diverticulitis within a clinical trial setting. Conservative management with antibiotics is recommended by the ASCRS [55], the EAES [59], and the WSES [60] for uncomplicated ACD and in patients with small mesocolic abscesses (range ≤ 2 cm to <5 cm). Pelvic abscesses require more aggressive therapy than mesocolic abscesses, with percutaneous drainage, and elective surgery if unsuccessful.

What Is the Role of Oral, Rectal, and Intravenous Contrast When Imaging Known or Suspected ACD on CT?

Summary of Evidence Although positive contrast in the colon can increase the visibility of small and subtle diverticuli on CT [73], the cardinal imaging findings of diverticulitis, particularly segmental colonic wall thickening with associated inflammatory changes in the mesenteric fat, should be readily visible with or without positive intraluminal contrast material, particularly in patients with average or above average body mass indices [74–77].

Support of Evidence In a recently published retrospective analysis of 2008 CT examinations, Kammerer et al. found that delineation of the small and large bowel was possible across all segments irrespective of the presence or absence of enteric contrast, although a slight impairment in delineation of complications, particularly fistulas and abscesses, occurred without oral contrast [78].

In their recently updated Appropriateness Criteria [62], the American College of Radiology advises that intravenous and oral contrast should be administered in all patients with ACD if possible, prior to abdominal abscess drainage, in an effort to minimize the risk of nontarget catheter

placement. Rectal contrast is rarely used in day-to-day CT practice to our knowledge and based on the ACR Criteria but may be valuable to confirm patency of a suspected fistula to adjacent pelvic structures or to the skin. Furthermore, the ACR also recommends that low-dose CT techniques be employed routinely according to local availability if possible, given that radiation dose reductions of 75–90% have been achieved in patients with suspected ACD on CT but without significant reductions in sensitivity and specificity [62].

Take-Home Tables

Tables 20.4, 20.5, and 20.6 highlight key information regarding diagnostic performance of imaging in acute colonic diverticulitis and specific information a physician needs to know.

Imaging Case Study

Case 2

In Fig. 20.2, a 68-year-old woman presents with right lower quadrant abdominal pain.

Suggested Imaging Protocols

CT

Imaging protocols can vary depending on the particular practice/institution. The majority of centers/practices scan patients with IV contrast at a portal venous phase [74]. Dual-phase CT is not necessary for the diagnosis of acute diverticulitis in most patients. Non-contrast CT is a valuable alternative in patients with contraindications to injection of IV contrast [75]. Presently, the use of

Table 20.4 Diagnostic performance of US in patients suspected of having acute colonic diverticulitis

Ultrasound	TP	FN	TN	FP	Sensitivity	Specificity	PPV	NPV
Zielke, 1997 [64]	62	12	64	5	0.84	0.93	0.93	0.84
Pradel, 1997 [65]	28	5	26	5	0.85	0.84	0.85	0.87
Hollerweger, 2001 [66]	96	6	71	2	0.94	0.97	0.98	0.92
Summary estimate (95% CI)					0.90 (0.76–0.98)	0.90 (0.86–0.94)	0.93 (0.84–0.98)	0.88 (0.82–0.92)

Adapted with permission from Andeweg CS, Wegdam JA, Groenewoud J, van der Wilt GJ, van Goor H, Bleichrodt RP. Toward an evidence-based step-up approach in diagnosing diverticulitis. *Scand J Gastroenterol* 2014;49:775–784

Table 20.5 Diagnostic performance of CT in patients suspected of having acute colonic diverticulitis

CT	TP	FN	TN	FP	Sensitivity	Specificity	PPV	NPV
Cho, 1990	25	2	29	0	0.93	1.00	1.00	0.94
Stefánsson, 1997	36	16	36	0	0.69	1.00	1.00	0.69
Pradel, 1997	30	3	24	7	0.91	0.77	0.81	0.89
Rao, 1998	62	2	86	0	0.97	1.00	1.00	0.98
Werner, 2003	65	2	52	1	0.97	0.98	0.98	0.97
Tack, 2005	36	3	70	1	0.92	0.99	0.98	0.96
Summary estimate (95% CI)					0.95 (0.91–0.97)	0.96 (0.90–1.00)	0.97 (0.92–0.99)	0.91 (0.82–0.97)

Adapted with permission from Andeweg CS, Wegdam JA, Groenewoud J, van der Wilt GJ, van Goor H, Bleichrodt RP. Toward an evidence-based step-up approach in diagnosing diverticulitis. *Scand J Gastroenterol* 2014;49:775–784

Table 20.6 Acute colonic diverticulitis: what the referring physician needs to know

Location and length of involved segment
Presence or absence of pericolic phlegmon or abscess
Presence or absence of pelvic abscess
Presence or absence of localized “walled-off” perforation
Presence or absence of pneumoperitoneum
Presence or absence of feculent peritoneal contamination

**Fig. 20.2** 68-year-old woman with right lower quadrant abdominal pain. Axial contrast-enhanced CT demonstrates a thickened loop of cecum. There is an inflamed cecal diverticulum with an enhancing wall. Note marked inflammation in the pericolonic fat

combined oral and rectal contrast administration for imaging patients with known or suspected acute diverticulitis is controversial but is used in some institutions [76].

Future Research

- Accuracy of sonography in detecting diverticulitis and its complications, especially in younger patient populations
- Cost-effectiveness of MRI for following up of complications of diverticulitis in younger patients requiring multiple, sequential imaging examinations
- Identifying imaging features that might better predict early cases that are at risk for complications, particularly abscess and fistula formation

Summary

- Acute diverticulitis is a common cause of abdominal pain in middle age and older patients presenting to an emergency department.
- CT is widely available and reproducible for the identification of diverticulitis and for the diagnosis of complications associated with it, including abscess and fistula formation.

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Acute Biliary Disorders in Adults: Evidence-Based Emergency Imaging of Acute Calculous and Acalculous Cholecystitis, Bile Duct Obstruction, and Choledocholithiasis

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Key Points

- Ultrasonography should be performed at the initial consultation for all patients with suspected acute cholecystitis with cholescintigraphy being considered in clinically equivocal cases (strong evidence).
- Cholescintigraphy is significantly more accurate than ultrasonography in the diagnosis of acute calculous cholecystitis (ACC) (strong evidence).
- The use of ultrasonography and cholescintigraphy has been advocated for acute acalculous cholecystitis (AAC); however, there is no single highly accurate test for the diagnosis of AAC (moderate evidence).
- Magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasonography (EUS) are superior to transabdominal ultrasonography in visualizing the entire bile duct and establishing the level of bile duct obstruction (strong evidence).
- Magnetic resonance cholangiopancreatography and endoscopic ultrasonography are useful in patients with a low/intermediate probability of choledocholithiasis to select individuals with common duct stone for therapeutic ERCP (strong evidence).
- Patients with a high likelihood of choledocholithiasis based on clinical, laboratory, and ultrasonography findings should proceed directly to therapeutic endoscopic retrograde cholangiopancreatography (ERCP) without further cholangiographic studies (strong evidence).

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Definition and Pathophysiology

Acute cholecystitis is caused by chemical or bacterial inflammation of the gallbladder leading to mucosal ulceration, wall edema, and fibrinosuppurative serositis. In up to 90% of patients, gallstones are the causative factor/etiology leading to acute calculous cholecystitis (ACC), and in the remaining 10% of patients, gallbladder inflammation occurs in the absence of stones resulting in acute acalculous cholecystitis (AAC) [1, 2].

Extrahepatic bile duct obstruction can result from intraluminal, mural, or extramural lesions of the biliary tract. The most common cause of biliary obstruction is choledocholithiasis, or biliary sludge [3]. Other causes include tumor and benign or malignant strictures. Malignant biliary obstruction may be due to primary neoplasms of the bile ducts such as cholangiocarcinoma or from extrabiliary neoplasm causing extrinsic mass effect like pancreatic head carcinoma, duodenal carcinoma, or metastatic lymph node enlargement. Most benign strictures of the bile duct are traumatic, infective, or inflammatory in origin [2].

Epidemiology

Acute biliary pathologies continue to be one of the common causes for emergency hospital visits. Approximately 20–25 million (10–15%) adults in the USA have gallstones [4]. Each year, between 1% and 4% of these individuals become symptomatic [5]. Gallstones occur far more commonly in women than men, with around 50% of women and 16% of men having gallstones by the eighth decade [1]. Prevalence is higher in fair-skinned people of Northern European descent but is highest in specific races such as the Pima Indians (up to 75%) [2]. It is least prevalent in African-Americans, unless there are underlying genetic disorders such as sickle cell disease or thalassemia.

The prevalence of acute cholecystitis is approximately 5% in patients presenting with

acute abdominal pain to the emergency department [6]. It typically occurs in women of reproductive age of 30–50 years. Although traditionally considered a disease of adults, acute cholecystitis has been increasing in incidence in the pediatric population over the last three decades [7]. The prevalence is increased in children with chronic hemolysis such as hemolytic anemia. However, the cholecystectomy rate in children without the diagnosis of chronic hemolysis has doubled in the USA in recent years possibly due to the rise in childhood obesity [8].

Acute acalculous cholecystitis occurs most commonly in critically ill or injured patients. It accounts for approximately 10% of all cases of acute cholecystitis and occurs in about 0.2% to 0.4% of all critically ill patients [9]. However, the development of acute acalculous cholecystitis is not limited to the intensive care unit; diabetes, malignant disease, abdominal vasculitis, shock, cardiac arrest, and viral infections are also associated with acute acalculous cholecystitis [10]. It occurs more commonly in males with a male-to-female ratio of 2–3:1 and occurs at an average age of over 50 years [9]. It is more frequent in the pediatric population compared to adults.

The incidence of biliary obstruction in the USA is approximately five cases per 1000 people, with gallstones being by far the commonest cause [11]. However, the vast majority of patients with gallstones are asymptomatic, with only 20% presenting with related symptoms. Malignancy is the second commonest cause of biliary obstruction with cholangiocarcinoma and pancreatic adenocarcinoma being the commonest lesions [12]. Benign strictures of the extrahepatic bile duct are the third commonest cause of bile duct obstruction with traumatic, infective, and inflammatory lesions being the leading causes [12, 13].

Overall Cost to Society

Cholecystectomy is currently the most common elective abdominal surgery performed in the USA, with >750,000 operations being performed

annually [4]. In addition, 15% of cholecystectomies performed in the USA each year require common bile duct exploration. The resultant direct and indirect cost of gallstone disease represents a consumption of approximately \$6.2 billion annually, constituting a major health burden in the USA [4].

The advent of laparoscopic surgery has served to reduce some of these costs, although due to the large volume of cases, the health economic burden still remains high. There is very little information on the cost of managing patients with bile duct obstruction, particularly that due to malignancy. Only the minority of patients undergoes curative surgery. The majority are palliated with stent placement or chemoradiotherapy.

Goals of Imaging

The goals of imaging in patients with suspected gallbladder pathologies include (1) diagnosing the gallbladder abnormality, (2) identifying underlying etiology, (3) assessing the degree and cause of obstruction, and (4) evaluating for associated complications.

Methodology

A search of the MEDLINE/PubMed (National Library of Medicine, Bethesda, MD) was performed using a single or combination of keywords including *imaging, ultrasonography, computed tomography, magnetic resonance cholangiopancreatography, cholescintigraphy, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography, acute cholecystitis, acalculous cholecystitis, bile duct obstruction, choledocholithiasis, and neoplasm*. Reviewing the reference list of relevant papers identified additional articles. No time limits were applied for the searches, which were repeated up to several times up to April 16, 2015. Limits included English language, abstracts, and human subjects. A search of the National Guideline Clearinghouse at <http://www.guideline.gov> was also performed.

Discussion of Issues

What Is the Best Imaging Strategy for the Diagnosis of Acute Calculous Cholecystitis (ACC)?

Summary of Evidence Ultrasonography is useful primarily for the diagnosis of gallstones and biliary obstruction and secondarily in the diagnosis of acute cholecystitis. Its accuracy for diagnosis of cholelithiasis is over 95%, but its accuracy for diagnosis of acute cholecystitis is reduced to around 80% (strong evidence). Cholescintigraphy is the most accurate test for the diagnosis of acute cholecystitis with an accuracy exceeding 90% (strong evidence) [14]. However, in the appropriate clinical setting, sonographic findings of gallstones and specific gallbladder changes are sufficient for the management of most patients with suspected ACC. According to the American College of Radiology (ACR) appropriateness criteria [15], ultrasound is preferred as the initial imaging test, with supplemental cholescintigraphy used in problematic cases where doubt exists (strong evidence) [15].

Supporting Evidence ACC usually presents with a triad of right upper quadrant pain, fever, and leukocytosis; however, the symptoms and laboratory parameters are often very nonspecific posing a challenge and dilemma for clinical diagnosis [16, 17]. Imaging thus plays key role in diagnosis of suspected ACC as well as in assessing for related complications thereby directing the clinical management. Of all the imaging tests available, ultrasonography and cholescintigraphy have proven to be the two most useful tests for this task [18].

Ultrasonography

While ultrasonography (US) is highly accurate in diagnosing gallstones, exceeding 95%, it has a lower sensitivity in diagnosing acute cholecystitis [16, 19]. A meta-analysis by Shea et al. [14] showed that ultrasonography has an overall adjusted sensitivity of only 85% and a specificity of 80% in the diagnosis of acute cholecystitis. A more recent meta-analysis by Kiewiet et al.

reported a lower sensitivity of 81% and a slightly higher specificity of 83% for ultrasonography diagnosis of ACC [5].

Despite this, some findings on ultrasonography have been more strongly associated with acute cholecystitis than others: a positive Murphy's sign is reported to have sensitivity as high as 88% [20]; and an increased gallbladder wall thickness of >3.5 mm has been found to be a reliable and independent predictor of acute cholecystitis [21]. In addition, combinations of ultrasonography findings have been found to be very predictive of acute cholecystitis. In a study by Ralls et al. [22], a positive Murphy's sign and the presence of gallstones had a positive predictive value of 92%. In the same study, the findings of gallbladder wall thickening and gallstones had a positive predictive value of 95%. However, a single specific finding or several nonspecific findings alone were unreliable for the diagnosis of acute cholecystitis [20]. Thus, although ultrasonography is reduced in accuracy when broadly applied, in the right clinical setting and taken together with the abovementioned specific imaging signs, ultrasonography alone is sufficient to direct patient management [23]. The 2013 revised Tokyo guidelines for acute cholecystitis suggest that abdominal ultrasonography should be performed at the initial consultation for all cases of suspected acute cholecystitis (level 1A evidence) [24].

Cholescintigraphy

In the recent meta-analysis published by Kiewiet et al. [5], the summary estimate of sensitivity for cholescintigraphy was 96%, which was significantly higher than that for ultrasonography. The mean specificity of 90% was not significantly different from that of ultrasonography. Sensitivity estimates ranged from 78% to 100%, with specificities ranging from 50% to 100%. When studies directly comparing cholescintigraphy with ultrasonography were evaluated, Kiewiet et al. [5] reported both sensitivity and specificity to be significantly higher for cholescintigraphy than for ultrasonography. In another recent study by Kaoutzanis et al. [25], cholescintigraphy compared to ultrasonography had a sensitivity of

91.7% versus 73.3%, and the sensitivity of cholescintigraphy and ultrasonography combined was 97.7% (Table 21.1). Nevertheless, due to greater availability, shorter study time, lack of ionizing radiation, and identification or exclusion of alternative diagnoses, ultrasound remains the initial test of choice for imaging of patients with suspected ACC with cholescintigraphy being considered in clinically equivocal cases [5, 15].

Computed Tomography

Evidence does not support the routine use of computed tomography (CT) as the primary modality in the initial assessment of ACC [35]. CT has poor sensitivity for detection of cholelithiasis (75%) compared to ultrasonography. However, Nyman et al. [36] reported a sensitivity of 94% for CT in the detection of acute cholecystitis. Also, a more recent study by Bennett et al. [37] showed an extremely good overall sensitivity, specificity, and accuracy of 91.7, 99.1, and 94.3%, respectively, for the CT diagnosis of acute cholecystitis. Nevertheless, in practice, CT is more commonly used for detection of complications of acute cholecystitis such as emphysematous cholecystitis, perforation, or abscess formation, rather than for primary diagnosis of acute cholecystitis [38–40].

Magnetic Resonance Imaging

Studies assessing the role of magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) in ACC have shown mixed results [41–43]. While MRCP is superior to ultrasound and CT in detecting distal biliary obstruction and etiologies (stones, stricture, tumors, and secondary causes of strictures like pancreatitis/mass effect), its utility in an acute setting is still not validated [41–43]. The recent meta-analysis by Kiewiet et al. [5] showed a sensitivity of 85% and a specificity of 81% for MRI, which was not significantly different from ultrasonography. However, the lack of widespread availability of MRI and the relatively high cost prohibit its primary use for now, making it a useful alternative in patients with technically limited ultrasonography examinations or in high suspicion of biliary obstruction [5, 35].

Table 21.1 Accuracy of ultrasonography compared with cholescintigraphy in the diagnosis of acute cholecystitis

Investigators	Year	Number of patients	Cholescintigraphy sensitivity/specificity (%)		Ultrasonography sensitivity/specificity (%)	
Worthen et al. [26]	1981	113	95	100	67	100
Ralls et al. [27]	1982	59	86	84	86	90
Freitas et al. [28]	1982	195	98	90	81	60
Samuels et al. [29]	1983	190	97	93	97	64
Gill et al. [30]	1995	47	100	100	91	92
Lauritsen et al. [31]	1988	67	95	–	91	–
Chatziioannou et al. [32]	2000	107	92	89	40	89
Kalimi et al. [33]	2001	132	86	–	48	–
Alobaidi et al. [34]	2004	117	91	–	62	–
Kaoutzanis et al. [25]	2014	406	92	–	73	–

Adapted from Varghese JC, Lucey BC, Soto JA. Imaging of Biliary Disorders: Cholecystitis, Bile Duct Obstruction, Stones, and Stricture. In Medina LS, Blackmore CC (eds.): *Evidence-Based Imaging: Optimizing Imaging in Patient Care*. New York: Springer Science+Business Media, 2006

Imaging Strategy

Based on available evident literature, there is no doubt that cholescintigraphy is the most accurate test for the diagnosis of acute cholecystitis; however, its clinical utility in evaluation of suspected cases of ACC is not uniformly accepted, possibly from a combination of reasons including availability, broad imaging capability, and clinician referral pattern. Ultrasonography thus remains the first-line imaging modality for the diagnosis ACC, with cholescintigraphy reserved for sonographic equivocal cases. An evidence-based algorithmic approach for evaluation of patients with clinically suspected ACC is provided in Fig. 21.1.

What Is the Best Imaging Strategy for the Diagnosis of Acute Acalculous Cholecystitis (AAC)?

Summary of Evidence There is no ideal test for the diagnosis of AAC (moderate evidence). Ultrasonography, CT, and cholescintigraphy are all moderately accurate, with cholescintigraphy being the most accurate. Occasionally, an empirical trial of percutaneous cholecystostomy may be the only way to make the diagnosis.

Supporting Evidence There are two well-documented reasons why it is important to promptly diagnose and treat patients with AAC: first, delay in treatment is associated with a high mortality ranging from 10 to 50% [44–47]; and second, percutaneous cholecystostomy is effective in ameliorating sepsis [45–49].

Ultrasonography

Ultrasonography of the abdomen and pelvis is often the first test requested in the critically ill patient with sepsis of unknown etiology [49]. Although easy to perform, evidence shows that ultrasonography is limited in the diagnosis of AAC [35, 44], the reasons being that many of the usual indicators of acute cholecystitis are absent or difficult to elicit: gallstones are absent by definition, and the other helpful pointers such as sonographic Murphy's sign may not be elicited due to the patient's medical condition or heavy sedation [44]. Thus, the diagnosis is dependent on the other findings such as gallbladder luminal distention (>5 cm transverse), presence of echogenic sludge, wall thickening (>4–5 mm), subserosal edema, and pericholecystic fluid [9, 44, 50]. Unfortunately, these are all nonspecific findings that can also be found with other comorbidities that commonly afflict the critically ill or injured patient [50]. The sen-

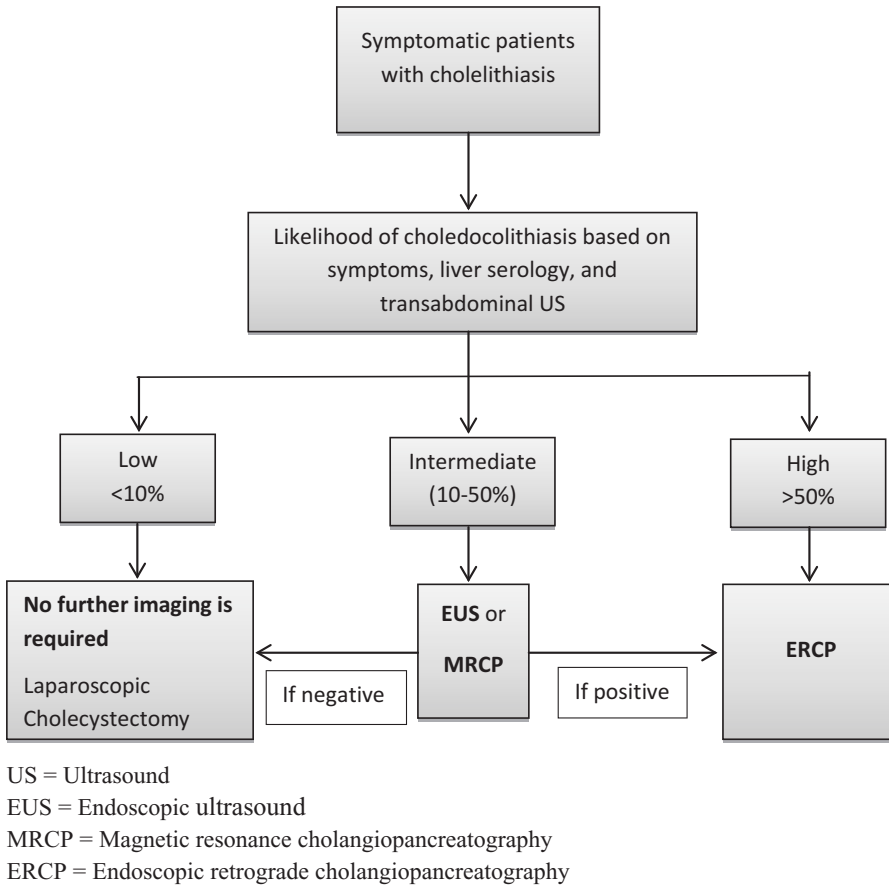


Fig. 21.1 A suggested evidence-based management algorithm for patients with symptomatic cholelithiasis based on the degree of probability for choledocholithiasis (Modified with permission from The American Society for Gastrointestinal Endoscopy Guideline as in Maple JT, Ben-Menachem T, Anderson MA, Appalaneni V, Banerjee

S, Cash BD, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. *Gastrointestinal endoscopy*. 2010;71(1):1–9; and in Tse, F., Barkun, J.S., and Barkun, A.N. The elective evaluation of patients with suspected choledocholithiasis undergoing laparoscopic cholecystectomy. *Gastrointest Endosc*. 2004;60:437–448)

sitivity and specificity of US are variable ranging from 30% to 100% [9]. The variance in sensitivity and specificity partly stems from the small, mostly retrospective studies with the use of different sonographic criteria for diagnosis. Kalliafas et al. [51] and Puc et al. [50] found very low sensitivities for ultrasonography in the diagnosis of AAC. They came to the conclusion that despite its convenience as a bedside imaging modality, ultrasonography was too insensitive to justify its use and that a more sensitive diagnostic tool was required. However, others have found better sensitivities ranging from 60

to 90%. In two other prospective studies, Imhof et al. [21] and Raunest et al. [52] found ultrasonography to be a valuable tool for early detection of AAC. Overall, the reported accuracy for AAC is not sufficiently high to make ultrasonography definitive in the evaluation of patients with possible AAC.

Cholescintigraphy

Cholescintigraphy may be a more sensitive tool for diagnosis of AAC, considering that most cases of AAC are associated with cystic duct obstruction [15]. The reported sensitivities of

Table 21.2 Accuracy of cholescintigraphy in the diagnosis of acute acalculous cholecystitis

Investigators	Year	No. of pts	Sensitivity (%) Number of patients/total number of patients	Specificity (%) Number of patients/total number of patients
Weissmann et al. [53]	1983	15	93 (14/15)	
Shuman et al. [54]	1984	19	76 (14/19)	
Ramanna et al. [55]	1984	11	100 (11/11)	
Mirvis [56]	1986	45	90 (9/10)	62 (21/34)
Swayne [57]	1986	41	93 (37/40)	
Fig et al. [58]	1990	51	94 (15/16)	69 (22/32)
Flancbaum and Choban [59]	1995	45	75 (12/16)	100 (29/29)
Kalliafas et al. [51]	1998	10	90 (9/10)	
Prevot et al. [60]	1999	32	64 (9/14)	100 (18/18)
Mariat et al. [61]	2000	28	67(8/12)	100 (16/16)
Puc et al. [50]	2002	20	100 (12/12)	88 (7/8)
Total			86 (150/175)	82 (113/137)

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cholescintigraphy in the diagnosis of AAC have ranged from 64 to 100%, with a mean of 86% (Table 21.2). Diagnostic specificity of cholescintigraphy can be limited due to false-positive scans (e.g., in prolonged fasting). The reported specificities range from 62 to 100%, with a mean of 82% (Table 21.2). While some investigators have suggested cholescintigraphy be the primary modality for diagnosis of AAC [51, 53, 57], others have suggested that ultrasonography and cholescintigraphy are complementary, with each independently improving the overall diagnostic accuracy [60, 61].

Computed Tomography

Computed tomography of the abdomen and pelvis is sometimes the first test performed in the critically ill or injured patient, particularly when gastrointestinal symptoms predominate. However, the high prevalence of nonspecific abnormalities in the gallbladder of critically ill patients limits the diagnostic value of CT in detecting AAC. Nevertheless, when the gallbladder appears totally normal on CT, AAC is very unlikely [15, 62].

Imaging Strategy

There is as yet no ideal imaging test available for the diagnosis of AAC. The use of ultrasonography and scintigraphy has been advocated for AAC [15]. Overall, cholescintigraphy has better test characteristics than ultrasonography. However, due to logistical and technical reasons, many studies have focused on bedside modalities, namely, ultrasonography. While ultrasonography has poor sensitivity and specificity [39], it is still the initial imaging modality used as the findings of gallstones, bile duct obstruction, or extrabiliary source of sepsis would alter patient management.

The management of patients with potential AAC remains difficult and controversial. The best strategy is for the interventional radiologist and the referring physician concerned to evaluate each patient based on the clinical, laboratory, and ultrasonography findings. Percutaneous cholecystostomy, which can be both diagnostic and therapeutic, is often a safe approach in hospitalized patients with suspected AAC [15]. Ideally, ultrasonography, CT, or cholescintigraphy should be performed before percutaneous cholecystos-

Table 21.3 Imaging criteria for acute acalculous cholecystitis

Modality	Criteria	Diagnosis	
Ultrasound			
	Major	<ul style="list-style-type: none"> • 3.5 to 4 mm (or more) thick wall (if at least 5 cm distended longitudinally with no ascites or hypoalbuminemia) • Pericholecystic fluid (halo)/ subserosal edema • Intramural gas • Sloughed mucosal membrane 	2 major or 1 major and 2 minor (most studies have favored the diagnostic triad of wall thickness, sludge, hydrops)
	Minor	<ul style="list-style-type: none"> • Echogenic bile (sludge) • Hydrops = distension greater than 8 cm longitudinally or 5 cm transversely (with clear fluid) 	
Computed tomography			
	Major	<ul style="list-style-type: none"> • 3 to 4mm wall thickness • Pericholecystic fluid • Subserosal edema • Intramural gas • Sloughed mucosa 	2 major or 1 major and 2 minor
	Minor	<ul style="list-style-type: none"> • Hyperdense bile (sludge) • Subjective distension (hydrops) 	
Cholescintigraphy			
		<ul style="list-style-type: none"> • Nonvisualization of the gallbladder 1 h after injection of radiolabeled technetium^a • Nonvisualization of the gallbladder 30 min after injection of morphine (after initial radiolabeled technetium)^b 	RC alone or RC and MC have been used

Adapted from Huffman JL, Schenker S. Acute acalculous cholecystitis: a review. Clin Gastroenterol Hepatol. 2010;8(1):15–22

^aRadionuclide cholescintigraphy (RC)

^bMorphine cholescintigraphy (MC)

tomy [15]. Sometimes when this is not possible or the imaging results are equivocal, it is optimal to proceed with a trial of percutaneous catheter drainage [46, 63]. While the definitive management is cholecystectomy, given that often these patients are critically ill and thus at high risk for surgery, therapy is directed to percutaneous cholecystostomy and rarely transpapillary endoscopic biliary drainage [64]. The imaging criteria for acute acalculous cholecystitis are given in Table 21.3.

What Is the Best Imaging Strategy for the Evaluation of Bile Duct Obstruction?

Summary of Evidence Ultrasonography is the initial test for detection of biliary obstruction by identifying intrahepatic and/or common bile duct dilatation. However, MRCP and endoscopic ultrasound (EUS) are superior to ultrasonography in visualizing the whole of the bile duct and establishing the level of bile duct obstruction (strong evidence).

Supporting Evidence The diagnosis of bile duct obstruction is based on a combination of clinical, laboratory, and imaging findings. The clinical findings of jaundice, pruritus, pale stools, and dark urine, in association with laboratory findings of elevated bilirubin, alkaline phosphatase, and transaminases, are highly suggestive of biliary tract obstruction [65, 66]. The imaging modalities used for the evaluation of patients with suspected biliary tract obstruction include ultrasonography, CT, MRCP, endoscopic retrograde cholangiopancreatography (ERCP), and EUS. The utility of these imaging modalities is based on a number of factors including their diagnostic accuracy, invasiveness, complication rate, availability, ease of use, local expertise, operator preference, and cost.

Ultrasonography

Transabdominal ultrasonography is universally accepted as the test of choice for distinguishing hepatocellular disease from mechanical bile duct obstruction, with a sensitivity of 70–95% and a specificity of 80–100% [19, 67, 68]. Thus, together with the high sensitivity for diagnosis of bile duct obstruction, availability, ease of use, noninvasiveness, safety, and low cost, ultrasonography has established itself as the first-line imaging modality in the investigation of patients with suspected hepatobiliary disease [19].

Pitfalls in the ultrasonography diagnosis of bile duct obstruction include [1] non-obstructed but dilated common bile duct (CBD) in the elderly or post-cholecystectomy patient, giving rise to a false-positive result; [2] bile duct dilatation lagging (as much as 1 week) behind the onset of mechanical obstruction, giving rise to a false-negative result; and [3] obstructive lesion not associated with significant bile duct dilation (as occurs in 10% to 25% of choledocholithiasis), resulting in a false-negative result [19, 69]. The major limitation of ultrasonography is its variable accuracy in differentiating the level and cause of biliary obstruction ranging from 27 to 95% and 23 to 88%, respectively [70]. Ultrasonography has also been shown to have poor sensitivities for detecting choledocholithiasis and also differentiating benign from malignant masses.

Computed Tomography

Computed tomography with intravenous contrast is superior to ultrasonography in the diagnosis of bile duct obstruction by revealing intrahepatic and extrahepatic bile duct dilatation [71]. It is 96% accurate in determining the presence of biliary obstruction, 90% accurate in determining its level, and 70% accurate in determining its cause [71, 72]. It is better able to visualize the middle to distal CBD compared to ultrasonography, particularly in the obese patient or those with overlying bowel gas [71]. Recently, negative-contrast CT cholangiopancreatography (nCTCP) has been reported to provide comparable performance to MRCP for the diagnosis of obstructive biliary

diseases [73, 74]. Therefore, nCTCP may serve as a valuable alternative in patients not eligible for MR examinations.

Magnetic Resonance Cholangiopancreatography

Magnetic resonance cholangiopancreatography (MRCP) is an established and effective noninvasive diagnostic modality for bile duct obstruction. With good-quality MRCP, the normal CBD is visualized in up to 98% of patients [75]. A recent meta-analysis of 67 MRCP studies performed over a period of 16 years (from January 1987 to March 2003) evaluating a mixture of benign and malignant conditions found an overall sensitivity of 97% for the presence of obstruction and a sensitivity of 98% for determination of the level of obstruction on MRCP [76]. In a recent study by Zhang et al. [73], MRCP correctly diagnosed all (31/31) patients with benign biliary obstruction and 94.9% (37/39) of patients with malignant biliary obstruction. The overall accuracy of MRCP in making specific diagnosis of the cause of biliary obstruction was 84.3%. Another recent study by Parashari et al. [77] reported the diagnostic accuracy of MRCP in identifying the level and the cause of obstruction to be 96 and 88%, respectively.

Endoscopic Ultrasonography

Endoscopic ultrasonography (EUS) is rapidly gaining momentum in the evaluation of the extrahepatic biliary system [71, 78–83] and other upper gastrointestinal disorders [84]. It combines endoscopy with high-frequency (7.5–20 MHz) ultrasonography to visualize the whole of the bile duct in up to 96% of patients [71, 85]. In a meta-analysis by Garrow et al., EUS was found to have a high overall pooled sensitivity of 88% and specificity of 90% for biliary obstruction. In a more recent large cohort of patients with presumed biliary obstruction, EUS was shown to be accurate in predicting the need for therapeutic ERCP (diagnostic accuracy of 92 and 90% for benign and malignant obstructions, respectively) [80].

What Is the Best Imaging Strategy for the Diagnosis of Choledocholithiasis?

Summary of Evidence Ultrasonography is insensitive in the diagnosis of choledocholithiasis. Both MRCP and EUS are highly accurate alternatives in the diagnosis of choledocholithiasis. ERCP is reserved for therapeutic intervention. Patients with a high likelihood of choledocholithiasis based on clinical, laboratory, and ultrasonography findings should be referred directly for therapeutic ERCP, without further imaging (strong evidence).

Supporting Evidence The presence of clinical and sonographic imaging features of biliary obstruction without convincingly evident choledocholithiasis warrants the use of noninvasive modality MRCP for evaluating the cause. However, presence of choledocholithiasis on ultrasonography is an indication of therapeutic intervention with ERCP. CT has shown to have poor sensitivity for biliary sludge and tiny bile duct stones. Diagnosis and therapeutic intervention in obstructive biliopathy are clinically important to avoid complications such as cholangitis and intrahepatic biliary abscesses.

Ultrasonography

Most of the bile duct stones are found within the middle to distal portion of the CBD [86], a particularly difficult region of the biliary tract to visualize using ultrasonography often due to obscuration by overlying bowel gas shadow [69, 71]. There is a further reduction in diagnostic information in patients who are obese. This results in a poor sensitivity for ultrasonography diagnosis of choledocholithiasis, ranging from 18 to 75% depending on the operator experience, patient population studied, and quality of equipment used [71, 87–89]. The specificity for diagnosis of choledocholithiasis can be as high as 95% [71], with false positives occurring due to pneumobilia, hemobilia, and overlying gas shadows from adjacent bowel [19, 69].

Computed Tomography

Bile duct stones are directly visualized as a hyperdense focus against hypodense bile duct or found by using the target or crescent signs [72]. The sensitivity for CT diagnosis of choledocholithiasis is only slightly higher than that for ultrasonography, ranging from 60 to 88%, with a specificity of 73 to 97% [71, 90–94]. Optimization of CT technique, such as using thin sections and unenhanced helical CT [95], can improve the detection of filling defects and has been shown to have greater accuracy for the diagnosis of choledocholithiasis [94]. The decreased detection rate of CT is predominantly related to the varying density of gallbladder stones based on their cholesterol and calcium content [94]. Up to 20–25% of stones are isodense with bile, making them almost impossible to detect. A very recent study has shown that with efficient imaging capability and powerful spectral image-processing software, spectral CT has a high diagnostic value for isodense gallstones or bile duct stones [96]. However, it is not clear yet that whether spectral CT is more accurate than other available diagnostic modalities (e.g., MRCP).

Computed tomography cholangiography is a relatively new technique that is developed to overcome some of the limitations of CT in the diagnosis of bile duct disease. It provides cholangiographic images by opacification of the bile duct with contrast material administered through the oral or intravenous route. The low-density stones are seen as filling defects within the contrast opacified bile duct. Improved stone detection rates with sensitivity and specificity of 92 and 92%, respectively, have been reported [93]. However, this technique has not gained wide acceptance due to the small but finite incidence of contrast hypersensitivity reactions, the poor bile duct opacification in patients with hepatocellular dysfunction/high-grade obstruction, and the availability of other more robust techniques such as MRCP and EUS. Also, in one study comparing CT cholangiography with fiber-optic cholangioscopy, CBD stones < 5 mm were missed by CT cholangiography in several cases [97].

Magnetic Resonance Cholangiopancreatography

A recent meta-analysis has shown MRCP to have a high sensitivity of 93% and a specificity of 96% in the diagnosis of choledocholithiasis [98]. The specificities have ranged from 73 to 99% and the sensitivities from 77 to 100% [98]. In general, false-negative results occur due to small stones (<5 mm) found within non-dilated bile ducts, particularly impacted at the ampulla [87, 99–101]. False-positive results may occur due to the presence of other low signal intensity foci such as sludge, blood clots, air bubbles, and tumor, on the MRCP images [86, 87, 100]. The major drawback of MRCP is its cost. A recent study has suggested that MRCP is not a cost-effective strategy in the management of silent CBD stones [102]. Thus, MRCP is of greatest use in symptomatic patients in order to avoid unnecessary ERCP [103, 104].

Endoscopic Retrograde Cholangiopancreatography

In a very recent meta-analysis, sensitivity estimates for endoscopic retrograde cholangiopancreatography (ERCP) ranged from 67% to 94%, with specificities ranging from 92% to 100%. The summary sensitivity was 83%, and specificity was 99% [105]. Although long considered the gold standard test, compared to EUS and MRCP, accuracy of ERCP is suboptimal, being reduced in the case of CBD dilation and small CBD stones [78, 106–109]. Currently, ERCP is used predominantly as a therapeutic tool, and it is usually preceded by other diagnostic tests such as EUS or MRCP especially in patients with moderate to intermediate risk of carrying CBD stones [109]. A recent Cochrane review found that performing EUS or MRCP prior to ERCP can potentially decrease the rate of unnecessary invasive testing by 30–70% [98].

Endoscopic Ultrasonography

In a recent meta-analysis, the summary estimate of sensitivity and specificity for EUS was 95 and 97%, respectively. The sensitivities ranged

between 75 and 100%, and the specificities ranged between 85 and 100%. In particular, EUS is sensitive (more sensitive than MRCP) in detecting small stones (<3 mm), even when situated at the distal bile duct or within a non-dilated bile duct [71, 78, 110, 111]. In patients with “idiopathic” pancreatitis, EUS was able to diagnose a cause in 77–92% patients where their symptoms were caused by small gallstones missed by conventional imaging [112, 113]. EUS is increasingly used for diagnosis of CBD stones, often as the first step of a potential double-technique procedure (EUS and ERCP/endoscopic sphincterotomy) [107, 109, 114]. A positive EUS can be followed immediately with a therapeutic ERCP, allowing for a single session of sedation.

Imaging Strategy

To help direct therapy, classifications based on clinical, laboratory, and transabdominal ultrasonography findings have been developed to stratify patients according to their likelihood (low, intermediate, and high) of harboring CBD stones at presentation [86, 115–124]. Calvo et al. [86] validated such a classification by finding bile duct stones at ERCP in 65.3, 33, and 0% of their patients with a high, intermediate, and low probability classification, respectively. Even better selection was achieved by Liu et al. [120], who found bile duct stones in over 90% of their patients classified as a high-probability group.

Evidence suggests that patients with a high probability for choledocholithiasis should directly undergo diagnostic ERCP with intent to treat [103, 117–120]. The needlessness of performing screening tests in such a high-probability group of patients was shown by Sahai et al. [117], who found that a screening MRCP would have prevented ERCP in only less than 4% of their patients. A recent cost-effectiveness study comparing MRCP-, EUS-, and ERCP-based strategies has also shown that outcomes were highly dependent on the pretest probability for choledocholithiasis and that at probabilities of >45%, ERCP alone was the most cost-effective option [118].

In patients with a low/intermediate or intermediate probability for choledocholithiasis, the literature suggests that a relatively noninvasive screening test such as MRCP or EUS should be used first to select patients with common duct stone for therapeutic ERCP [86, 108, 116, 125, 126]. In such a group of patients, Calvo et al. [86] showed that MRCP may replace ERCP without missing pronounced choledocholithiasis. A systematic review of 28 studies with economic evaluation has shown that the preliminary use of MRCP can also reduce cost and improve quality of life outcomes when compared to diagnostic ERCP [108]. The role of EUS has also been validated in a number of studies [125, 126]. In a study of 55 patients with intermediate probability for choledocholithiasis by Kohut et al. [125], EUS selection for therapeutic ERCP only failed in one of five patients with CBD stones. Canto et al. [123] found EUS to be a useful test in the low- to intermediate-probability group of patients. Performing EUS first, before ERCP, has also been shown to be cost-effective when patients were at a medium risk for CBD stones [127]. Evidence such as this has prompted the National Institutes of Health (NIH) state-of-the-art science statement that in patients with a low likelihood of biliary stone disease, diagnostic ERCP should be avoided [126]. Recent suggested management algorithms by the American Society for Gastrointestinal Endoscopy (ASGE) [103] advise MRCP or EUS for triage purposes only in patients with intermediate risk of choledocholithiasis (level 1B, strong evidence). According to the suggested algorithms, no further imaging is required in patients with a low probability for choledocholithiasis [103] (level 1B, strong evidence) (Fig. 21.1).

The question of whether to use MRCP or EUS as the primary screening tool has not yet been fully settled. The two tests are similar in terms of diagnostic accuracy with both consistently showing accuracies of greater than 90% in the diagnosis of choledocholithiasis [98]. MRCP has the advantages of being quick to perform, not requiring sedation, and being completely noninvasive. EUS is less costly and facilitates interven-

tions that are not possible with MRCP [83, 118, 128, 129]. A recent cost-effective analysis by Morris et al. [130] showed that using MRCP to select patients for ERCP was the most cost-effective option with the highest monetary net benefit. In practice, which of these two tests is used is dictated more by the availability of equipment, local expertise, physician preference, and contraindications to each test, rather than by strict clinical or economic criteria.

Thus, it would appear that patients with a high pretest probability for choledocholithiasis should directly undergo ERCP for diagnosis and treatment of their probable stones. Performing screening tests such as MRCP or EUS would only serve to add a time and cost burden to the patient. However, in patients with an intermediate pretest probability for choledocholithiasis, a test such as MRCP or EUS should be performed to select patients for therapeutic ERCP. Typically, those with negative EUS or MRCP do not need further invasive tests. Doing so would result in considerable clinical benefit and cost savings by avoiding unnecessary diagnostic ERCP in the vast majority of these patients. Finally, patients with symptomatic cholelithiasis who have a low probability for choledocholithiasis should undergo laparoscopic cholecystectomy without any further investigations (Fig. 21.1).

Take-Home Tables and Figure

Tables 21.1 and 21.2 present the accuracy of ultrasonography compared with cholescintigraphy in the diagnosis of acute cholecystitis and the accuracy of cholescintigraphy in diagnosing acute acalculous cholecystitis, respectively. Table 21.3 highlights the imaging criteria for acute acalculous cholecystitis, while Table 21.4 presents the CT protocol for suspected biliary pathology. Table 21.5 summarizes the parameters for performing magnetic resonance cholangiopancreatography.

Figure 21.1 is an algorithm for the management of patients with symptomatic cholelithiasis based on the degree of probability for choledocholithiasis.

Imaging Case Studies

Case 1

In Fig. 21.2a–f, a 63-year-old male is presenting to the emergency room with right upper quadrant pain.

Case 2

In Fig. 21.3a–c, a 59-year-old man presents with a history of abdominal pain, leukocytosis, and abnormal liver function tests.

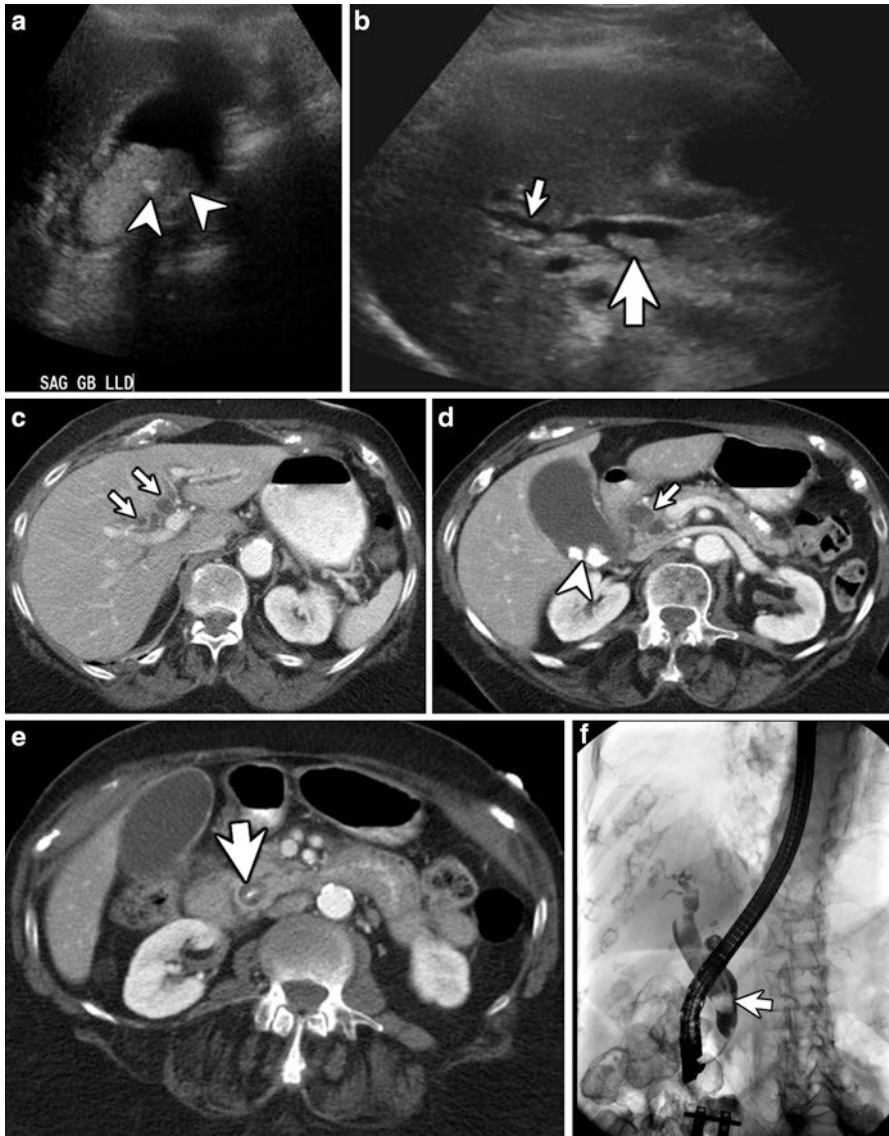


Fig. 21.2 (a) Ultrasound image of the gallbladder showing multiple stones and sludge (*arrowhead*). (b) Ultrasound image of the common bile duct (CBD) shows a hypochoic stone (*thick arrow*) with dilated intrahepatic biliary ducts (*short arrow*). (c–e) Axial contrast-enhanced

CT of the abdomen confirms dilated intrahepatic biliary ducts (*short arrow*), gallstone (*arrowhead*), and CBD stone (choledocholithiasis, *thick arrow*). (f) Endoscopic retrograde cholangiogram confirms the filling defect stone in the CBD (*thick arrow*) which was removed

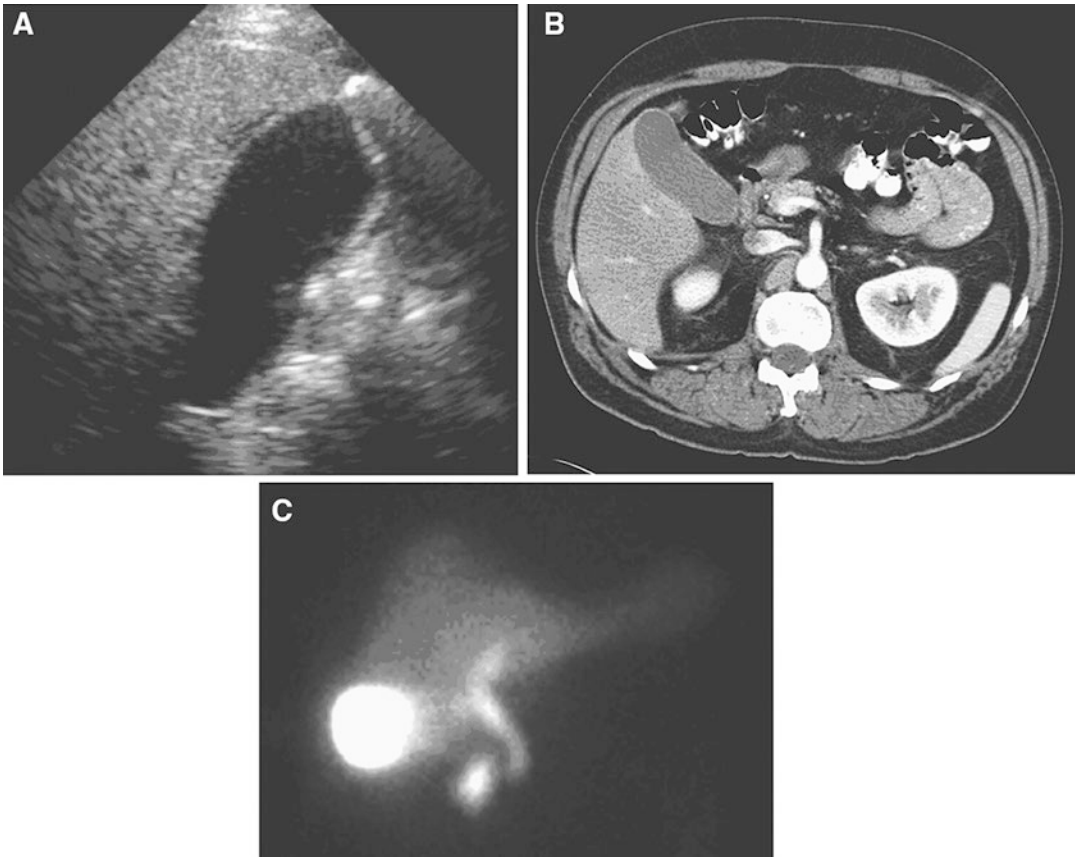


Fig. 21.3 (a) Ultrasonography shows a thin layer of fluid around the fundus of the gallbladder. Patient had an associated positive sonographic Murphy's sign. (b) Intravenous and oral contrast-enhanced CT shows a normal gallbladder. (c) Technetium diisopropyl iminodiacetic acid (Tc-DISIDA) cholescintigraphy shows normal intense filling of the gallbladder, ruling out the diagnosis of acute

cholecystitis (Reprinted with kind permission of Springer Science+Business Media from Varghese JC, Lucey BC, Soto JA. Imaging of Biliary Disorders: Cholecystitis, Bile Duct Obstruction, Stones, and Stricture In Medina LS, Blackmore CC (eds.): *Evidence-Based Imaging: Optimizing Imaging in Patient Care*. New York: Springer Science+Business Media, 2006)

Case 3

In Fig. 21.4a, b, a 49-year-old female presents with intermittent right upper quadrant colicky pain.

Case 4

In Fig. 21.5a, b, a 69-year-old male presented to ED with epigastric pain.

Suggested Imaging Protocols

Suggested imaging protocols are given in Tables 21.4 and 21.5; with Table 21.4, suggested CT

protocols for evaluation of suspected biliary pathology are presented, and with Table 21.5, suggested parameters for performing magnetic resonance cholangiopancreatography (MRCP) (for 1.5 T scanner with torso phased array coil) are presented.

Future Direction

- Studies to assess most cost-effective and specific imaging strategy for diagnosing acute acalculous cholecystitis
- Comparative study between negative-contrast CT cholangiopancreatography (nCTCP) and

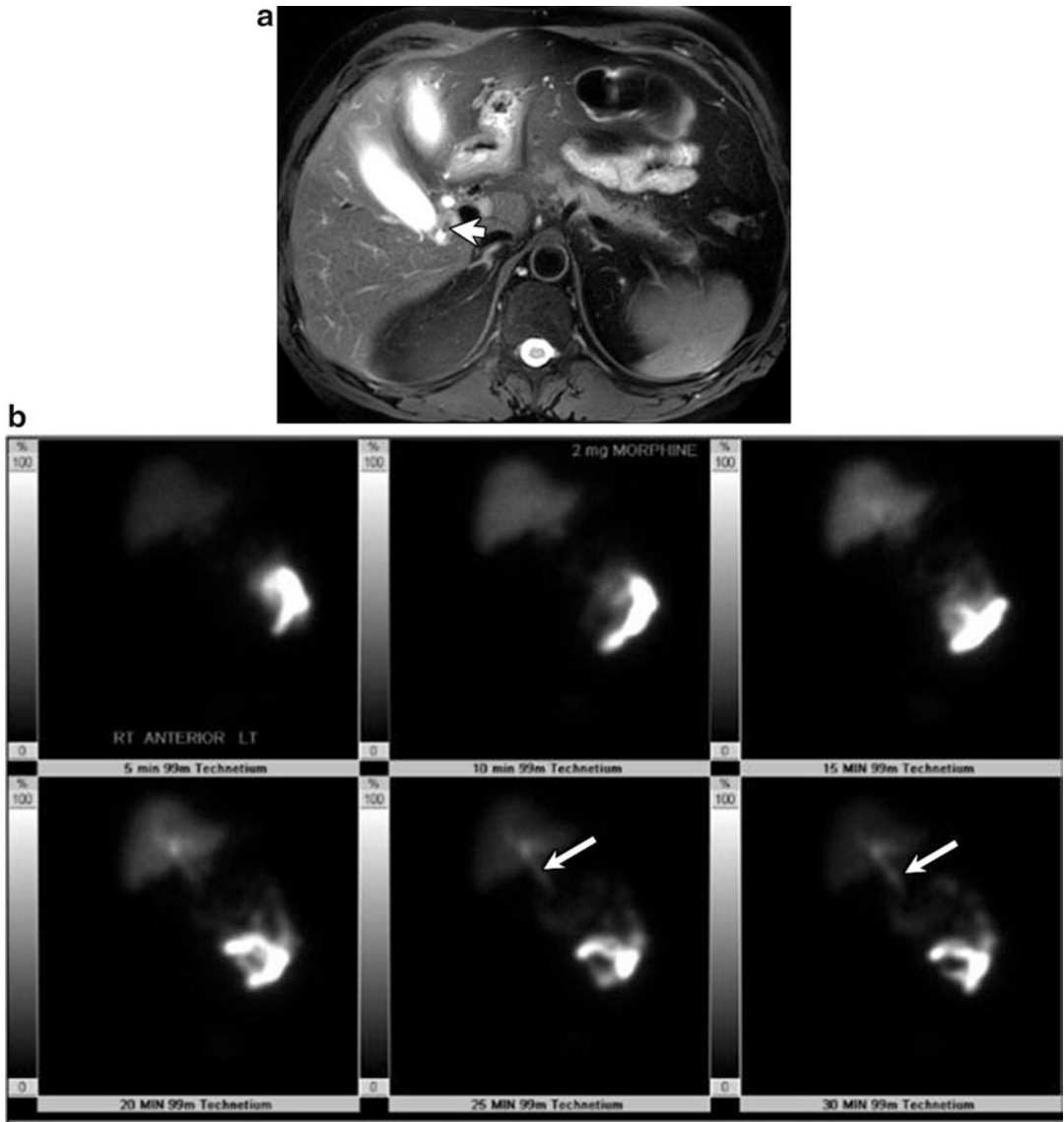


Fig. 21.4 (a) Axial T2-weighted image of the upper abdomen shows a hypointense filling defect in the gallbladder neck (*thick arrow*) suggesting impacted gallstone. (b) Cholescintigraphy (HIDA scan) shows excretion of the tracer into the common bile duct at 20–30 min (*arrows*) but no filling of the gallbladder consistent with findings of acute cholecystitis

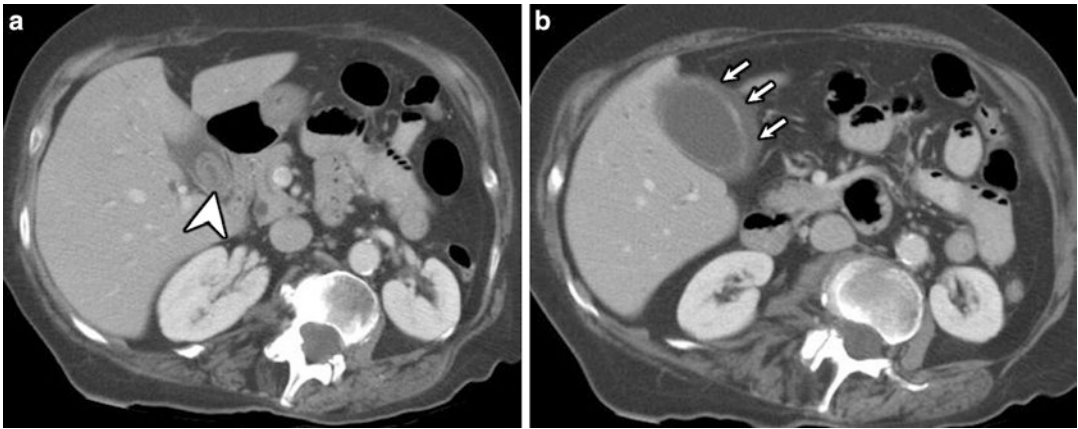


Fig. 21.5 (a, b) Axial contrast-enhanced CT through upper abdomen demonstrates gallstone (*arrowhead*) and diffuse gallbladder wall thickening and pericholecystic fluid (*arrows*) consistent with acute cholecystitis

MRCP for the diagnosis of obstructive biliary diseases

- Utility of cholecystikinin cholescintigraphy in patients undergoing percutaneous cholecystostomy

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Small and Large Bowel Obstruction in Adults: Evidence- Based Emergency Imaging

22

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Key Points

- Radiography is an easily accessible, low-cost and low-radiation investigation to “rule in” small bowel obstruction (SBO) in the emergency department (ED). Ultrasound is a better test to “rule out” SBO, especially if radiography is negative (strong evidence).
- Multidetector computed tomography (MDCT) is the gold standard investiga-

tion to diagnose SBO, to determine the level and cause of SBO and to diagnose ischemia as a complication of SBO (strong evidence).

- MDCT has high negative predictive value for ischemic bowel in subjects with small bowel obstruction.
- MDCT may help to more appropriately risk-stratify patients for surgical versus nonsurgical management at admission.
- Water-soluble contrast follow-through is an excellent test to predict if SBO secondary to adhesions will resolve spontaneously or will require surgery (strong evidence).
- In large bowel obstruction (LBO), MDCT is the investigation of choice to identify the level and cause of LBO, but water-soluble contrast enema is the investigation of choice to determine if the obstruction is partial or complete (weak to moderate evidence).

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Definitions and Pathophysiology

Small bowel obstruction (SBO) continues to pose a dilemma for surgeons. Nonsurgical treatment of SBO is now common with bowel rest and

nasogastric tube decompression replacing routine surgical treatment in most patients suspected of having SBO. However, failure of conservative treatment and subsequent delayed surgery may lead to the development of bowel ischemia and result in prolonged hospitalization, with a concomitant increase in cost and the risk of nosocomial infections.

Small bowel obstruction in the majority of studies is defined as the presence of continuous dilated loops of bowel >2.5 cm proximal to collapsed loops of bowel. These criteria were first described by Maglinte et al. [1]. However, several studies also use >3 cm as a cut-off. Predictors of SBO in patients presenting to the emergency department include a previous history of abdominal surgery, constipation, abnormal bowel sounds and/or abdominal distention on examination [2]. SBO with a single transition zone can be caused by (a) extrinsic and (b) intrinsic bowel wall and (c) intraluminal pathologies [3]. Extrinsic causes include adhesive bands, external hernias (e.g. inguinal, femoral, Spigelian, umbilical, obturator or incisional), extension of a disease process from the mesentery to the bowel serosal surface (e.g. peritoneal carcinomatosis and endometriosis) and any inflammatory or infectious process adjacent to the small bowel that can cause reactive bowel wall oedema [4, 5]. Intrinsic causes of SBO include the causes of bowel wall inflammation or fibrosis (e.g. Crohn's disease, ischemia, anastomotic stricture, hematoma, radiation enteritis), as well as intussusception and primary and secondary bowel neoplasms [3–7]. Intraluminal pathologies causing SBO include gallstone ileus, phytobezoars, thick intestinal secretions (distal intestinal obstruction syndrome in cystic fibrosis) and ingested foreign body [3].

The transition zone is the point at which there is a change of calibre between dilated proximal and collapsed distal bowel loops in mechanical bowel obstruction [8]. Diffusely dilated small bowel loops and colon without a transition zone signify a paralytic ileus, rather than a mechanical obstruction.

Strangulating small bowel obstruction is defined as small bowel obstruction associated with intestinal ischemia from various causes

including internal or external hernia and small bowel volvulus.

Closed loop obstruction is identified when there is more than one transition zone in adjacent loops of small bowel. A single pathology obstructs the bowel at two or more adjacent points, obstructing the bowel proximal to the closed loop and within the closed loop [4]. The bowel often demonstrates a U- or C-shaped configuration, converging at the site of obstruction. Continued distension leads to venous compression with hampered venous outflow followed by arterial compression with obstruction to arterial inflow leading to strangulation or arterial ischemia. The finding of a closed loop obstruction, even without evidence of ischemia, is associated with a high risk of transmural necrosis at surgery [9]. The causes of closed loop obstruction include adhesions, hernia (internal or external) and volvulus [3].

Incarceration is fixation of a bowel segment and its mesentery within an internal or external hernia. Hernias are the second most common cause of SBO [5]. *Internal hernia* occurs when bowel prolapses through defects or potential spaces in the peritoneum or mesentery and becomes obstructed at both the entry and exit sites [6, 10]. Internal hernias account for less than 1% of all cases of bowel obstruction, but their presentation is frequently non-specific with intermittent symptoms, making their diagnosis difficult. A high index of suspicion is needed to guide imaging and make the diagnosis. The defect or potential space can be congenital (most commonly right and left paraduodenal, foramen of Winslow and pericaecal) or acquired from prior abdominal or pelvic surgery (e.g. trans-mesenteric hernia) [3]. Paraduodenal hernias account for 53% of internal hernias unrelated to prior surgery. Roux-en-Y gastric bypass surgery causes internal hernia in an estimated 5% of patients undergoing laparoscopic bypass [11]. Imaging findings include abnormal grouping of bowel loops in unusual locations, as well as adjacent transition zones at the entry site into the hernia sac [10].

External hernias occur at sites of muscular or ligamentous weakness in the abdominal wall. Inguinal, femoral and ventral hernias usually can be detected on clinical examination. SBO caused by hernia is often a closed loop obstruction, and

symptomatic hernias have a 28% risk of developing ischemia. Therefore, all patients with symptomatic hernias should undergo surgical repair [12].

Non-strangulating or simple mechanical obstruction is any process that obstructs bowel lumen without causing obstruction to arteries or major veins. If small bowel obstruction persists, it will impair venous return leading to oedema and eventually bowel ischemia.

Adhesions are not visible on imaging. Kinking or tethering of the bowel at the transition zone without any other identifiable causes, particularly in a patient with a history of surgery, is highly suggestive of an adhesion [7]. Therefore, adhesion is a diagnosis of exclusion.

Intraluminal obstruction, such as gallstone ileus, is a rare cause of SBO. The site of obstruction is usually at the ileocecal valve, where the lumen of the bowel is narrowest.

Tumours with a tendency to cause widespread peritoneal metastases, such as ovarian, colonic, and gastric neoplasms, may lead to multiple serosal implants on the surface of small bowel, forming confluent soft-tissue masses that surround and cause extrinsic compression of the small bowel lumen or tethering of bowel loops.

Large bowel obstruction has been defined as the absence of gas or bowel movements for greater than 24 h associated with abdominal distension and the visualization of dilated colon on an abdominal radiography [13]. Acute large bowel obstruction is a common presentation of advanced colorectal cancer. Other causes of LBO include sigmoid and caecal volvulus, pseudo-obstruction and hernia. Patients may or may not have nausea and vomiting, depending on the competence of the ileocaecal valve.

Sigmoid volvulus is the wrapping of the sigmoid colon around itself and its mesentery [14]. Caecal volvulus is the twisting of the caecum on itself and on its mesentery.

Acute colonic pseudo-obstruction is characterized by clinical and radiological evidence of acute large bowel obstruction in the absence of a mechanical cause [15]. It was first described by Sir William Heneage Ogilvie in 1948, hence the eponym Ogilvie's syndrome [16]. Acute pseudo-

obstruction usually affects elderly patients with multiple comorbidities.

Epidemiology

Annual rates for SBO range from 579 to 654 per 100,000 population [17]. Annual rates per 100,000 population varied by age category, ranging from 28.9 to 41.6 for age 15–44, from 120.8 to 155.8 for ages 45–64 and from 402.5 to 480.6 for those age 65 or older [17]. The prevalence of SBO in the emergency department has been estimated at 2% of patients presenting with abdominal pain [2]. Small bowel obstruction accounts for as many as 12–16% of surgical admissions and more than 300,000 operations annually in the United States [18]. Ischemia complicates less than 20% of SBOs due to adhesion [19]. Strangulating small bowel obstruction is estimated to account for about 10% of all cases of small bowel obstruction. The most common cause of SBO is due to adhesions, followed by Crohn's disease, neoplasia, hernias and radiation [20].

LBO accounts for approximately 2% of acute surgical admissions [21]. Pseudo-obstruction is estimated to account for approximately 20% of cases of LBO [15].

Overall Cost to Society

The healthcare expenses associated with SBO are substantial, accounting for more than 300,000 hospitalizations annually. The cost of SBO to the US health system was estimated at more than \$2.3 billion per year in 2005 [18, 22]. More recent estimates would suggest \$3 billion in medical care per year in the United States with approximately 70% of these patients being admitted through an ED [7, 23].

Goals of Imaging

The goals of imaging are to diagnose bowel obstruction and to identify the level and cause of obstruction, as well as any associated complications

such as ischemia or perforation. Imaging is an adjunct to clinical and laboratory assessment of the patient and assists the surgeon in the decision to treat the patient operatively or nonoperatively.

Methodology

A comprehensive Medline search (United States National Library of Medicine database) for original articles published between May 2005 and May 2015 using the Ovid and PubMed search engines was performed using a combination of the following key terms: (“diagnosis”) AND “small bowel obstruction”) AND (computed tomography OR magnetic resonance imaging OR ultrasound OR follow through) and (“diagnosis”) AND “large bowel obstruction”) AND (computed tomography OR magnetic resonance imaging OR ultrasound OR follow through).

The search was limited to English language articles and human studies. The abstracts were reviewed and selected based on well-designed methodology, clinical trials, outcomes and diagnostic accuracy. Additional relevant articles were selected from the references of reviewed articles and published guidelines.

To determine the most appropriate investigations in this population, graphs of conditional probability (GCTs) have been used to compare tests (see Take Home section). GCTs are generated from the sensitivity and specificity of a test and show posttest probabilities for both positive and negative test results over the full range of pretest probabilities [24].

Discussion of Issues

Small Bowel Obstruction

What Is the Imaging Modality of Choice to Rule Out Small Bowel Obstruction (SBO) in Adults Attending the Emergency Department?

Summary of Evidence MDCT is the most sensitive and specific modality for the diagnosis of SBO (strong evidence). With the advent of MDCT,

multiplanar reformatting and thinner detectors and the speed and accessibility of CT, it is the gold standard for the imaging of patients with suspected complicated SBO.

Radiography is a cheap, widely available and fast investigation. If abdominal radiography is positive in the setting of a high pretest probability for SBO, it is a useful test. However, radiography is a weak test when it is negative in the setting of an intermediate or high pretest probability, as it cannot reliably exclude SBO, particularly when the bowel loops are fluid-filled.

Stable patients with suspected uncomplicated SBO may not need a CT to rule out SBO and may be spared the exposure to unnecessary radiation. Ultrasound, as an alternative imaging modality to radiography, is a useful adjunct for the initial work-up of patients with suspected SBO in the ED (strong evidence). When ED physicians are trained in ultrasound for SBO, it is an excellent test to rule out SBO.

MRI has high sensitivity and specificity for the diagnosis of SBO, but its restricted access, higher cost and longer scan times mean it is usually reserved for special cases, such as stable pregnant patients, or for the imaging of subacute or chronic obstruction, such as in Crohn's disease.

Supporting Evidence

Computed Tomography

Findings consistent with SBO on CT scan include continuous dilated loops of small bowel >2.5 cm proximal to collapsed loops of bowel and a decompressed colon [1]. MDCT is very useful for the diagnosis of SBO in the presence of either air- or fluid-filled dilated small bowel loops. It is a very sensitive modality for the identification of the transition zone between dilated and collapsed bowel loops. Failure of intraluminal contrast to pass beyond the transition zone signifies high-grade or complete obstruction [25].

Due to the significant advancement in CT technology over the past 20 years, many studies show tremendous variability in terms of the type of CT scanner used, the image slice thickness (ranging from 5.0 to 0.75 mm) and the use and

timing of both intravenous (IV) and oral contrasts [2]. The majority of systematic reviews on the diagnosis of SBO appear to have diluted the diagnostic performance of modern MDCT scanners by including such a mixture of historical and modern studies [2, 25, 26]. One such systematic review showed a positive likelihood ratio (+LR) of 3.6 (95% CI = 2.3–5.4) and a negative likelihood ratio (–LR) of 0.18 (95% CI = 0.09–0.35) for CT using 5–10 mm slices with sensitivities ranging from 63 to 100% and specificities ranging from 57 to 100% [2].

For the purposes of this discussion, the main focus is on studies assessing the diagnosis of SBO in the era of 64-slice MDCT with 0.75 to 5 mm image slice thickness, so as not to underestimate the diagnostic performance by dilution from now-obsolete technology. One level 3 (limited evidence) study showed a sensitivity of MDCT for the diagnosis of SBO of 96% (95% CI = 80–100%) with a specificity of 100% (95% CI = 69–100%) and +LR infinity and –LR of 0.04 (Fig. 22.1a) [27].

Two likely explanations for the superiority of MDCT for diagnosis are the ability to post process the images and make sagittal and coronal reformats and the use of thinner slices [8, 28]. The improved spatial resolution of these scanners and the ability to simultaneously review images in different planes have greatly improved the diagnostic performance.

Ultrasound

Several studies have shown that ultrasound is reliable for the diagnosis of SBO in the emergency department and has a higher sensitivity and specificity compared to radiographs [2]. A number of prospective studies have been carried out, some involving radiologists [29–33] and some involving emergency department physicians who have received training in bedside ultrasound [33, 34]. A systematic review showed summary results for formal radiologist-interpreted ultrasounds with a sensitivity of 90% (86–93, 95% CI), specificity of 96% (91–99, 95% CI), +LR of 14.1 (3.6–55.6, 95% CI) and –LR of 0.13 (0.08–0.2, 95% CI) (Fig. 22.1b) [2].

The emergency department physician studies showed a summary sensitivity of 97% (92–99, 95% CI), specificity of 90% (84–95, 95% CI), +LR of 9.5 (2.1–42.2, 95% CI) and –LR of 0.04 (0.01–0.13, 95% CI) (Fig. 22.1c) [2].

The real-time capability of graded compression ultrasound makes it a very fast investigation and avoids exposure to radiation. Once adequate training has been provided, it is easy to use. Point-of-care ultrasound is now widely used in the ED to assess for free fluid in abdominal trauma or in suspected ruptured abdominal aortic aneurysm, and expanding its use to include assessment for SBO could be easily achieved. It can be used to measure bowel diameter, assess for presence or absence of peristalsis and look for ascites.

Radiography

The low cost and ease of accessibility to radiography mean it is still very often the first-line imaging modality performed in the work-up of patients with small bowel obstruction. It remains the first step in several imaging algorithms [26]. In a large systematic review and meta-analysis of the imaging modalities associated with the diagnosis of SBO, radiography was determined to be the least useful modality for the diagnosis. Four similar studies extracted from the meta-analysis give a summary positive likelihood ratio (+LR) of 1.55 (95% confidence interval [CI] = 1.10–2.19) [2]. These four similar studies showed sensitivities ranging from 69 to 77% and specificities ranging from 57 to 67% [29, 34–36]. These results may be explained by the fact that fluid-filled SBO often leads to false-negative plain radiography. Therefore, radiography is a useful test when positive in the setting of a high pretest probability and when negative in the setting of a low pretest probability, but it is a poor test when negative if there is a high or intermediate pretest probability of SBO (Fig. 22.1d).

Magnetic Resonance Imaging

The diagnostic performance of MRI is very high. Half-fourier acquisition single-shot turbo spin-echo (HASTE) MRI has been shown to diagnose SBO

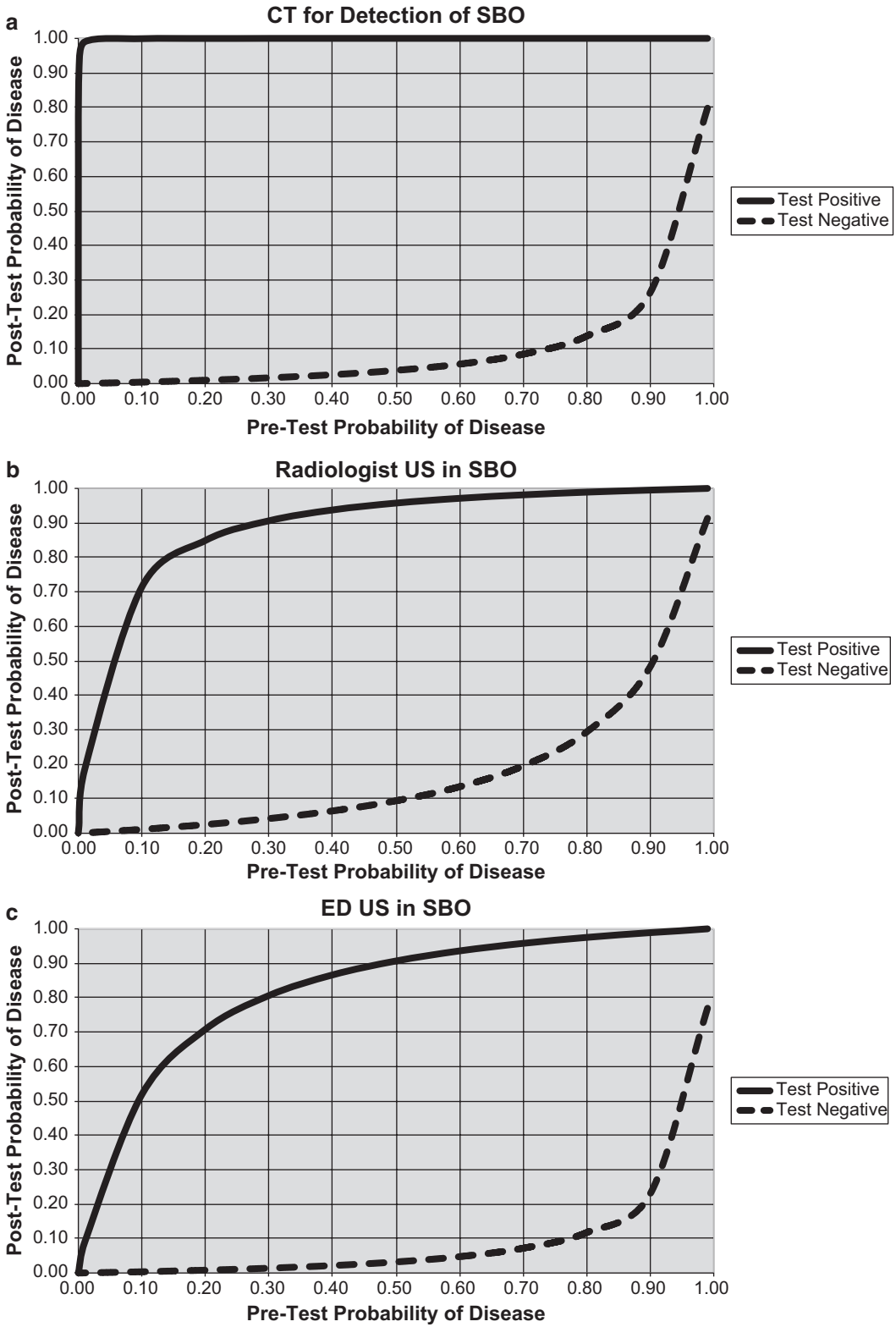


Fig. 22.1 (a) Multiple-detector computed tomography (MDCT) for the detection of small bowel obstruction. (b) Radiologist interpreted ultrasound for the detection of small bowel obstruction. (c) ED physician performed ultrasound for the detection of small bowel obstruction.

(d) Radiography (using upper limits of four studies summary sensitivity and specificity) for the detection of small bowel obstruction. (e) Magnetic resonance imaging (MRI) for the detection of small bowel obstruction

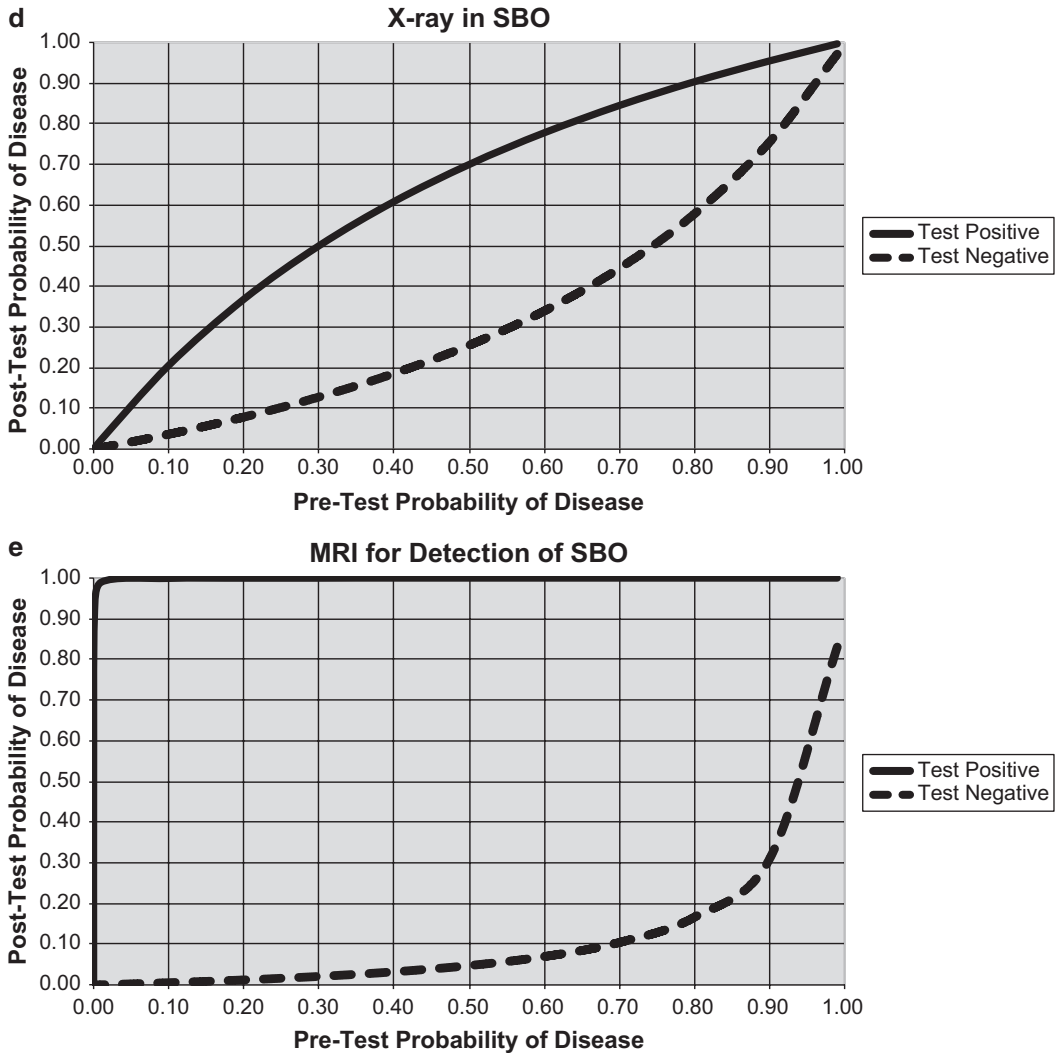


Fig. 22.1 (continued)

with a sensitivity of up to 95% and a specificity of up to 100% with a PPV of 100% and a NPV of 80% (Fig. 22.1e) [2, 25, 37]. For practical purposes, the use of MRI in the diagnosis of acute SBO is limited, as it is not always suitable for the emergency investigation of unstable patients due to the long scan times, lack of accessibility and lower availability, especially out of hours. As a result, it is usually reserved for special patient groups such as stable pregnant patients or for the investigation of patients with subacute or chronic obstruction, often in the setting of Crohn's disease.

In stable pregnant patients, MRI is the modality of choice for the diagnosis of SBO as it avoids exposing the foetus to potentially harmful ionizing radiation. The evidence is quite limited in this area, but one level 4 study showed MRI to be superior to ultrasound for diagnosis in this patient group [38]. In unstable pregnant patients, CT is still recommended as the first-line modality. In these cases, the risk of radiation to the foetus is outweighed by the much greater risk of pregnancy loss due to an acute abdomen [39].

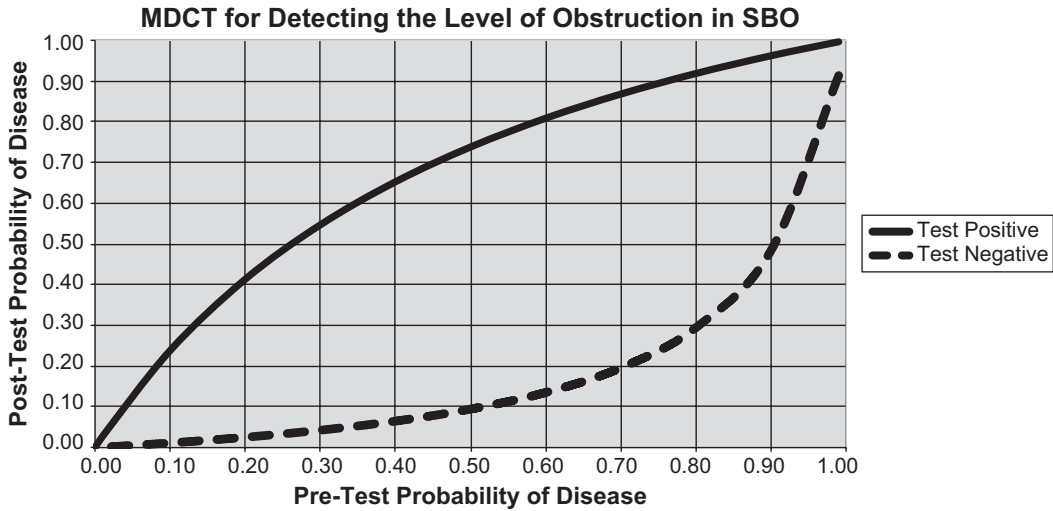


Fig. 22.2 MDCT for the detection of level of obstruction in small bowel obstruction

What Is the Imaging Modality of Choice for the Detection of the Level and Cause of SBO in Adults?

Summary of Evidence Once SBO has been diagnosed, the radiologist must then look for signs to determine the level and cause of the obstruction. The level of obstruction is most often at the transition zone between proximal dilated and distal collapsed bowel loops. It is also at this level that the signs of the cause of obstruction are apparent. If there is more than one transition zone, closed loop obstruction should be considered. If there is a single transition zone and a cause is not seen, it is likely to be secondary to adhesions, the most common cause of SBO in the Western world, which occurs in patients with a history of abdominal surgery or previous abdominal sepsis. If the obstruction is due to an internal hernia, abnormal orientation of the bowel is often seen. If the cause is volvulus, twisting of the mesentery is usually identified, the so-called swirl sign. Inguinal and femoral hernias are usually fairly obvious. The small bowel faeces sign refers to solid feculent material within the lumen of the small bowel and is seen in more chronic or subacute obstruction, such as proximal to a stricture in Crohn's disease or in distal intestinal obstruction syndrome (DIOS) secondary to cystic fibrosis. This sign can also be seen in the absence of dilated bowel

loops, and then it only signifies slow transit or bacterial overgrowth. Therefore, the small bowel faeces sign is only reliable in the setting of bowel dilatation [40]. As all of these signs are best seen on CT, it comes as no surprise that MDCT is the modality of choice for the detection of the level and cause of obstruction (strong evidence) [25].

Supporting Evidence

Computed Tomography

MDCT with its high spatial resolution and multiplanar reformatting has led to improved diagnostic performance for the diagnosis of bowel obstruction. The improved technology has also led to improved diagnosis of the level and cause of SBO. One level 2 prospective study of all patients who were admitted with SBO and went to surgery looked at the correlation between transition zones on MDCT and at surgery and found that 64-slice MDCT had a 93% sensitivity (95% CI 0.86–1.0), 67% specificity (95% CI 0.13–1.0), 98% positive predictive value and 33% negative predictive value with a prevalence of 95%. The +LR was 2.79, and the –LR was 0.107 (Fig. 22.2) (moderate evidence) [8].

Historical studies involving helical CT (now out-of-date technology) have shown it to be accurate at determining the cause of obstruction in

80–91% of patients [25, 29, 36, 41]. While there are limited studies of the more modern MDCT scanners in the diagnosis of the cause of SBO, it is well established that the true diagnostic performance of MDCT is far superior to its helical ancestor.

Magnetic Resonance Imaging

With the advent of faster MRI sequences which are less susceptible to artefact due to peristalsis, half-fourier acquisition single-shot turbo spin-echo (HASTE) MRI has been shown to be effective at determining the level and cause of SBO [25, 37]. In one prospective study of 44 patients presenting with clinical symptoms of SBO comparing HASTE sequence MRI to helical CT from the late 1990s, HASTE MRI was found to be more accurate at determining the transition zone than helical CT. This was felt to be due to the multiplanar capability of MRI, which was not available for CT at that time [37]. Obviously, the technology used in this study is now very much out of date, but there is a paucity of data available using newer technologies.

MRI may not be widely available at all centres, especially outside of normal working hours. The longer scan time may not be appropriate for very ill patients. It is not clear if MRI is as reliable as MDCT at identifying the cause of obstruction, due to limited evidence in this area.

What Is the Best Imaging Modality to Predict If the Patient Should Undergo Nonoperative or Operative Management?

Summary of Evidence Patients with SBO who require operative intervention may be divided into different subgroups:

1. SBO secondary to adhesions, which is slow to resolve or fails nonoperative management
2. SBO complicated by ischemia (see section “What Is the Imaging Modality of Choice to Assess for Associated Bowel Ischemia or Strangulation?”) or at high risk of ischemia, which should proceed directly to surgical management, e.g. incarcerated hernia and closed loop obstruction

The first group are generally clinically stable patients with SBO secondary to adhesions that do not have a history of surgery within the previous 6 weeks, have no signs of strangulation or peritonitis and have no evidence of carcinomatosis or irreducible hernia. This uncomplicated adhesive SBO group is initially treated with nasogastric tube aspiration and intravenous fluid replacement. In this group, water-soluble contrast follow-through has been shown to be an excellent test which is both diagnostic (predicting which patients will resolve nonoperatively and which will require surgery) and potentially therapeutic (as the water-soluble contrast medium can act to improve small bowel motility and help relieve the obstruction).

Supporting Evidence

Water-Soluble Contrast Follow-Through

There is level 1 (strong) evidence to support the use of water-soluble contrast follow-through for the prediction of success of nonoperative management in adhesive uncomplicated SBO. Abbas et al. performed a systematic review of primary evidence and included patients who had undergone abdominal surgery more than 6 weeks before admission and who were admitted to the hospital with abdominal pain, vomiting and abdominal distension with dilated small bowel loops and air-fluid levels on abdominal radiography, without signs of large bowel obstruction. The exclusion criteria were similar for all studies included in the systematic review. The exclusion criteria included patients who had surgery within 6 weeks before the episode of SBO, patients with signs of strangulation or peritonitis, patients with carcinomatosis or irreducible hernia and patients who showed signs of resolution of obstruction at the time of admission [42]. This good-quality systematic review showed a summary sensitivity of 97% and specificity of 96% for the appearance of water-soluble contrast agent in the colon on an abdominal radiograph within 24 h of its administration to predict resolution of adhesive SBO (Fig. 22.3) [42]. Patients who did not have water-soluble contrast in the colon after 24 h had complete obstruction and were much more likely to

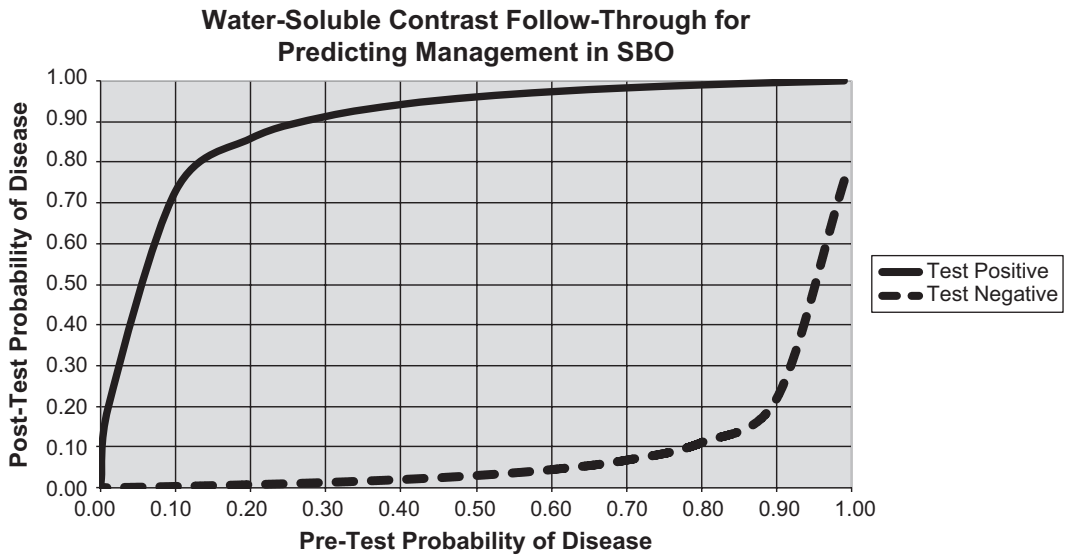


Fig. 22.3 Water-soluble contrast follow-through for predicting management in small bowel obstruction

require surgical intervention [43]. Several other studies have looked at water-soluble contrast follow-through using different time limits from 4 to 24 h [42–45]. Abbas et al. in their systematic review showed similar positive and negative likelihood ratios in the studies using 4–8 h compared with studies using 24 h. All studies had the same exclusion criteria and the same prevalence. The negative predictive value was higher using 24 h instead of the shorter intervals [42].

The most commonly used water-soluble contrast medium in these studies is Gastrografin (Schering, Berlin, Germany), a mixture of sodium diatrizoate and meglumine diatrizoate with an osmolality of 1900 mosm/l. It may also play a therapeutic role and aid in the resolution of obstruction as it activates movement of water into the small bowel lumen, decreases oedema in the wall and increases smooth muscle contractility [25, 42].

Computed Tomography

MDCT is also useful for determining if nonoperative management of SBO is more likely to fail. One prospective level 2 study of patients with SBO assessing the ability of MDCT to predict the need for surgery showed a sensitivity of 100%, specificity of 46%, positive predictive value of

43% and negative predictive value of 100% in the setting of high-grade or complete bowel obstruction (Fig. 22.4a). In the presence of a transition zone, it showed a sensitivity of 100%, specificity of 23%, PPV of 35% and NPV of 100% (Fig. 22.4b) [47]. Excluding patients with signs of ischemia, swirl sign or volvulus, MDCT was predictive of the need for surgery in the presence of an abnormal course of the mesenteric vessels where they converged together at the transition zone, with a sensitivity of 70%, specificity of 90%, PPV of 74% and NPV of 88% (Fig. 22.4c) [47]. High-grade or complete bowel obstruction is a greater predictor of need for surgery than low-grade or partial obstruction on CT [48].

What Is the Imaging Modality of Choice to Assess for Associated Bowel Ischemia or Strangulation?

Summary of Evidence This second group of patients requiring surgery for SBO are generally quite unwell and require urgent investigation and treatment to avoid significant morbidity and mortality secondary to bowel ischemia. Although ischemia only complicates approximately 10% of patients with SBO, it is the most feared complication [4]. Bowel obstructions associated with small bowel ischemia have a reported mortality

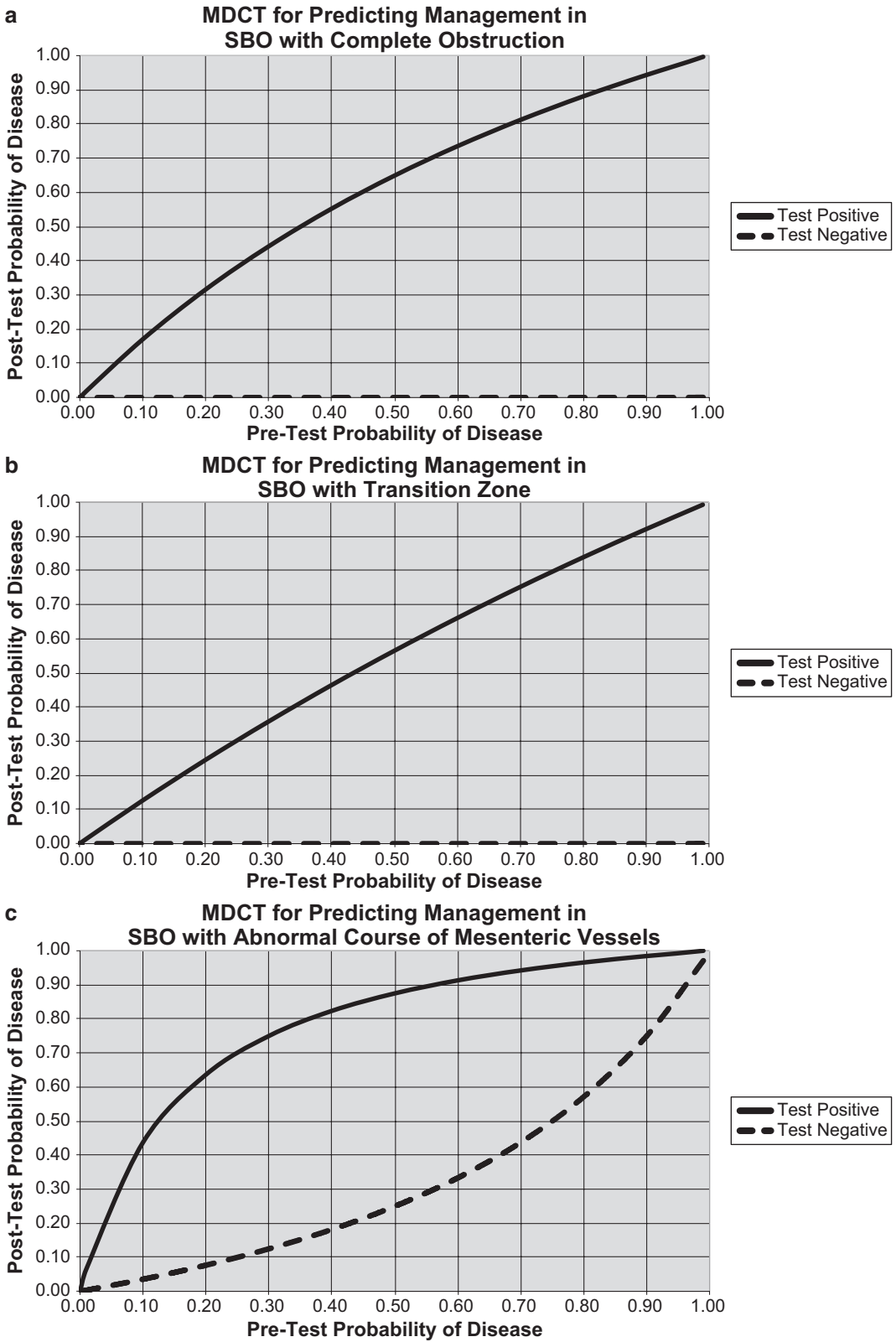


Fig. 22.4 (a) MDCT with complete SBO for predicting management in small bowel obstruction. (b) MDCT with transition zone for predicting management in small bowel obstruction. (c) MDCT with abnormal course of mesenteric vessels for predicting management in small bowel obstruction (Data from [46])

rate of 2–19% [49]. This high mortality rate is mainly attributed to a delay in establishing the diagnosis of ischemia. It is important to accurately identify these patients so that they are not mistakenly prescribed a course of nonoperative treatment. In patients with clinical symptoms and signs of ischemia such as peritonitis, leucocytosis, tachycardia and metabolic acidosis, urgent surgical exploration is recommended (strong evidence) [25].

The most common cause of ischemia related to SBO is closed loop obstruction, and surgery should be considered when these cases are identified, even in the absence of signs of ischemia on CT. Similarly, internal hernias also carry a high rate of associated ischemia, and prompt surgery is required to prevent significant associated morbidity [3, 10]. The aetiology of ischemia in this setting is due to venous compromise and infarction secondary to twisting of the mesentery, exacerbated by bowel dilatation and further reduced perfusion [50].

The mainstay for imaging of ischemia is MDCT, preferentially with intravenous contrast material enhancement and without oral contrast to allow adequate assessment of bowel wall thickening and bowel wall enhancement (strong evidence).

Supporting Evidence

Computed Tomography

Findings suggestive of ischemia on CT include reduced bowel wall enhancement, bowel wall thickening, mesenteric venous congestion, ascites, localized pneumatosis, high attenuation of the bowel wall on unenhanced images and unusual course of the mesenteric vasculature, e.g. swirl sign [25, 51–53]. These findings should prompt urgent surgical exploration (level 2, moderate evidence) [25].

In a systematic review of the diagnostic performance of CT in the setting of ischemia complicating SBO, Mallo et al. included only studies with primary data collection on patients who presented with clinical signs and symptoms of SBO and subsequently underwent CT scanning. They found that the aggregated performance characteristics for CT in the diagnosis of ischemia in SBO were a

PPV of 79% (range, 69–100%), NPV of 93% (range, 33–100%), sensitivity of 83% (range, 63–100%) and specificity of 92% (range, 61–100%) (Fig. 22.5a) [46]. This study was performed before the widespread availability of MDCT and refers to now-obsolete technology, single-detector CT.

A more recent level 3 study from Kato et al. showed that MDCT had a sensitivity of 85%, specificity of 96%–97%, PPV of 73%–79% and NPV of 97%–98% for the diagnosis of ischemia in SBO by consultant radiologists (Fig. 22.5b) (limited evidence) [54].

As with ischemic bowel in general, it is important to remember that early ischemia may be occult on MDCT. If there is clinical concern regarding ischemia or if internal hernia or closed loop obstruction is present, there should be a low threshold for proceeding to surgery.

Magnetic Resonance Imaging

Feasibility studies have been performed to assess the utility of MRI for the diagnosis of ischemia in SBO, but this remains largely experimental. One study showed the feasibility of using low b-value diffusion-weighted imaging [55]. Another study showed excellent results for the use of cine-loop MRI to assess for strangulated bowel in SBO. The sensitivity, specificity, PPV and NPV of cine MRI were 100%, 93%, 83% and 100%, respectively, according to this single study (Fig. 22.6) [56]. As discussed above, the longer scanning times and limited access to MRI, especially out of hours, limit its use in the assessment of these emergent patients.

Large Bowel Obstruction

What Is the Imaging Modality of Choice for the Detection of Large Bowel Obstruction (LBO) and the Diagnosis of the Level and Cause of LBO in Adults?

Summary of Evidence MDCT is the imaging modality of choice in the setting of acute large bowel obstruction (moderate evidence). It is

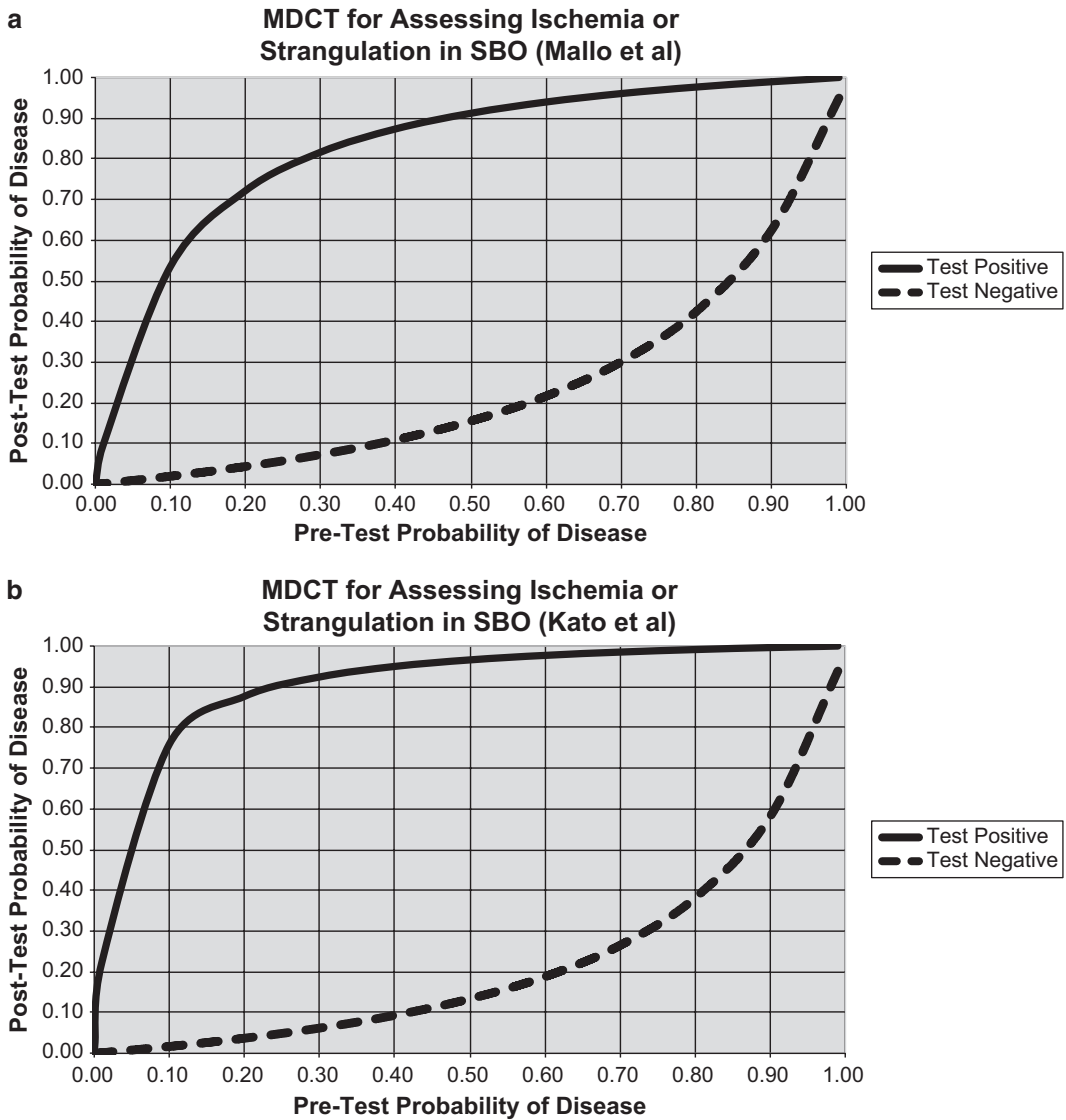


Fig. 22.5 (a) MDCT for assessing ischemia or strangulation in small bowel obstruction (Data from [46]). (b) MDCT for assessing ischemia or strangulation in small bowel obstruction

effective at diagnosing the presence of obstruction, as well as the level and cause of obstruction. It is the most reliable modality to assess for signs of ischemia as a complication of obstruction. In the setting of malignancy, MDCT can stage the disease, as well as localize the obstructing tumour.

There is a paucity of data available for the imaging of LBO in recent years, and much of the data relates to now-obsolete technology.

Water-soluble contrast enema and radiography also have important roles in the work-up of patients with suspected LBO, but neither is as reliable as MDCT.

**Supporting Evidence
Computed Tomography**

In the diagnosis of large bowel obstruction secondary to malignancy, CT has been shown to have a sensitivity of 96% and a specificity of

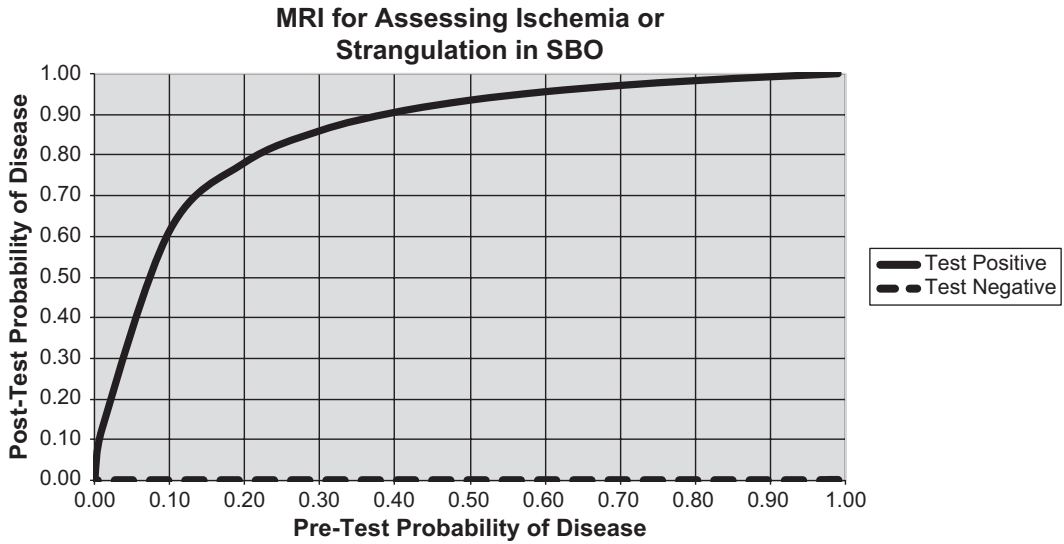


Fig. 22.6 MRI for assessing ischemia or strangulation in small bowel obstruction

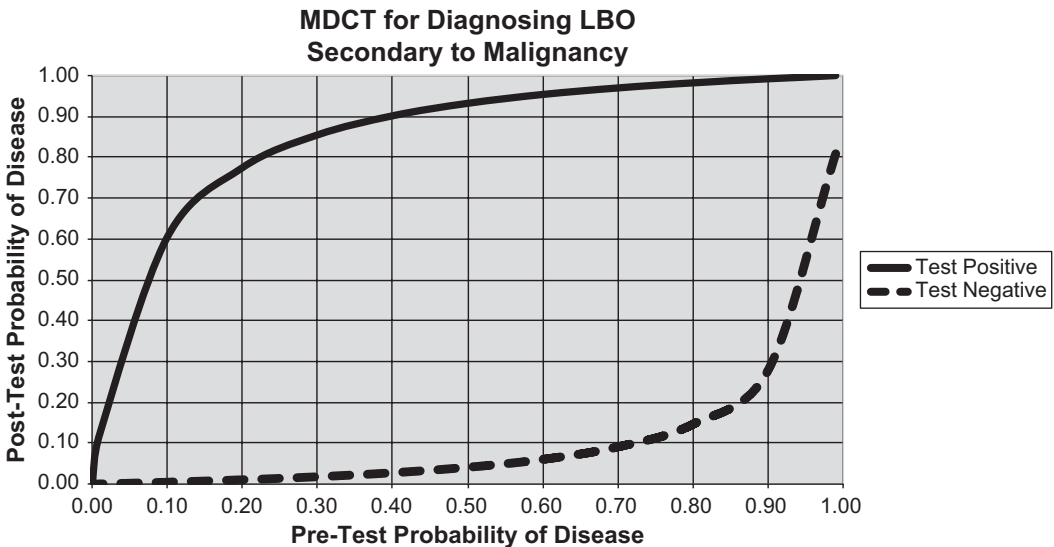


Fig. 22.7 MDCT for the detection of large bowel obstruction secondary to malignancy

93% in a large systematic review (Fig. 22.7) [13]. As in the case of SBO, several systematic reviews include studies on now-obsolete technology, which may underestimate the true sensitivity and specificity of modern MDCT scanners [13, 57]. MDCT with triplanar reformatting, higher spatial resolution and thinner collimation has greatly improved the diagnostic capabilities.

In the diagnosis of sigmoid volvulus, CT has been shown to have a sensitivity of 100% and a specificity of 100% in a retrospective review of 50 patients (Fig. 22.8b). The signs of sigmoid volvulus on CT include dilated sigmoid colon, air and fluid levels within proximal bowel loops and a whirl sign in the mesentery.

CT is useful in differentiating mechanical LBO from acute pseudo-obstruction and is supe-

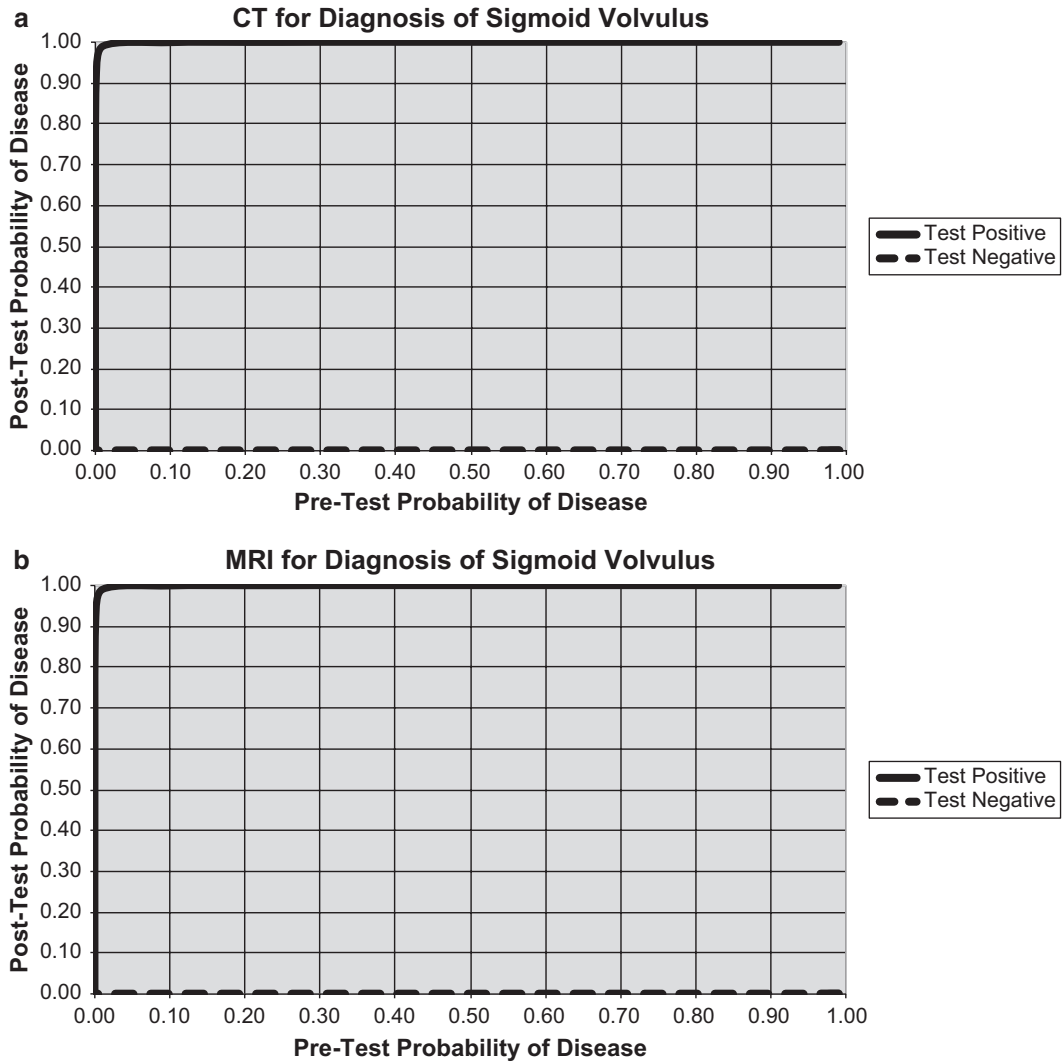


Fig. 22.8 (a) MDCT for the diagnosis of large bowel obstruction secondary to sigmoid volvulus. (b) MRI for the diagnosis of large bowel obstruction secondary to sigmoid volvulus

rior to water-soluble contrast enema in the detection of ischemia as a complication [15].

CT has the added advantage of locating the level and the cause of obstruction in the majority of patients and is accurate in staging the local and distant disease in the setting of malignancy. As such, when CT is available, it is recommended as the imaging modality of choice for the investigation of LBO [57].

Water-Soluble Contrast Enema

Water-soluble contrast enema is a useful tool in LBO and has been shown to have a sensitivity of 96% and a specificity of 98% and to be superior to radiographs in the diagnosis of LBO (Fig. 22.9) [58]. It is useful in making the diagnosis of LBO and determining the level of obstruction. It also determines if the obstruction is complete or partial.

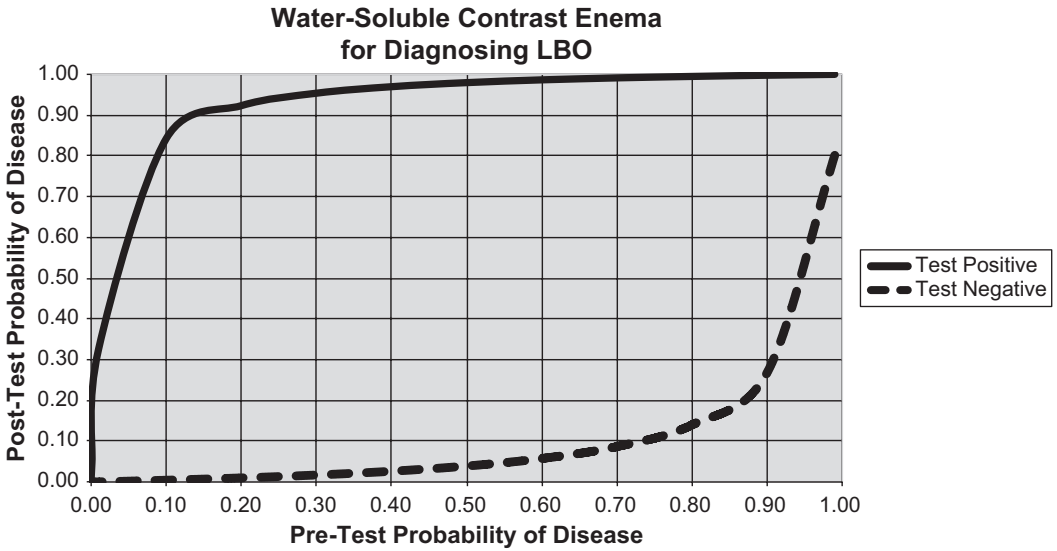


Fig. 22.9 Water-soluble contrast enema for diagnosing large bowel obstruction

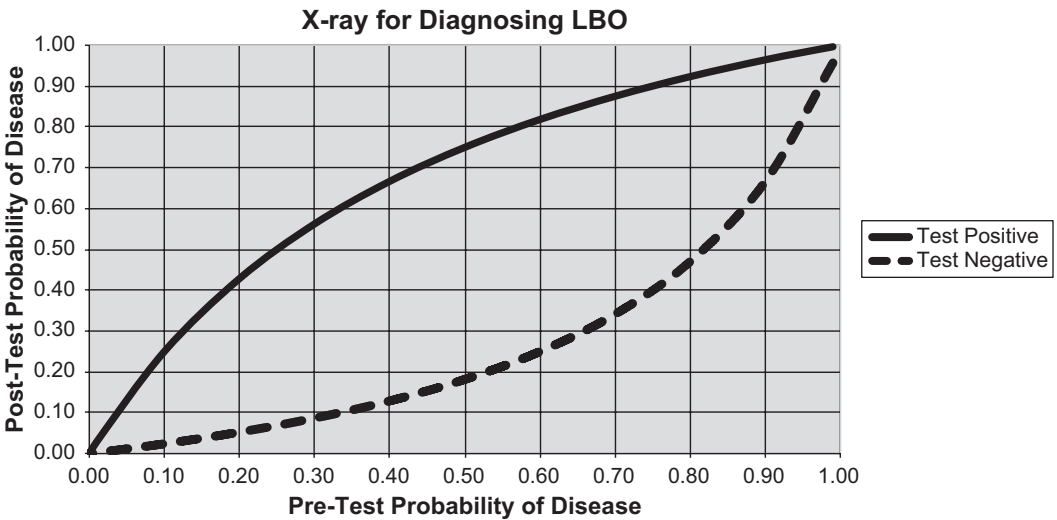


Fig. 22.10 Radiography for diagnosing large bowel obstruction

Water-soluble contrast enema can miss obstructing lesions if the obstruction is incomplete, leading to a misdiagnosis of pseudo-obstruction instead of malignancy. It does not provide information on the viability of the proximal obstructed bowel and therefore may miss associated ischemia [57]. Therefore, water-soluble contrast enema is better suited to use in large bowel volvulus and should not replace CT in the work-up

of LBO secondary to malignancy or if ischemia is suspected.

Radiography

While the low cost and ease of accessibility to radiography mean that it remains very often the first-line investigation for LBO, it is the least sensitive and specific of the modalities described for the diagnosis. Chapman et al. showed plain radio-

graph to have a sensitivity of 84% and specificity of 72% for the diagnosis of LBO when provided with the patient history (Fig. 22.10) [58].

and longer scan times. It is reserved for cases where CT is less desirable, such as in haemodynamically stable pregnant patients.

Magnetic Resonance Imaging

In a retrospective review of 34 patients with sigmoid volvulus, MRI has been shown to have 100% sensitivity and 100% specificity and, like CT, can demonstrate dilatation of the sigmoid colon, air and fluid levels in bowel loops and a whirl sign in the mesentery (Fig. 22.8b) [14]. MRI is rarely chosen over CT in the work-up of LBO due to its lack of availability, higher cost

Take-Home Tables and Figures

Tables

Tables 22.1 and 22.2 highlight and summarize the specificity and sensitivity of various imaging modalities for the detection and management of LBO and SBO.

Table 22.1 Imaging modalities to rule out SBO, for the detection of the level and cause, to predict if the patient should undergo nonoperative or operative management and to assess for associated bowel ischemia or strangulation in adults attending the emergency department

Imaging modalities to rule out SBO in adults attending the emergency department							
	Sensitivity	Specificity	PPV	NPV	Accuracy	+LR	-LR
MDCT	0.96 (0.80–1.00)	1.00 (0.69–1.00)			1.0	Infinity	0.04
US (radiologist’s interpretation)	0.90 (0.86–0.93)	0.96 (0.91–0.99)			0.87	14.1 (3.6–55.6)	0.13 (0.08–0.2)
US (ED physician interpretation)	0.97 (0.92–0.99)	0.90 (0.84–0.95)			0.81	9.5 (2.1–42.2)	0.04 (0.01–0.13)
Radiography	0.69–0.77	0.57–0.67			0.63	1.55 (1.10–2.19)	
MRI	Up to 0.95	Up to 1.00	1.00	0.80	1.00		

Imaging modality for the detection of the level and cause of SBO in adults							
	Sensitivity	Specificity	PPV	NPV	Accuracy	+LR	-LR
CT	0.93 (0.86–1.0)	0.67	0.98	0.33	0.65	2.79	0.11

Imaging modality to predict if the patient should undergo nonoperative or operative management								
	Sensitivity	Specificity	PPV	NPV	Accuracy	+LR	-LR	
WSCFT	0.97	0.96			0.87			
CT	1.00	0.46	0.43	1.00	0.59			
CT—with transition zone	1.00	0.23	0.35	1.00	0.53			
CT—with abnormal course of the mesenteric vessels at the transition zone	0.70	0.90	0.74	0.88	0.77			

Imaging modalities to assess for associated bowel ischemia or strangulation							
	Sensitivity	Specificity	PPV	NPV	Accuracy	+LR	-LR
CT	0.83 (0.63–1.00)	0.92 (0.61–1.00)	0.79 (0.69–1.00)	0.93 (0.33–1.00)	0.81		
MDCT	0.85	0.96–0.97	0.73–0.79	0.97–0.98	0.88		
MRI	1.00	0.93	0.83	1.00	0.84		

Numbers in parenthesis are 95% confidence intervals
 CT computed tomography, +LR positive likelihood ratio, -LR negative likelihood ratio, MDCT multiple-detector computed tomography, MRI magnetic resonance imaging, NPV negative predictive value, PPV positive predictive value, SBO small bowel obstruction, US ultrasound, WSCFT water-soluble contrast follow-through

Table 22.2 Imaging modalities for the detection of LBO and the diagnosis of the level and cause of LBO in adults

	Sensitivity	Specificity	PPV	NPV	Accuracy	+LR	-LR
CT	0.96	0.93			0.84		
CT—with sigmoid volvulus	1.00	1.00			1.00		
WSCE	0.96	0.98			0.90		
Radiography	0.84	0.72			0.66		
MRI with sigmoid volvulus	1.00	1.00			1.00		

Numbers in parenthesis are 95% confidence intervals

CT computed tomography, +LR positive likelihood ratio, -LR negative likelihood ratio, LBO large bowel obstruction, MDCT multiple-detector computed tomography, MRI magnetic resonance imaging, NPV negative predictive value, PPV positive predictive value, WSCE water-soluble contrast enema

Graph of Conditional Probability and Area Under the Curve

Figures 22.1–22.10 show graphs of conditional probability for the different imaging modalities in the different clinical scenarios. For assistance in interpreting these graphs, the x-axis represents the pre-test probability of the disease in question, and the y-axis represents the posttest probability. The pretest probability is chosen, and a vertical line is drawn from the corresponding point on the x-axis to the “test negative” or “test positive” curve. From this point of intersection, a horizontal line is drawn to the y-axis. The posttest probability is the value at the point where the horizontal line intersects the y-axis.

Figure 22.1a demonstrates that MDCT is a strong test for the diagnosis of SBO; most pretest probabilities result in a clinically useful (low or high) posttest probability whether the test is negative or positive. Figures 22.1b and 22.1c demonstrate that Ultrasound is a strong test for the diagnosis of SBO when carried out by a radiologist or a trained ED physician; most pretest probabilities result in a clinically useful (low or high) posttest probability whether the test is negative or positive. See Fig. 22.1b and Fig. 22.1c. Figure 22.1d demonstrates that a negative radiograph is a weak test for the diagnosis of SBO, as most pretest probabilities result in a high posttest probability of SBO. See Fig. 22.1d. Figure 22.1e demonstrates that MRI is a strong test for the diagnosis of SBO; most pretest probabilities result in a clinically useful (low or high) posttest probability whether the test is negative or positive. See Fig. 22.1e.

MDCT for detecting the level of obstruction in SBO is more reliable when negative than when positive. With a pretest probability of 0.50, a positive test is only correct 75% of the time, whereas a negative test is correct 90% of the time. See Fig. 22.2.

Figure 22.3 demonstrates that Water soluble contrast follow-through is a strong test for predicting the need for operative versus conservative management of SBO; most pretest probabilities result in a clinically useful (low or high) posttest probability whether the test is negative or positive. See Fig. 22.3.

MDCT is a poor test when positive but a good test when negative to predict management in the setting of complete SBO. See Fig. 22.4a. MDCT is a poor test when positive but a good test when negative to predict management in the setting of a transition zone. See Fig. 22.4b. MDCT is a moderate test in the setting of abnormal course of the mesenteric vessels for predicting management in SBO. See Fig. 22.4c.

MDCT is a strong test when positive in the setting of SBO with ischemia but less reliable when negative. See Fig. 22.5a. MDCT is a strong test when positive in the setting of SBO with ischemia but less reliable when negative. See Fig. 22.5b.

MRI is a strong test when positive and when negative for the diagnosis of ischemia or strangulation in SBO. See Fig. 22.6.

MDCT is a good test when positive and when negative in the setting of LBO secondary to malignancy. See Fig. 22.7.

Figure 22.8a demonstrates that MDCT is a strong test for the diagnosis of LBO secondary

to sigmoid volvulus; most pretest probabilities result in a clinically useful (low or high) posttest probability whether the test is negative or positive. See Fig. 22.8a. Figure 22.8b demonstrates that MRI is a strong test for the diagnosis of LBO secondary to sigmoid volvulus; most pretest probabilities result in a clinically useful (low or high) posttest probability whether the test is negative or positive. See Fig. 22.8b.

Water-soluble contrast enema is a good test when positive and when negative for the diagnosis of LBO. See Fig. 22.9.

Radiography is a weak test when positive and when negative for the diagnosis of LBO. See Fig. 22.10.

Algorithms

Figures 22.11, 22.12 and 22.13 highlight suggested clinical pathways for suspected small bowel obstruction in the Emergency Department (ED), conservative vs operative management of small bowel obstruction and suspected large bowel obstruction in the ED, respectively.

2. Ultrasound is a better test to “rule out” SBO in the ED, especially if the radiographs are considered negative.
3. Multidetector computed tomography (MDCT) is the gold standard investigation to diagnose SBO, determine the level and cause of SBO and to diagnose ischemia as a complication of SBO.
4. MRI has excellent diagnostic performance for the diagnosis of SBO, but due to its restricted availability and longer scanning times, it is usually reserved for use in stable pregnant patients and those with Crohn’s disease.
5. Water-soluble contrast follow-through is an excellent test to predict if adhesion-related SBO will resolve spontaneously or will require surgery, in suitable patients with no evidence of ischemia, hernia or carcinoma and who are more than 6 weeks post-surgery.
6. Patients with a suspected high-grade obstruction do not require oral contrast medium.
7. In LBO, MDCT is the investigation of choice to identify the level and cause of LBO.
8. In LBO, water-soluble contrast enema is the investigation of choice to determine if the obstruction is partial or complete.

Take-Home Points

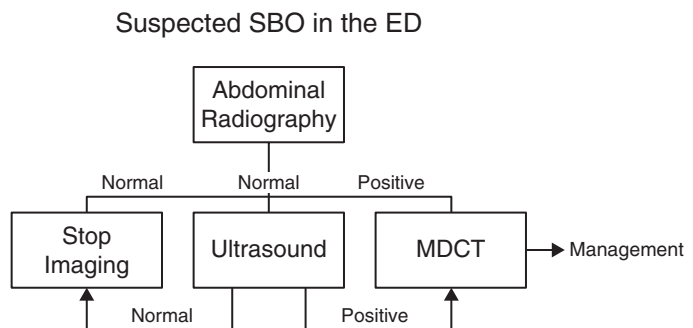
1. Radiography is an easily accessible, low-cost and low-radiation investigation to “rule in” SBO in the ED. However, the limitations of its use should be recognized by ordering physicians.

Imaging Case Studies

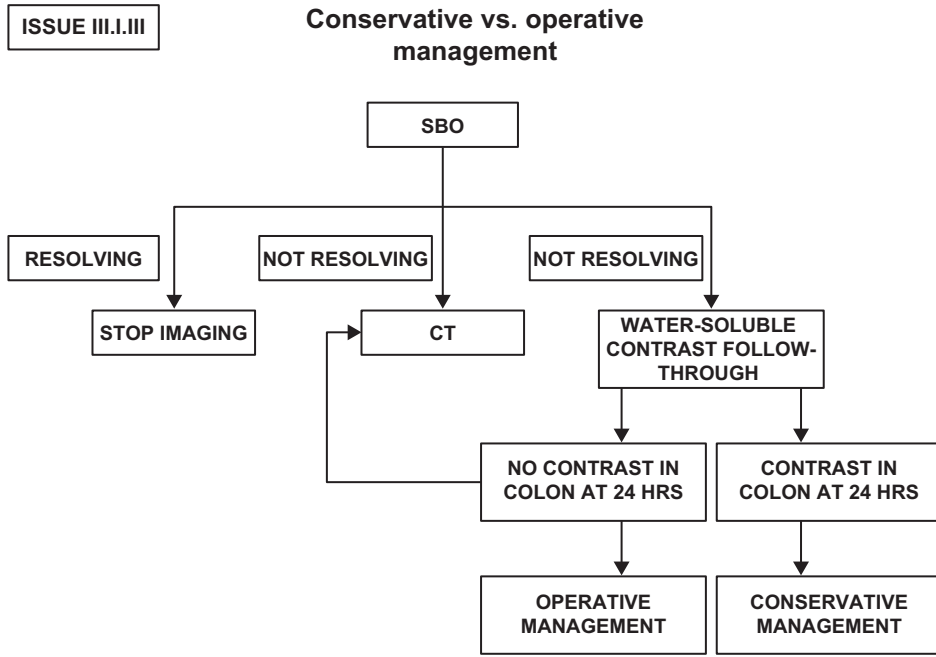
Case 1

Figure 22.14a–d focuses on a 37-year-old female, who presented acutely to the ED 5 days post shoulder surgery, with no bowel motions since

Fig. 22.11 Suspected small bowel obstruction in the emergency department



CT = Computed Tomography
 PFA = Abdominal Radiograph
 US = Ultrasound



CT = Computed Tomography
PFA = Abdominal Radiograph
SBO = Small Bowel Obstruction
US = Ultrasound

Fig. 22.12 Conservative versus operative management of small bowel obstruction

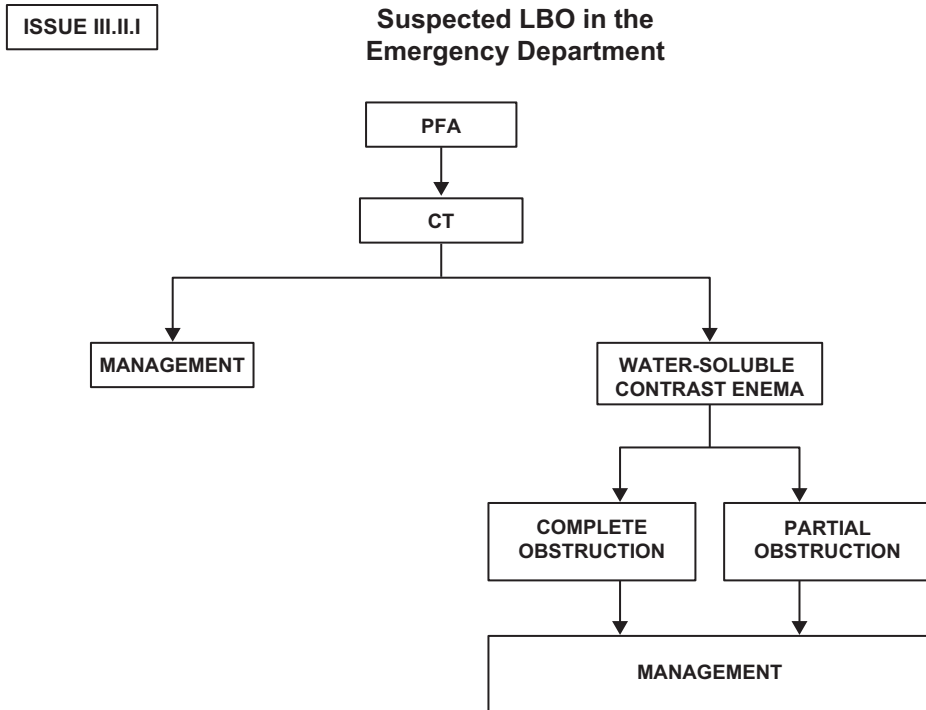


Fig. 22.13 Suspected large bowel obstruction in the emergency department

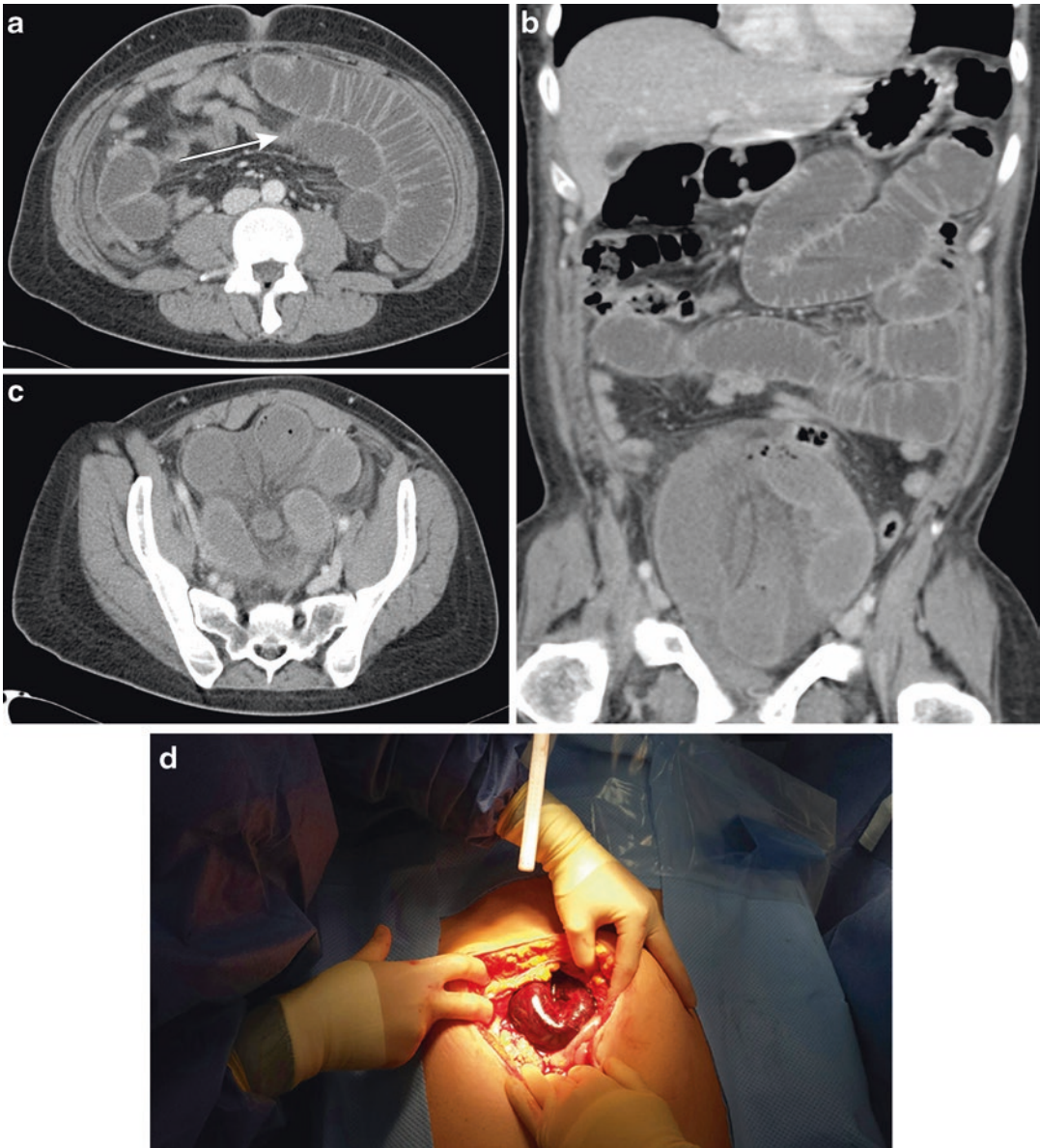


Fig. 22.14 A 37-year-old female, who presented acutely to the ED 5 days post shoulder surgery. No bowel motions since the surgery. Now vomiting with significant abdominal distension and diffuse severe abdominal tenderness. White cell count = 20.5, neutrophils = 16.9 and CRP = 359. (a) Axial MDCT image with intravenous contrast material enhancement showing dilated small bowel loops in the right flank and a transition zone (see *arrow*) to collapsed small bowel loops in the central abdomen. (b) Coronal MDCT image with intravenous contrast material enhancement only demonstrating acute SBO with poorly

enhancing bowel loops in the pelvis consistent with a closed loop obstruction, complicated by ischemia. (c) Axial MDCT with intravenous contrast material enhancement only in the same patient demonstrating acute SBO with abnormally twisted poorly enhancing small bowel loops in the pelvis consistent with an ischemic closed loop obstruction. (d) Ischemic closed loop obstruction at laparotomy in the same patient (With thanks to Ms. Ruth Pritchard and Ms. Niamh O'Farrell for this intraoperative photograph)

the surgery and with new vomiting, significant abdominal distension and diffuse severe abdominal tenderness.

White cell count = 20.5, neutrophils = 16.9 and CRP = 359.

Case 2

Figure 22.15a, b illustrates a 69-year-old female who presented to the ED with acute abdominal pain, distension and vomiting and had no previous abdominal surgery.

White cell count was 7.6 and CRP 2.4.

Case 3

Figure 22.16a, b focuses on a 61-year-old female with history of liver transplant who is presenting with acute onset abdominal pain associated with nausea and vomiting. She was observed on the floor for 3 days with persistent high output from NG tube and failure to pass flatus suggesting failure of conservative management.

Case 4

Figure 22.17a, b focuses on a 73-year-old male with history of radical cystoprostatectomy who presented to the ED with abdominal pain for 1 day. Patient had bowel motion in the morning before going to work. Patient had worsening pain and nausea and started with frequent emesis at work that day. CT scan of the abdomen/pelvis showed SBO with transition point at the ileal anastomosis. Patient was managed conservatively and was discharged home a couple of days later after he had a bowel movement.

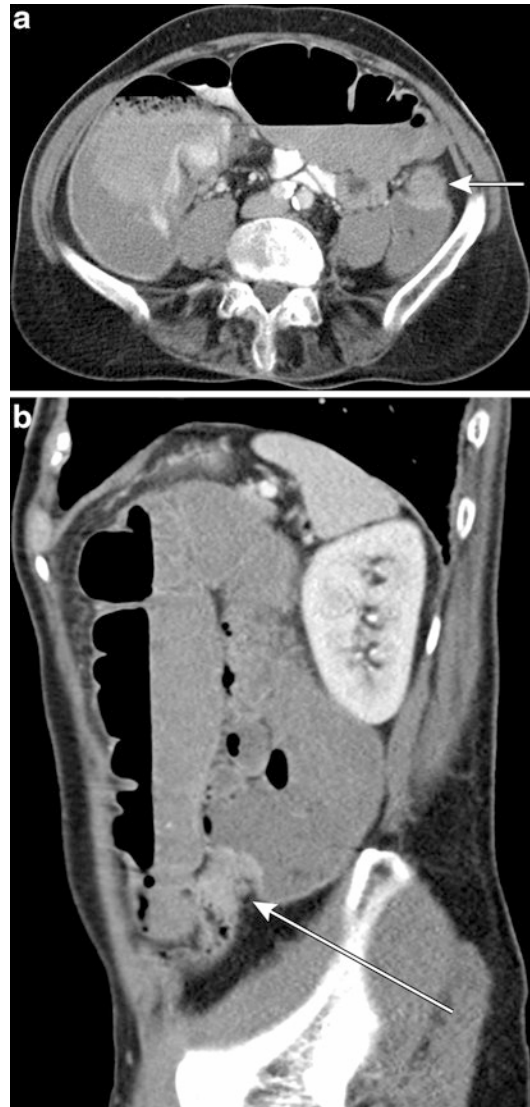


Fig. 22.15 A 69-year-old female who presented to the ED with acute abdominal pain, distension and vomiting. No previous abdominal surgery. White cell count 7.6 and CRP 2.4. (a) Axial MDCT with oral and intravenous contrast material enhancement showing dilated large bowel loops with air-fluid levels, consistent with acute LBO secondary to an obstructing tumour in the descending colon (see *arrow*). (b) Sagittal MDCT with oral and intravenous contrast material enhancement in the same patient showing acute LBO secondary to an obstructing apple core lesion in the descending colon (see *arrow*), which was confirmed to be a primary colonic tumour at laparotomy

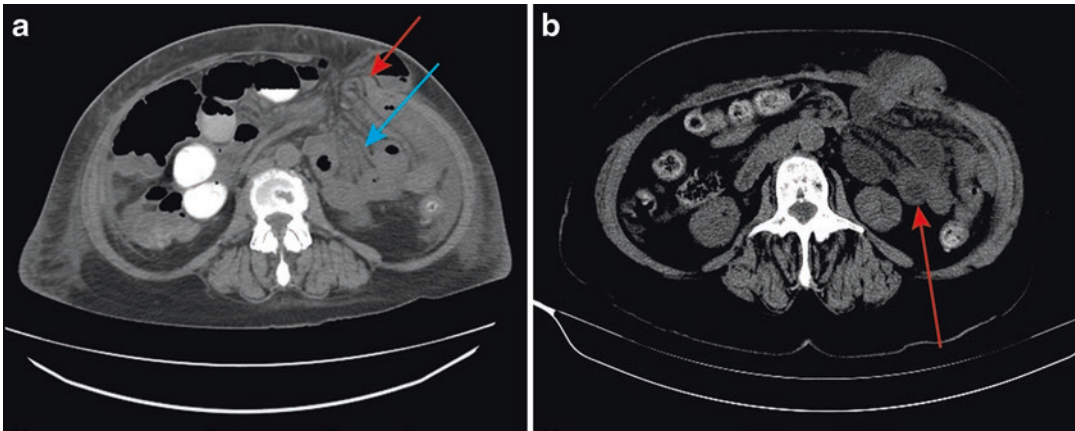


Fig. 22.16 A 61-year-old female with history of liver transplant presenting with acute onset abdominal pain associated with nausea and vomiting. She was observed on the floor for 3 days with persistent high output from NG tube and failure to pass flatus suggesting failure of conservative management. CT scan of the abdomen/pelvis without intravenous contrast material enhancement shows SBO with transition zone at the incisional hernia.

(a) Axial image show dilated loops of small bowel with associated mesenteric oedema (*blue arrow*). A beak sign (*red arrow*) can also be seen at the site of incisional hernia indicating location of transition zone. (b) Axial image shows thickening and hyperdense appearance of the bowel wall (*red arrow*) on the non-intravenous contrast-enhanced CT

Case 5

Figure 22.18a–c illustrates a 77-year-old male with history of prior laparotomy who presented with acute onset nausea, vomiting and abdominal pain. Patient was taken to the OR after the CT findings for an exploratory laparotomy. Intraoperative findings included small bowel obstruction secondary to an adhesive band which had caused small bowel volvulus.

Suggested Imaging Protocols

MDCT Technique

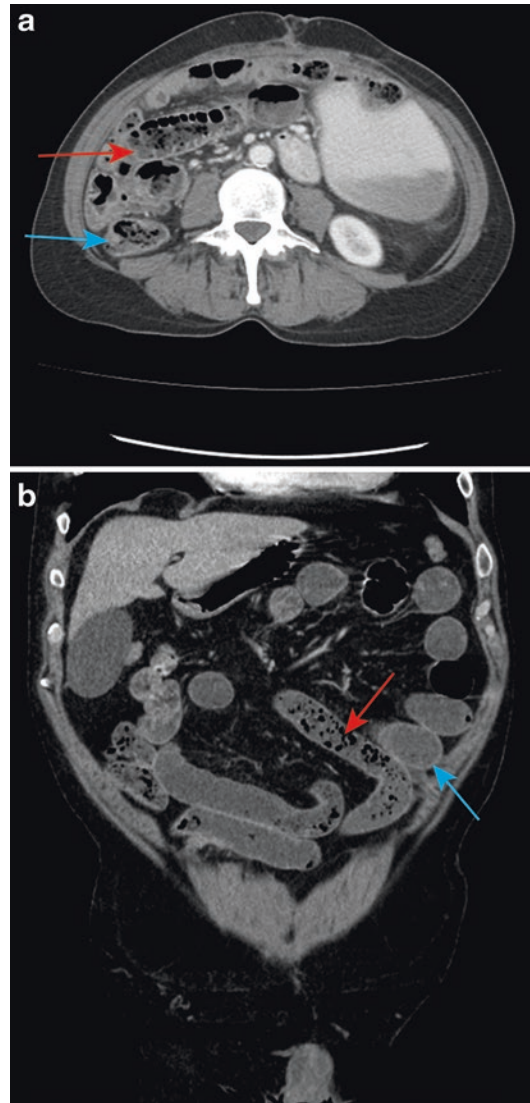
Optimal CT evaluation of patients with suspected or known SBO should ensure complete coverage of the gastrointestinal tract, starting above the diaphragm and extending to the bottom of the

pelvis (to include both the inguinal and femoral regions) in the supine position during a single breath-hold. A collimation of 0.6 mm is used.

Administration of intravenous contrast material is essential to assess the patency of the mesenteric vessels and to evaluate the bowel wall enhancement pattern (to identify potentially ischemic or necrotic bowel). Defining the mesenteric branches on a contrast-enhanced examination is also helpful to detect the presence of vascular engorgement or swirling that can be present in certain types of obstructions (e.g. volvulus) [3]. In patients presenting with acute symptoms, CT is most commonly performed as a single acquisition in the portal venous phase at 65–70 s after the start of an IV contrast injection (100–150 ml/s of 300–370 mg iodine/ml concentration) delivered at the rate of 2–4 ml/s [3].

The use of oral contrast is dependent on the individual patient. Generally in bowel obstruc-

Fig. 22.17 A 73-year-old male with history of radical cystoprostatectomy presented to ED with abdominal pain for 1 day. Patient had bowel motion in the morning before going to work. Patient had worsening pain and nausea and started with frequent emesis at work that day. CT scan of the abdomen/pelvis showed SBO with transition point at the ileal anastomosis. Patient was managed conservatively and was discharged home a couple of days later after he had a bowel movement. CT abdomen/pelvis with intravenous and oral contrast material enhancement shows a low-grade obstruction. Axial (**a**) and coronal (**b**) images show mildly dilated loops of bowel with segments containing faecalized stool (*red arrow*). Bowel wall enhancement (*blue arrow*) and lack of mesenteric oedema suggest adequate bowel perfusion



tion, the intraluminal fluid acts as its own contrast material, obviating the need for oral contrast. Positive oral contrast can be a disadvantage if it makes the patient vomit excessively with a risk of aspiration or if it obscures underlying bowel ischemia. However, in subacute bowel obstruction, water-soluble oral contrast medium can be useful to assess for complete or partial bowel obstruction by determining if the contrast passes beyond the transition zone or not. The radiograph can be assessed along with the clinical information to decide if oral contrast medium should be used for an individual patient. Data reconstruction is performed using a smooth

body kernel and 1 mm slice thickness. Multiplanar reformats are useful to improve diagnostic performance [8, 28].

Future Research

More research is needed into the role of ultrasound as an adjunct to radiography in the ED and as an alternative to MDCT for the investigation of suspected uncomplicated SBO. If proven to be a safe alternative, the use of ultrasound in appropriate patients may reduce unnecessary radiation exposure.

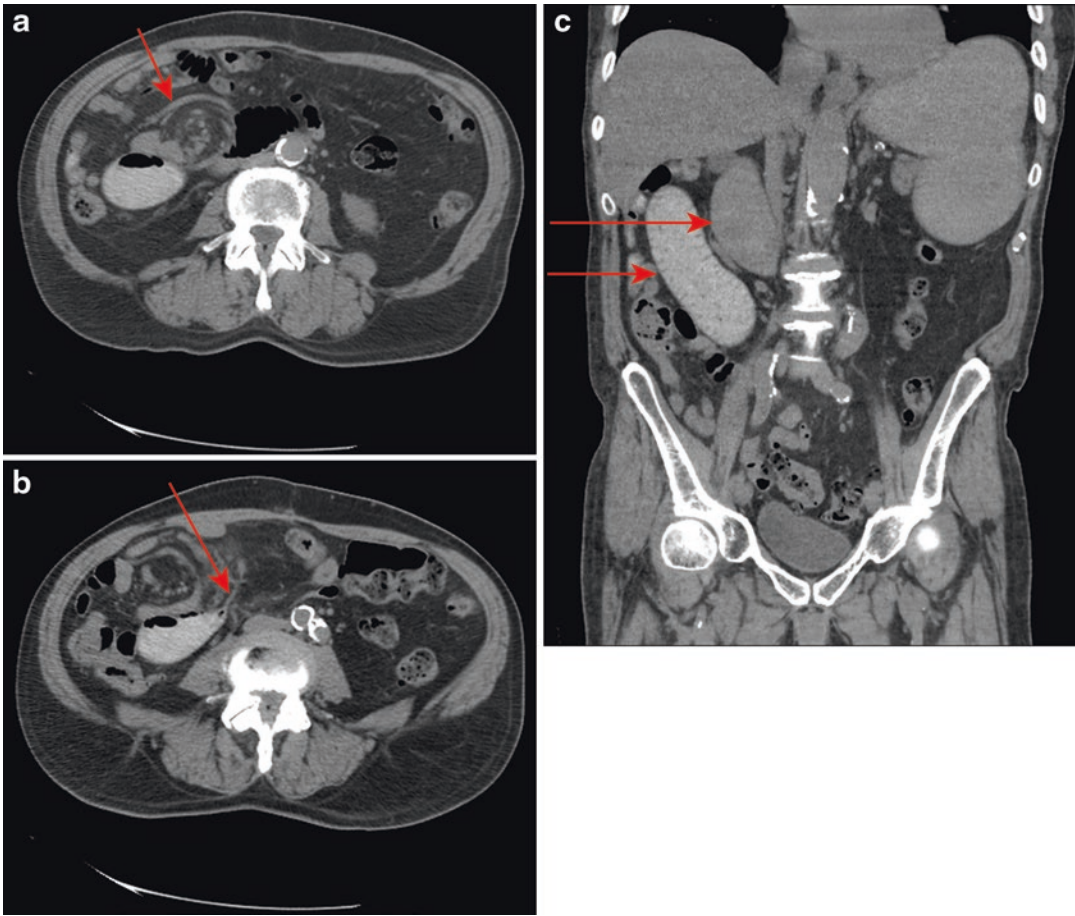


Fig. 22.18 CT scan of the abdomen/pelvis with oral contrast material enhancement. (a) Axial—dilated segment of proximal small bowel and classic swirl sign (red arrow).

(b) Axial—shows a beak sign at the transition zone (red arrow). (c) Coronal—shows dilated loops of small bowel confined to the right abdomen (red arrows)

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Acute Gastrointestinal Bleeding in Adults and Children: Evidence-Based Emergency Imaging

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Key Points

- Computed tomography (CT) angiography has high diagnostic performance in the setting of acute lower gastrointestinal (GI) hemorrhage (strong evidence). CT angiography should be performed prior to catheter angiography where possible as it increases the likelihood of successful angiographic localization of bleeding (moderate evidence). CT angiography may be superior to colonoscopy as the initial investigation/evaluation in acute lower GI bleeding, but further studies are required to support this (limited evidence).

- Superselective microcoil embolization is a safe and effective treatment for acute lower GI bleeding (moderate evidence). CT angiography should be performed prior to embolization where possible (moderate evidence). A randomized study comparing colonoscopy with CT angiography and embolization has not been performed.
- Endoscopy is currently accepted as the first-line investigation in upper GI bleeding. CT angiography is the imaging modality of choice in cases where endoscopy has failed to localize or control the bleeding (strong evidence). It has been proposed that CT angiography may be useful as a first-line investigation prior to endoscopy, but more research is required to support this claim (limited evidence).
- Superselective microcoil embolization is the initial treatment of choice in acute non-variceal upper GI bleeding refractory to endoscopic management and has been shown to have a lower 30-day mortality rate when compared with surgery (moderate evidence). In acute variceal upper GI bleeding, emergent transjugular intrahepatic portosystemic shunt (TIPSS) formation may control hemorrhage in cases refractory to endoscopic management (moderate evidence).

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Definitions and Pathophysiology

This chapter focuses on the radiological investigation and management of acute hemorrhage originating in the upper and lower GI tracts. As the radiologist plays a central role not only in the investigation but the treatment of GI bleeding (often during the same procedure by means of catheter angiography and embolization), both subjects are addressed. Upper gastrointestinal bleeding is defined as originating proximal to the ligament of Treitz, with lower gastrointestinal bleeding arising distally. Upper GI bleeding accounts for approximately 76% of cases [1]. Causes of upper GI bleeding include duodenal ulcers (24%), gastric erosions (23%), varices (10%), Mallory-Weiss tears (7%), esophagitis (6%), duodenitis (6%), neoplasia (3%), and esophageal ulcers (2%) [2, 3]. Common causes of lower GI bleeding are diverticular hemorrhage (42%), colorectal malignancy (9%), and ischemic colitis (9%) [4]. Other less frequent causes include vascular ectasia, Crohn's ileitis, Meckel's diverticula, and small bowel tumors [5]. Risk factors associated with an increased risk of gastrointestinal hemorrhage include age, aspirin, nonsteroidal anti-inflammatories, selective serotonin reuptake inhibitors, warfarin, and chronic liver disease [2, 3, 5–7].

Epidemiology

The estimated annual incidence of upper GI bleeding in the United States in 2009 was 66.0/100,000, a decrease from 78.4/100,000 in 2001 [8]. Bleeding ascribed to gastroduodenal ulcers or gastritis/duodenitis decreased by more than one third between 2001 and 2009, with a decrease in the prevalence of *Helicobacter pylori* and an increase in the use of acid-suppressing medications proposed as potential explanations [8]. The mortality rate in 2009 for cases of upper GI bleeding was 2.95%. The incidence of lower GI bleeding in 2009 was estimated at 25.7/100,000 in 2009 compared with 41.8/100,000 in 2001, with a case fatality rate of 1.93%. Both upper and lower GI bleeding have

a significantly higher incidence in patients aged over 75 [8].

Overall Cost to Society

The estimated annual cost of upper GI bleeding in the United States has been estimated to be \$2.5 billion, with 300,000 hospital admissions every year [9]. The annualized US healthcare costs for a patient with an upper GI bleeding event have been estimated to be \$20,405 [9]. While no formal estimates for the annual cost of lower GI bleeding in the United States are available, the cost of diverticular hemorrhage, the most common cause of lower gastrointestinal hemorrhage, was estimated to be \$1.3 billion in 2001 [10].

Goals of Imaging

The primary goal of imaging in patients presenting with acute gastrointestinal bleeding is to correctly identify the site and cause of bleeding and to triage the patient to the correct management pathway, whether that be endoscopy, catheter angiography and embolization, surgery, or conservative management.

Methodology

A comprehensive MEDLINE search (US National Library of Medicine database) for original articles published between 1995 and 2015 using the PubMed search engine was performed using a combination of the following MeSH headings: *Gastrointestinal Hemorrhage; Tomography, X-Ray Computed; Nuclear Medicine; Radiopharmaceuticals; Angiography; Angiography, Digital Subtraction; Embolization, Therapeutic; Adolescent; Infant; Child; Pediatrics; Costs and Cost Analysis; and Epidemiology*. The abstracts were reviewed and selected on the basis of relevance and methodology. Additional relevant articles were identified from the references of the reviewed articles and by use of the reverse citation trail [11].

Discussion of Issues

What Is the Most Appropriate Imaging Modality for the Diagnosis of Acute Lower GI Bleeding?

Summary of Evidence Computed tomography angiography (CTA) has high diagnostic performance for detecting and localizing lower gastrointestinal hemorrhage (strong evidence). It is superior to technetium-99m-labeled red blood cell scintigraphy for accurately localizing the source of bleeding (moderate evidence). Performing CTA prior to catheter angiography improves localization of the bleeding site compared with catheter angiography alone (moderate evidence) suggesting CTA should be performed if catheter angiography is being considered, where clinical circumstances permit. One small prospective study found CTA to be more sensitive and specific than colonoscopy (limited evidence) [12] suggesting it may be useful as the initial test in lower GI bleeding; further data is required to substantiate this.

Supporting Evidence

CT Angiography

The role of imaging in the patient presenting acutely with lower gastrointestinal bleeding is to identify the site and source of bleeding and to triage the patient to the appropriate management pathway. Endoscopy has long been the initial test of choice, and current guidelines from the American Society of Gastrointestinal Endoscopy and the Scottish Intercollegiate Guidelines Network continue to recommend upper and lower GI endoscopy as the first investigations in patients presenting with hematochezia, with radiological investigations reserved for those in whom endoscopy fails to identify or control the source of bleeding [13, 14]. However in the setting of active large-volume bleeding, colonoscopy can be challenging, and its ability to treat the cause of bleeding may be limited [15]. For this reason, the American College of Radiologists Appropriateness Criteria on lower GI bleeding suggest catheter angiography is more appropriate

than colonoscopy in the unstable patient with lower GI bleeding, although CT is still deemed second line [16]. Similarly, guidelines from the American College of Gastroenterology suggest that angiography may be more appropriate than colonoscopy in severe active bleeding [17]. Recent developments in multi-detector CT technology and its widespread dissemination have led to increased interest in its role in the setting of acute lower GI bleeding, both in patients failing endoscopic management and also as a potential first-line investigation [12].

A meta-analysis and systematic review of 22 studies published in 2012 by Garcia-Blazquez et al. found CT angiography to have high diagnostic performance in detecting and localizing acute gastrointestinal bleeding (both upper and lower) with an overall sensitivity of 85.2% (95% confidence interval 75.5%–91.5%), overall specificity of 92.1% (95% confidence interval 76.7%–97.7%), likelihood ratio for a positive test result of 10.8 (95% confidence interval 3.4–33.4), likelihood ratio for a negative test result of 0.16 (95% confidence interval 0.1–0.027), and an area under the curve (AUC) of 0.935 (95% confidence interval 0.693–0.989) (strong evidence) [18]. These high sensitivity and specificity values were replicated in two earlier systematic reviews of the diagnostic performance of CT angiography published in 2008 and 2010 [19, 20]. The studies included in these three systematic reviews demonstrate somewhat variable methodological quality with a minority being prospective in design, and they show significant differences in the reference standards used [21–37]. The majority of the primary studies in these meta-analyses utilized multi-detector CT technology with a minority utilizing single-detector technology.

CTA has previously been shown to be capable of detecting bleeding rates of as little as 0.3 ml/min [38], compared with 0.1 ml/min for radionuclide scans [39] and 1 ml/min for first-order aortic branch-selective digital subtraction angiography [40]. While CTA may be less sensitive for slow active bleeding than radionuclide scanning, it has significant advantages when it comes to availability and speed of imaging, and it also performs superiorly at correctly localizing the

bleeding source. A 2015 study comparing CTA and technetium-99m red blood cell (RBC) scintigraphy prior to catheter angiography found that although CTA and RBC scintigraphy had similar sensitivity and specificity, localization of the bleeding site was more precise and consistent with CTA (moderate evidence) [41]. The same study showed that performing CTA prior to catheter angiography improved localization of the bleeding site when compared with catheter angiography alone. These findings suggest CTA should be performed prior to catheter angiography where possible.

In addition, a retrospective review published in 2015 by Chan et al. showed that of 115 patients undergoing urgent CTA for lower GI bleeding, 77% of patients with a negative CTA did not rebleed [42] and a negative CTA may therefore be useful for identifying those that will not need emergent intervention (moderate evidence). A small retrospective review of 20 patients published in 2010 showed that of ten patients with a negative CTA, only one required intervention to secure hemostasis, and a positive CTA allowed patients to be triaged to either catheter angiography or surgery (limited evidence) [43]. CT angiography may therefore be a useful tool in deciding which patients are likely to respond to endovascular management.

A study of 29 patients with acute non-variceal GI bleeding (11 upper and 18 lower) compared the diagnostic performance of endoscopy and CTA [12]. Although limited by small patient numbers, the study showed CT to be more sensitive and specific than endoscopy in identifying the site and cause of bleeding (limited evidence). The authors propose CTA as a first-line test (prior to endoscopy) in patients with GI bleeding; however, further well-designed prospective studies comparing CTA and endoscopy as initial investigations in acute lower GI bleeding are required.

The literature on the imaging of GI bleeding in children is scarce; however, there has been recent interest in the utility of CT angiography in the pediatric population. A review of 27 infants and children with lower GI bleeding found that arterial phase CT imaging identified the source of bleeding in 20 cases [44]. A small case series

in 2013 described two cases of lower GI bleeding in children with causes successfully diagnosed by CT angiography [45]. While there may be a role for CTA in children with acute lower GI bleeding, further investigation is required (limited evidence).

Nuclear Medicine

Prior to the advent of CT angiography, technetium-99m-labeled red blood cell scintigraphy had been considered (along with catheter angiography) a first-line imaging test in those patients for whom endoscopy failed to identify a source of acute lower GI bleeding. The primary advantage of RBC scintigraphy is its ability to detect active bleeding rates as low as 0.1 ml/min [39], making it more sensitive to slow rates of bleeding than CT angiography and catheter angiography, which can detect bleeding at rates of 0.3 ml/min and 1 ml/min respectively [38, 40]. Technetium-99m-labeled RBC scintigraphy has been shown to be superior to technetium-99m-labeled sulfur colloid and is considered the radiopharmaceutical of choice [46].

The reported sensitivities of RBC scintigraphy for the detection of active GI bleeding vary widely, ranging from 23 to 83% (limited evidence) [46–51]. These values are based on retrospective studies using a variety of reference standards including endoscopy, angiography, and surgery. Technetium-99m RBC scans are more likely to be positive in hemodynamically unstable patients, with one study showing 62% of studies to be positive in unstable patients versus 21% in stable patients [52]. In the emergency setting, the availability of RBC scintigraphy in most institutions is limited when compared with that of CTA.

Significantly, RBC scintigraphy performs poorly when localizing the site of bleeding. A review of 162 patients undergoing RBC scans showed accurate localization of the site of bleeding in only 52% of cases (moderate evidence) [49]. Four similar smaller studies showed that RBC scintigraphy incorrectly localized the site of bleeding in 48–83% of patients [48, 53–55]. In one retrospective study of 80 patients undergoing single-photon emission computed tomography

(SPECT)-enhanced RBC scintigraphy, there were 8 false positives leading to 5 inappropriate operations [56]. A retrospective study comparing CTA and nuclear scintigraphy prior to catheter angiography found similar sensitivity and specificity between the two studies, but CTA was superior in correctly identifying the site of bleeding (moderate evidence) [41]. A prospective study performed in 2008 comparing contrast-enhanced multi-detector CT and technetium-99m RBC scintigraphy showed CT to be effective for the detection and localization of active lower GI bleeding and further showed significant disagreement between the CT and RBC scintigraphic findings (moderate evidence) [57]. Thus in the acute setting, CT is preferred over RBC scintigraphy in the imaging of lower GI bleeding.

The literature examining the role of nuclear scintigraphy in children with lower GI bleeding mainly relates to technetium-99m pertechnetate imaging for the detection of ectopic gastric mucosa in Meckel's diverticula. A systematic review of 40 such studies found technetium-99m pertechnetate imaging to have a sensitivity of 92%, specificity of 95%, positive likelihood ratio of 16.5, negative likelihood ratio of 0.15, and diagnostic odds ratio of 120.7 (strong evidence) [58]. A review of technetium-99m RBC scintigraphy in 22 children presenting with acute lower GI bleeding found it to be a sensitive but nonspecific method for detecting the bleeding source (moderate evidence) [59]. Further evidence is required to more accurately define the role of technetium-99m RBC scintigraphy in these patients.

Catheter Angiography

CT angiography has largely supplanted catheter angiography in the imaging of acute lower GI bleeding, with catheter angiography usually reserved for cases where there is intent to treat. A significant disadvantage of catheter angiography is the invasive nature of the procedure, in contrast to CTA and RBC scintigraphy. An *in vitro* study comparing CTA and catheter angiography found CTA to be more sensitive for the detection of slow rates of bleeding than first-order aortic branch-selective digital subtraction angiography [40]. Significant active bleeding

may need to be present in order to be detectable by catheter angiography. A 2013 retrospective study showed that in 33 patients in whom CTA identified active extravasation, only 27% of the subsequent catheter angiograms were positive (limited evidence) [60]. Similarly, another 2013 retrospective study showed that only 24% of catheter angiograms were positive following a positive technetium-99m-labeled RBC scan (moderate evidence) [61]. A 1993 study evaluating the role of angiography found that in 49 patients with a history of overt non-variceal GI bleeding, 29 yielded true positive results with 16 being false negatives giving a sensitivity value of 64% [62] although note should be made of the fact that this group contained some patients with subacute presentations (limited evidence). Factors shown to increase the likelihood of a positive angiogram include hemodynamic instability, a transfusion requirement of 5 units of red blood cells or more, a hemoglobin drop of 5 g/dL or more, and a hemoglobin level of 10 g/dL or less [60, 63, 64]. Given the challenges of performing colonoscopy in unstable patients with active bleeding [15], and the increased likelihood of a positive angiogram in these cases, the American College of Radiology (ACR) Appropriateness Criteria currently recommend angiography over colonoscopy as the initial investigation of choice in unstable lower GI bleeding (insufficient evidence) [65].

A negative catheter angiogram appears to predict a low risk of rebleeding although the risk of a recurrent massive hemorrhage remains. A study that followed 75 patients for an average of 8 months after negative angiograms found that rebleeding occurred in 12 patients (16%) and in 6 of these patients (8%); this rebleeding resulted in death within 4–9 h [66]. Provocative angiography using anticoagulants and fibrinolytics has yielded some success in cases of occult GI lower bleeding [67–69] although it has largely been replaced by newer techniques such as capsule endoscopy, CT enterography and MR enterography.

Catheter angiography is not frequently used as a primary diagnostic modality in children presenting with lower GI bleeding, and the evidence relating to its utility is limited. A review of 27

such cases utilizing catheter angiography published in 1984 found that a correct diagnosis was made in 64% of patients and 36% of results were false negatives (limited evidence) [70]. Noninvasive imaging methods, particularly CT angiography, mean that the performance of diagnostic catheter angiography is now rarely undertaken, except in those cases where treatment with embolization is intended.

What Is the Most Appropriate Approach to the Radiological Management of Acute Lower GI Bleeding?

Summary of Evidence Numerous retrospective studies demonstrate the efficacy and safety of superselective microcoil embolization as a treatment in acute lower GI bleeding (moderate evidence). One randomized trial showed technetium-99m RBC scintigraphy followed by catheter angiography to be inferior to colonoscopy in localizing bleeding without a significant difference in outcomes, although intra-arterial vasopressin was used as treatment rather than superselective microcoil embolization (limited evidence) [71]. Performing CTA prior to catheter angiography has been shown to increase the ability to successfully localize the bleeding source at angiography (moderate evidence) [41]. CTA should therefore be performed prior to catheter angiography where clinical circumstances permit. Based on the current evidence, the most appropriate approach to the radiological management of acute lower GI bleeding is CTA followed by embolization when bleeding is identified.

Supporting Evidence A 2005 randomized controlled trial by Green et al. comparing urgent colonoscopy with standard care (technetium-99m RBC scintigraphy which if positive was followed by catheter angiography and subsequent expectant colonoscopy) in acute lower GI bleeding found no significant difference in patient outcomes, although a definitive source of bleeding was identified more often in the urgent colonoscopy group than in the standard care group

(42% vs. 22%) [71]. This study appeared to demonstrate the superiority of colonoscopy over radiological management; however, of note superselective microcoil embolization was not performed, with a nonselective infusion of vasopressin being utilized as the transcatheter treatment (limited evidence). The widespread adoption of CTA as the imaging test of choice in acute lower GI bleeding means that the site of bleeding is now frequently known to the operator prior to commencing the angiographic procedure, thus increasing the likelihood of successful targeting of the bleeding vessel. A 2015 study showed that performing CTA prior to catheter angiography improves the localization of the source of bleeding when compared with catheter angiography alone (moderate evidence) [41]. Chang et al. showed that visualization of contrast extravasation at angiography allows targeting of the bleeding vessel directly leading to higher success rates (moderate evidence) [72]. This suggests that identifying the bleeding vessel on CTA may allow more accurate targeting at the time of embolization and higher success rates. A small retrospective review of 20 patients found that a negative CTA was associated with spontaneous cessation of bleeding, while a positive CTA allowed patients to be triaged to catheter angiography or surgery (limited evidence) [43]. For these reasons, where possible, it is suggested that CTA should be performed prior to proceeding to catheter angiography. While the previously referenced 2005 randomized controlled trial by Green et al. found colonoscopy to be superior to standard radiological investigation (nuclear scintigraphy and angiography) in localizing bleeding, CTA offers significant advantages over nuclear scintigraphy in this respect. In an ideal world, a randomized study comparing colonoscopy with CTA followed by catheter angiography would be of use, but in practice such a study is unlikely to take place.

In the hemodynamically unstable patient with active bleeding and high blood transfusion requirements, the likelihood of a positive catheter angiogram is increased [60, 63, 64] and it may be reasonable to proceed directly to angiography without a preceding CT. As previously noted, the

ACR Appropriateness Criteria on Radiological Management of Lower GI Bleeding recommend catheter angiography as the most appropriate initial intervention in these circumstances, relegating colonoscopy and CT to second line (insufficient evidence) [65], although modern multi-detector CT can be performed emergently even in the setting of hemodynamic instability.

Superselective microcoil embolization has gained widespread acceptance as a treatment of lower GI bleeding. A large number of retrospective reviews have been performed demonstrating its safety and efficacy, with reported technical success rates ranging from 73 to 100%, clinical success rates ranging from 63 to 96%, and rebleeding rates ranging from 11 to 50% (moderate evidence) [16, 61, 73–97]. Most series report ischemic complications in 3% or less of cases. Some small series have demonstrated good technical success rates with transcatheter embolization using *N*-butyl-2-cyanoacrylate (limited evidence) [98, 99]. One small recent patient cohort study found transcatheter pharmacologically induced vasospasm using epinephrine followed by vasopressin to be safe and effective in inducing hemostasis, although the exact circumstances in which this would be preferred to microcoil embolization have not yet been clarified (limited evidence) [100].

Rebleeding rates after superselective microcoil embolization are higher in the small bowel than the large bowel, probably due to its richer vascular supply (limited evidence) [97]. A meta-analysis of six series showed the rates of rebleeding to be lowest in diverticular hemorrhage, occurring in 15%, with rebleeding seen in 40% of patients with non-diverticular sources (limited evidence) [101]. Malignancy has been found to be a risk factor for rebleeding (limited evidence) [102], and one study examining tumor sources of GI bleeding demonstrated a 68% short-term success rate following embolization without any ischemic complications [103]. Studies comparing arterial embolization with surgery have not been performed. Similarly lacking are cost-effectiveness analyses comparing colonoscopy, arterial embolization and surgery in the management of acute lower GI bleeding.

What Is the Most Appropriate Imaging Modality for the Diagnosis of Acute Upper GI Bleeding Refractory to Endoscopic Treatment?

Summary of Evidence Endoscopy is currently accepted as the first-line investigation in patients presenting with acute upper GI bleeding. CTA has high diagnostic performance in identifying sources of both upper and lower GI bleeding (strong evidence) and should be performed in cases where endoscopy failed to localize or control the bleeding. One study examining the role of CTA prior to endoscopy showed that it inconsistently identified the source of bleeding but significantly shortened endoscopic procedure times (limited evidence). Further data is required before it can be recommended that CTA be performed before endoscopy. Technetium-99m RBC scintigraphy performs poorly at localizing bleeding in the upper GI tract and has no place in the diagnostic algorithm (limited evidence).

Supporting Evidence

CT Angiography

Upper GI endoscopy remains the initial investigation of choice in the presentation of acute upper GI bleeding due to its ability to provide both a diagnosis and a means of treatment. Current guidelines from the National Institute of Clinical Excellence, American Society for Gastrointestinal Endoscopy, American College of Gastroenterology, American College of Radiology, Annals of Internal Medicine Clinical Guidelines, and Scottish Intercollegiate Guidelines Network continue to recommend endoscopy as the first-line investigation [14, 104–108]. Endoscopy has previously been demonstrated to be an effective intervention with a meta-analysis of 30 studies finding a clinically important reduction in morbidity and mortality in patients with acute non-variceal upper GI hemorrhage (strong evidence) [109]. The current role of imaging in the acute setting is in those patients for whom endoscopy has failed to identify or control the bleeding source. In acute non-variceal bleeding, options for imaging are CT angiography and nuclear scintigraphy. Catheter angiography

may be utilized in those cases where embolization is intended.

In the emergency setting, the objective of CT angiography following failed endoscopy is to identify the source of bleeding and to triage the patient toward further management. CTA has been shown to be effective in detecting and localizing active bleeding in the gastrointestinal tract. While initially investigated in acute lower GI bleeding, studies examining the technique have since been performed including cases of both upper and lower GI bleeding. In a meta-analysis and systematic review of 22 studies examining CTA in GI bleeding, 12 studies included patients with upper or lower GI bleeding, while 10 dealt with lower GI bleeding alone (none of the studies addressed upper GI bleeding alone) [18]. This systematic review yielded sensitivity and specificity values for CTA of 85.2% and 92.1%, respectively, and likelihood ratios for positive and negative test results of 10.8 and 0.16, respectively. Similarly high sensitivity and specificity rates for CTA were found in two earlier systematic reviews [19, 20]. CT angiography can be considered to have high diagnostic performance in detecting and localizing active upper and lower gastrointestinal hemorrhage (strong evidence).

Due to its high diagnostic performance, CTA has been proposed as a potential first-line investigation prior to endoscopy in acute upper GI bleeding. A retrospective study found that a negative CTA in acute upper GI bleeding may be falsely reassuring; Chan et al. found that in 63 patients with a negative CTA in acute upper GI bleeding, 26 patients (41%) went on to rebleed with 24 of these requiring embolization or surgery (moderate evidence) [42]. A 2014 retrospective study of 577 patients who underwent urgent endoscopy for acute upper GI bleeding compared outcomes in those who were first investigated with CT and those who were not [110]. In endoscopy-confirmed non-variceal bleeding, contrast-enhanced CT identified the source of bleeding in 55% of cases. The proposed reason for this apparently low rate of detection was the inclusion of cases with slowly bleeding lesions including esophagitis, angioectasia, and shallow ulcers. Also of note is the fact that the CT images

were interpreted by endoscopists rather than radiologists. The average procedure time to endoscopic detection of the bleeding source was significantly shorter in the contrast-enhanced CT group. CT may therefore play a role as the initial test prior to endoscopy and may reasonably be requested by an endoscopist prior to endoscopy (limited evidence). A negative CTA should not prevent or delay endoscopy in these circumstances.

Studies in acute lower GI bleeding have found that performing CTA prior to catheter angiography can increase the likelihood of successfully identifying and treating the bleeding source [41, 72]. While it is now a common practice to obtain a CT angiogram prior to angiographic intervention in upper GI bleeding refractory to endoscopic treatment as part of treatment planning, there is no supporting evidence other than that extrapolated from lower GI bleeding data (insufficient evidence).

Endoscopy is the mainstay of diagnosis and treatment in patients with acute variceal upper GI bleeding [111]. CT is useful acutely in patients with refractory bleeding to assess for portal vein patency and as part of treatment planning prior to transjugular intrahepatic portosystemic shunt (TIPSS) formation or balloon-occluded retrograde transvenous obliteration (BRTO) of gastric varices [112].

Special consideration should be given to upper GI bleeding in the context of hemobilia, recent ERCP, hepatobiliary surgery, or pancreatitis. In these settings, endoscopy may have limited ability to identify and control the source of bleeding and may simply visualize bleeding from the duodenal papilla [113]. In these cases, CT is more useful than endoscopy in making a diagnosis and triaging toward further management with either transarterial embolization or surgery [114, 115]. Similarly, in patients with clinical suspicion of an aortoenteric fistula, CT is considered the first-line investigation, being preferred to endoscopy [116, 117].

Nuclear Medicine

The role of technetium-99m RBC scintigraphy in acute upper GI bleeding is limited. Although it is capable of detecting bleeding rates as low as

0.1 ml/min [39], its ability to accurately localize the source of hemorrhage has been shown to be poor (moderate evidence) [48, 49, 54, 55, 118]. Indeed, it appears to perform more poorly at localizing bleeding in the upper GI tract than in the lower GI tract. A retrospective review by Howarth et al. found that technetium-99m RBC scintigraphy accurately localized the source of foregut bleeding in only 7 of 21 cases (limited evidence) [54]. CT angiography is preferred in the acute setting, not least because of the significant logistical issues surrounding access to nuclear scintigraphy, both during the working day and out of hours.

What Is the Most Appropriate Approach to the Radiological Management of Acute Upper GI Bleeding Refractory to Endoscopic Treatment?

Summary of Evidence Superselective microcoil embolization is the initial treatment of choice in acute non-variceal upper GI bleeding refractory to endoscopic management, being preferred to surgery (moderate evidence). If treatment with embolization is intended, it should be undertaken early to improve outcomes (moderate evidence). In acute variceal upper GI bleeding, emergency transjugular intrahepatic portosystemic shunt (TIPSS) formation can be used in cases refractory to endoscopic management (moderate evidence). In both variceal and non-variceal bleeding, multiphase CT is often used for procedure planning.

Supporting Evidence CT angiography has largely replaced catheter angiography as a diagnostic modality for acute upper GI bleeding, and catheter angiography is now reserved for those cases in which treatment with embolization is intended. Upper GI endoscopy remains the initial diagnostic and therapeutic modality of choice in the emergent setting; therefore, the primary role of transcatheter arterial embolization is in those cases that are refractory to endoscopic management [107].

Numerous retrospective studies are available describing the high technical and clinical success rates of superselective microcoil embolization in acute non-variceal upper GI bleeding (moderate evidence) [72, 76, 79, 88, 98, 119–129]. One series which included patients with both upper and lower GI bleeding found that rebleeding rates after embolization were higher in those with upper GI bleeding (limited evidence) [127]. In a retrospective study comparing early and delayed embolization in patients with duodenal ulcer bleeding, the group treated early had significantly fewer deaths and ICU admissions (moderate evidence) [130]. If treatment with embolization is intended, it should therefore be undertaken early.

Given the potential roles for embolization and surgery in patients failing endoscopic management, of particular interest are studies comparing these two interventions. A retrospective study comparing embolization and surgery in these circumstances by Eriksson et al. found a clear trend toward a lower 30-day mortality rate in the embolization group compared with the surgical group (moderate evidence) [131]. In 2012 Ang et al. showed that embolization could avert the need for surgery in high-risk patients with upper GI bleeding [132]. Wong et al. examined 88 patients with bleeding peptic ulcers and showed that embolization reduced the need for surgery without increasing the overall mortality rate and was associated with fewer complications [133]. One study by Ripoll et al. in 2004 failed to demonstrate any significant differences between the two treatment groups in patients with bleeding peptic ulcers [134]. Overall, the evidence favors embolization as the treatment of choice in patients failing endoscopic management (moderate evidence).

TIPSS is an established treatment for patients with portal hypertension and variceal bleeding. The strongest evidence for TIPSS is in the secondary prevention of variceal bleeding, with numerous randomized controlled trials and meta-analyses supporting its use—a detailed review of this evidence is outside the scope of this discussion. In the setting of acute ongoing variceal hemorrhage refractory to endoscopic management, TIPSS is often employed as a salvage procedure. Numerous uncontrolled studies have

shown salvage TIPSS to be effective, with a review of 15 studies using uncovered stents showing bleeding cessation rates of 90–100% and rebleeding rates of 6–16% (moderate evidence) [135, 136]. A recent randomized controlled trial comparing emergency TIPSS with emergency surgical portocaval shunt formation in refractory esophageal variceal bleeding found surgery to be superior for long-term bleeding control, encephalopathy, and survival [137]. It is worth noting however that many of the stents used in the TIPSS arm were uncovered which is no longer considered standard of care, and recent data have demonstrated superior results with polytetrafluoroethylene (PTFE)-covered stents [138]. PTFE-covered stents are now considered standard of care. A randomized controlled trial comparing TIPSS using PTFE-covered stents with surgery is required. Updated guidelines issued in 2015 by the British Society of Gastroenterology continue to recommend TIPSS or surgery as viable options for salvage therapy in uncontrolled variceal bleeding, with the choice

depending on local availability [136]. Balloon-occluded retrograde transvenous obliteration (BRTO) is a procedure that has been pioneered in Japan for the treatment of gastric varices. A number of retrospective studies have shown it to be effective in the management of active gastric variceal bleeding (moderate evidence) [139–141]. In one small randomized trial with 15 patients comparing BRTO with TIPSS in active gastric variceal hemorrhage with a gastroduodenal shunt, immediate bleeding control, rebleeding rates and encephalopathy were similar in both groups [142]. BRTO may be considered as an alternative to TIPSS in acute gastric variceal bleeding (limited evidence).

Take-Home Table

In Table 23.1, the diagnostic performance of imaging modalities for the diagnosis of acute lower and upper GI bleeding is highlighted and summarized.

Table 23.1 Diagnostic performance of imaging modalities for the diagnosis of acute lower and upper gastrointestinal bleeding

Imaging modalities for the diagnosis of acute lower gastrointestinal bleeding						
	Sensitivity, %	Specificity, %	Accuracy	+LR	–LR	Evidence
MDCT angiography [18]	85 (76–92)	92 (77–98)	0.94 (0.69–0.989)	10.8 (3.4–33.4)	0.16 (0.1–0.027)	Strong
Nuclear medicine Tc-99m RBC scan Adult [22–82]	23–83 ^a					Limited
Nuclear medicine Tc-99m RBC scan Child [58]	92	95		16.5	0.15	Strong
Catheter angiography [62]	64 (49–78)					Limited
Imaging modalities for the diagnosis of acute upper gastrointestinal bleeding						
	Sensitivity, %	Specificity, %	Accuracy	+LR	–LR	Evidence
MDCT angiography [18]	85 (76–92)	92 (77–98)	0.94 (0.69–0.989)	10.8 (3.4–33.4)	0.16 (0.1–0.027)	Strong

Figures in brackets represent 95% confidence intervals

RBC red blood cell, MDCT multi-detector computed tomography, +LR positive likelihood ratio, –LR negative likelihood ratio

^aData based on heterogeneous results from 5 separate studies. A majority of these studies showed Tc-99m RBC scanning performs poorly at accurately localizing the site of bleeding

Take-Home Points

- CT angiography is the imaging modality of choice in acute GI bleeding.
- It has high diagnostic accuracy and can increase the likelihood of successfully localizing bleeding at catheter angiography.
- Superselective microcoil embolization is a safe and effective treatment for acute non-variceal bleeding.
- Further studies are required to investigate the role of CTA followed by embolization as the potential first-line treatment in acute lower GI bleeding.

- of 340 mg/ml iodinated contrast at 4 ml/s followed by a 50 ml saline flush.
- Portal venous phase scan acquired 35 s after the bolus-tracking trigger.
- Delayed phase scan acquired 135 s after the bolus-tracking trigger.
- The reconstructed section thickness should be 1 mm.
- The windowing of the arterial phase CT scan is adjusted at the discretion of the radiologist.

Imaging Case Studies

Case 1

Figure 23.1a–d presents diverticular hemorrhage: a 91-year-old female with sudden massive bleeding per rectum.

Case 2

In Fig. 23.2a–d, we see upper GI hemorrhage: a 30-year-old male with hematemesis necessitating numerous blood transfusions.

Case 3

Figure 23.3 shows technetium-99m-labeled RBC scintigraphy: a 79-year-old male with bleeding per rectum without hemodynamic compromise.

Suggested Imaging Protocol

GI bleeding protocol CT angiogram:

- Non-contrast scan of the abdomen and pelvis.
- Arterial phase scan using bolus tracking at the abdominal aorta after the injection of 150 ml

Future Research

Unanswered Clinical Questions

- CTA criteria for predicting response to endovascular management
- The role of CTA prior to endoscopy in upper GI bleeding
- Clinical outcomes and cost-effectiveness of colonoscopy versus embolization in acute lower GI bleeding
- Surgery versus PTFE-covered TIPSS in acute variceal hemorrhage not controlled at endoscopy

Clarification of Guidelines

- Clinical outcomes of CTA followed by embolization compared with embolization alone (as currently recommended by the ACR)
- CTA followed by embolization compared with colonoscopy as a first-line treatment strategy in lower GI bleeding (the ACG recommends angiography over colonoscopy in severe active bleeding)

Existing Weak Evidence of Uncertain Clinical Importance

- The role of CTA in children with acute GI bleeding

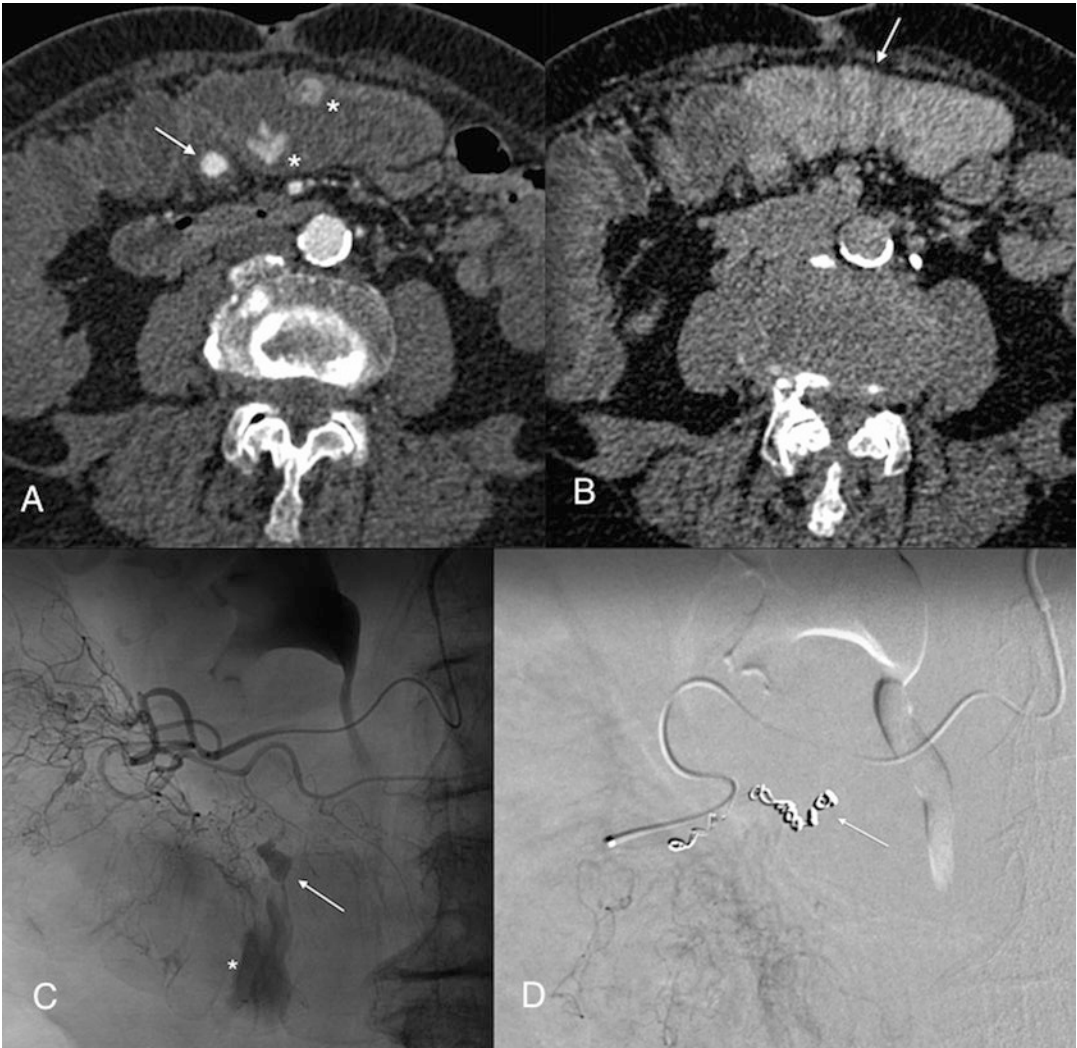


Fig. 23.1 (a–d) Diverticular hemorrhage. 91-year-old female presenting with sudden massive bleeding per rectum. There was hemodynamic instability with hypotension and tachycardia requiring multiple blood transfusions. The patient proceeded immediately to CT. **(a)** Arterial phase CT angiogram shows active extravasation into a diverticulum in the transverse colon (*arrow*) with accumulation of blood in the colonic lumen (*asterisks*). **(b)**

3-min delayed-phase CT shows significant volume acute hemorrhage in the colonic lumen (*arrow*). **(c)** Angiographic image shows bleeding from the colonic diverticulum (*arrow*) with significant active extravasation (*asterisk*). **(d)** Digital subtraction angiographic image shows coils deployed in the artery supplying the diverticulum and cessation of bleeding

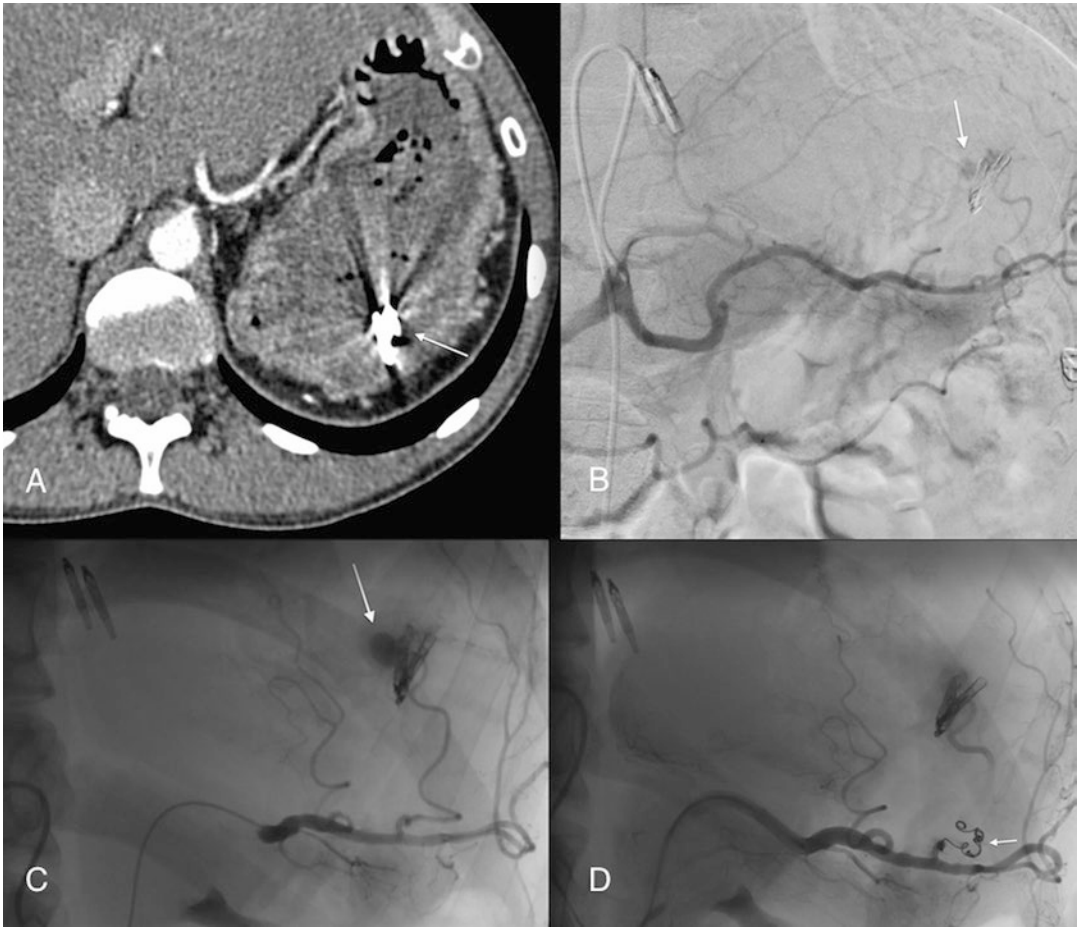


Fig. 23.2 (a–d) Upper GI hemorrhage. 30-year-old male presenting with hematemesis necessitating numerous blood transfusions. Upper GI endoscopy was performed with clipping of a Dieulafoy lesion although this failed to control the bleeding. CTA was then performed. (a) Arterial phase CT angiogram with streak artifact from the endoscopically placed clips in the stomach (*arrow*). The source of bleeding is not directly visualized. The endoscopically placed clips allow localization of the bleeding

source, and the subsequent procedure was planned accordingly. (b) and (c) Angiographic images show a rounded vascular abnormality immediately adjacent to the clips in keeping with a Dieulafoy lesion (*arrows*) being supplied by a short gastric artery from the splenic artery. (d) Angiographic image showing coils in the short gastric artery supplying the Dieulafoy lesion (*arrow*). There is a static column of contrast distal to the coils and no residual filling of the Dieulafoy lesion

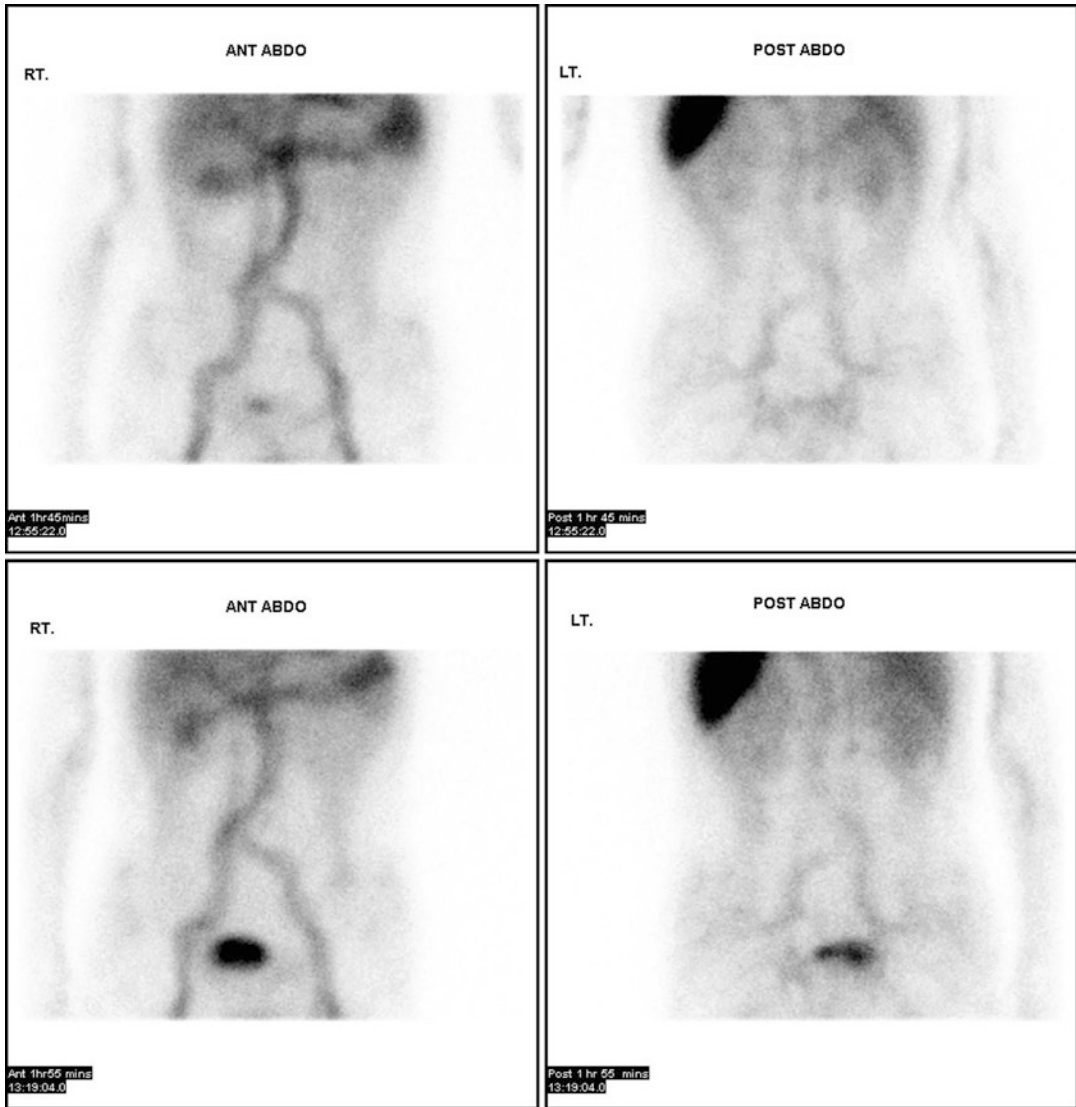


Fig. 23.3 Technetium-99m-labeled RBC scintigraphy. 79-year-old male presenting with bleeding per rectum without hemodynamic compromise. Colonoscopy showed blood throughout the colon, but no active source of bleeding was identified. No active extravasation was evident on

CTA. Delayed scintigraphic images show the accumulation of labeled red cells in a horizontally oriented viscus in the upper abdomen in keeping with the transverse colon. No active bleeding was identified on the subsequent catheter angiogram

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Acute Intestinal Ischemia in Adults: Evidence-Based Emergency Imaging

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Key Points

- Acute intestinal ischemia may be caused by arterial or venous occlusion or by nonocclusive hypoperfusion states.
- A high index of clinical suspicion is necessary for early detection and treatment of acute intestinal ischemia.
- Signs, symptoms, and laboratory tests for intestinal ischemia are nonspecific (strong evidence).
- Multiphase MDCT angiography should be used as a first-line imaging method and is highly sensitive and specific for the diagnosis of intestinal ischemia

(strong evidence). Patients should be scanned as soon as possible after imaging has been requested.

- Magnetic resonance angiography and ultrasound have limited roles in the evaluation of acute intestinal ischemia as alternative imaging modalities.
- Surgery is the mainstay of therapy.
- Percutaneous revascularization can be considered in acute intestinal ischemia in patients with no signs of advanced bowel ischemia or peritonitis and with a recent onset of symptoms (limited evidence).

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Definitions and Pathophysiology

Acute intestinal ischemia is defined as inadequate blood supply to the gut. Acute intestinal ischemia may be caused by arterial or venous occlusion or by nonocclusive hypoperfusion states. It has a high mortality rate, ranging between 32% and 93% depending on etiology [1, 2]. The incidence increases with age [1]. The majority of patients are over the age of 60. Accurate and prompt diagnosis is essential to prevent catastrophic complications including infarction, and a high clinical index of suspicion based on history and

examination is required. It remains a diagnostic challenge, however, as signs, symptoms, and laboratory tests are nonspecific.

The onset of symptoms is dependent on the cause of ischemia. Arterial occlusion classically presents with severe sudden persistent abdominal pain, which is disproportionately exaggerated relative to the unremarkable clinical examination [3]. Nausea, vomiting, fever, diarrhea, and anorexia are all commonly reported. Rectal bleeding is reported in approximately 15% of cases, and occult blood is detected in over 50% of cases [4]. Hypotension and peritonitis typically occur at a later stage as bowel becomes infarcted. A more gradual onset of symptoms occurs in venous occlusion and nonocclusive ischemia, with patients typically symptomatic for 2–3 days before the diagnosis is made [5].

To date, no reliable laboratory indicator of intestinal ischemia has been established. Serum lactate is a marker of cell hypoxia, but lactic acidosis is often a late finding concomitant with infarction. Other laboratory abnormalities include hemoconcentration and leukocytosis.

The consequences of acute intestinal ischemia are both local and systemic. Besides local complications such as bleeding, perforation, and abscess formation, ischemia can have serious systemic effects, including cardiac and renal failure, disseminated intravascular coagulation, and multi-organ failure. Treatment has traditionally focused on early diagnosis, mesenteric revascularization, bowel resection, and supportive care.

An understanding of gastrointestinal vascular anatomy and physiology is necessary to appreciate the pathology and etiology of intestinal ischemia. The gastrointestinal tract is perfused by three unpaired branches of the abdominal aorta: the celiac, superior mesenteric, and inferior mesenteric arteries. The celiac artery supplies many of the solid upper abdominal viscera and also the stomach and duodenum. The superior mesenteric artery supplies the jejunum, ileum, cecum, ascending colon, and the majority of the transverse colon. The inferior mesenteric artery supplies the remainder of the colon and rectum. The rectum is also supplied by the middle and inferior hemorrhoidal arteries, which arise from the inter-

nal iliac artery. Collateral pathways between the celiac and mesenteric arterial territories include the marginal artery of Drummond, the arc of Riolan, the hemorrhoidal arteries, the gastroduodenal and pancreaticoduodenal arteries, the arc of Buhler, and the arc of Barkow [6]. The superior and inferior mesenteric veins parallel their corresponding arteries and drain the respective parts of the intestinal tract. The inferior mesenteric vein drains into the splenic vein, which forms the portal vein with the superior mesenteric vein.

At rest approximately 15% of cardiac output is used to perfuse the small and large bowel, and this increases to 35% after a meal [6]. Of this blood flow, 70–90% supplies the mucosa and submucosa, while the remainder supplies the muscularis propria [7]. The mucosa is the layer most susceptible to ischemia. Compromise of blood flow results in ischemic damage ranging from superficial necrosis limited to the mucosa to life-threatening necrosis of all bowel wall layers. Wiesner et al. describe this in three stages; stage I is mucosal necrosis, stage II is submucosal and muscularis necrosis, and stage III is transmural necrosis [8]. They differentiate stage III from the others because of its association with a high mortality rate.

Ischemia is commonly followed by an inflammatory response due to the release of cytokines, platelet-activating factor, and tumor necrosis factor within the mesenteric circulation. These biologic mediators further damage the bowel wall and lead to additional bowel wall necrosis [9]. The bowel loses resistance to bacterial invasion, leading to bacteremia and sepsis.

The conditions that can cause intestinal ischemia can be classified into three groups (Table 24.1) [6]. These are presplanchnic (conditions causing reduced total mesenteric blood flow), splanchnic (conditions causing reduced blood flow at a local level), and postsplanchnic (venous conditions). Increased venous pressure causes reflex splanchnic arterial vasoconstriction [10].

Another term for presplanchnic ischemia is nonocclusive mesenteric ischemia (NOMI). It relates to decreased cardiac output from decreased preload, contractility, or afterload, resulting in

Table 24.1 Conditions causing intestinal ischemia

Presplanchnic: <i>reduced total mesenteric blood flow</i>
<ul style="list-style-type: none"> • Hemorrhage • Hypovolemia • Acute myocardial infarction • Congestive cardiac failure • Cardiac arrhythmias • Hemodialysis • Drugs, e.g., digitalis, cyclosporine, cocaine
Splanchnic: <i>reduced blood flow at a local level</i>
<ul style="list-style-type: none"> • Embolism • Thrombosis • Closed loop bowel obstruction • Arterial fibrodysplasia • Vasculitides • Trauma (direct vascular injury)
Postsplanchnic: <i>reflex arterial vasoconstriction secondary to increased venous pressure</i>
<ul style="list-style-type: none"> • Primary mesenteric venous thrombosis (hypercoagulable states) • Secondary mesenteric venous thrombosis, e.g., portal hypertension, inflammatory abdominal conditions • Trauma (mesenteric contusion causing venous obstruction)

intestinal hypoperfusion in the presence of patent vasculature. Common causes include dehydration, hemorrhage, acute myocardial infarction, congestive cardiac failure, and hemodialysis.

The commonest cause of acute intestinal ischemia is superior mesenteric artery (SMA) embolus. Embolic sources include left atrial or ventricular intraluminal thrombus and cardiac valve vegetation. Typically the embolus will lodge within 3–10 cm from the origin of the SMA, in a tapered segment distal to the origin of the middle colic artery [7]. In contrast, in situ thrombosis occurs more frequently at the origin of the SMA and patients affected usually have background atherosclerosis.

The initial physiological response to hypoxia is vasodilation. During this phase CT demonstrates parietal (wall) hyperdensity on the arterial phase, which persists on the portal venous phase relative to the normal adjacent loops. At this point ischemia has not yet caused irreversible damage. Vasodilation is followed by vasoconstriction, which results in reduced or absent enhancement of the ischemic bowel on CT after intravenous contrast injection. Vasoconstriction is followed by an

increase in capillary permeability causing submucosal edema. This gives rise to bowel wall thickening, which is the most frequently encountered CT finding [11]. The bowel wall may be hypodense reflecting submucosal edema, or it may be hyperdense representing submucosal hemorrhage [12]. Vascular occlusion with hypodense thrombus may be apparent. Distal emboli are more challenging to detect and may be limited to changes in the local bowel or surrounding mesenteric fat. The site and extent of involved intestine depends on the cause of ischemia and the availability of collateral vessels. For example, if the SMA is occluded the entire jejunum, ileum and proximal colon can be affected. Delayed CT findings include bowel dilatation due to interruption of the peristaltic activity. As ischemia progresses, pneumatosis and portal venous gas develop. These two findings are not specific to ischemia and can be seen in a number of other conditions [13]. Pneumoperitoneum can occur when there is transmural extension of necrosis.

Epidemiology

Acute intestinal ischemia is responsible for 0.1% of all hospital admissions and 1.0% of admissions with an acute abdomen [7]. The diagnosis is being made with increasing frequency due to the aging population, improved diagnostic tools, and more intensive treatment of critically ill patients [7].

Goals of Imaging

The goals of imaging patients with suspected intestinal ischemia include achieving a prompt and accurate diagnosis, excluding differentials and assessing bowel and surroundings for complications.

Methodology

A comprehensive Medline search for original articles published between January 2005 and May 2015 using the Ovid and PubMed search

engines was performed using a combination of the following key terms: acute mesenteric ischemia, diagnostic imaging, CT, US, MR, angiography, technology assessment, interventional radiology, evidence-based medicine, and cost. The search was limited to English-language articles and human studies. The abstracts were reviewed and selected based on level of evidence, well-designed methodology, clinical trials, outcomes, and diagnostic accuracy. Additional relevant articles were selected from the references of reviewed articles and published guidelines.

Discussion of Issues

What Is the Diagnostic Performance of CT for the Detection of Acute Intestinal Ischemia?

Summary of Evidence In practice CT is the most commonly used modality for the diagnosis of acute intestinal ischemia. Multiphase multidetector computed tomography (MDCT) angiography examination of patients with suspected intestinal ischemia is highly sensitive and specific in detecting small bowel ischemia and may be used as a first-line imaging method (strong evidence).

Supporting Evidence Conventional angiography was once considered the gold standard for diagnosis of acute intestinal ischemia; however, multiphase MDCT angiography is now becoming the imaging method of choice. It has many benefits including cost, rapid acquisition, accurate identification of mesenteric vessel pathology (arterial embolus, thrombosis, or venous thrombosis), localization of involved small bowel, and exclusion of differential diagnoses.

In 2010, Menke et al. performed a systematic review and meta-analysis on the diagnostic

accuracy of MDCT in acute mesenteric ischemia. Inclusion criteria included consecutive patients with clinically suspected acute mesenteric ischemia or acute or subacute abdomen of unknown origin. The review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [14]. Six studies were included in total, three were prospective, three were retrospective, and all were high quality according to the Quality Assessment of Studies of Diagnostic Accuracy included in Systematic Reviews (QUADAS) criteria [15]. In total, 619 cases were included, all of whom had been clinically examined before CT with findings of an acute or subacute abdomen and clinical suspicion of acute mesenteric ischemia. The prevalence of acute mesenteric ischemia ranged from 5.7 to 59.6%. The number of multidetector rows was four in most studies, with one study using 16 and one study using 16 or 40. Water was administered as oral contrast in three of the studies, and positive oral contrast was used in one study. Five of the studies used both arterial and portal venous phase protocols, and one study used portal venous phase CT of the abdomen and pelvis only [16–21]. The results included a summary sensitivity of 93.3% (95% CI, 82.8%–97.6%) and a summary specificity of 95.9% (95% CI, 91.2%, 98.2%) (Table 24.2) [23]. This systematic review was reviewed by the Cochrane Library and found to be a generally well-conducted study with the conclusions likely to be reliable.

In 2013, Cudnik et al. performed a further meta-analysis, including three additional studies to Menke’s meta-analysis, adding an additional 261 patients [24–26]. They found similar results—summary sensitivity of 94% (95% CI = 90% to 97%) and specificity of 95% (95% CI = 93% to 97%) with a positive likelihood ratio (+LR) for a positive CT of 17.5 (95% CI = 5.99

Table 24.2 Computed tomography for the diagnosis of acute intestinal ischemia

References	Sensitivity, %	Specificity, %	+LR	–LR	Evidence
[19]	93.3 (82.8–97.6)	95.9 (91.2–98.2)			Strong
[22]	94 (90–97)	95 (93–97)	17.5 (5.99–51.29)	0.09 (0.05–0.17)	Strong

Figures in parenthesis represent 95% confidence intervals

to 51.29) and a negative likelihood ratio ($-LR$) of 0.09 (95% CI = 0.05 to 0.17) [22]. Two of the additional studies used both arterial and portal venous phases, with one study performing a portal venous phase only.

CT protocols varied across the above different studies. In the early stages of arterial occlusion without reperfusion, appearances on a “survey” portal venous CT of the abdomen and pelvis performed with positive oral contrast and a lower dose of iodinated contrast injected at a slower rate may be within acceptable limits at this stage of the disease process. Multiphasic MDCT angiography allows evaluation on the arterial and portal venous phases. It is important to remember that if there is strong clinical suspicion of ischemia, a “normal” CT should not prevent a diagnostic laparotomy [23].

In Patients for Whom Computed Tomography Is Contraindicated, What Is the Best Alternative Modality?

Summary of Evidence Abdominal radiographs are of little value in the diagnosis of intestinal ischemia (limited evidence). Ultrasound and magnetic resonance angiography may be used as alternative imaging modalities in the evaluation of intestinal ischemia (limited evidence).

Supporting Evidence Radiographs are often performed initially in the setting of acute abdominal pain, but they are of limited value in the diagnosis of intestinal ischemia. Radiographic findings are usually nonspecific, showing no abnormality, a gasless abdomen, or intestinal dilatation. Specific findings such as pneumatosis or portal venous gas occur late when the bowel has infarcted and are therefore associated with a high mortality [27].

Ultrasound has been shown to be useful in demonstrating proximal mesenteric artery occlusion, but it has a limited role in diagnosing non-occlusive mesenteric ischemia and distal occlusion [27]. Technical issues such as operator-dependent quality, large patient body habitus, and bowel gas obscuration also limit the use of this modality. It can be helpful in excluding other

causes of acute abdominal pain such as cholecystitis, pancreatitis, etc.

Magnetic resonance angiography (MRA) has a high sensitivity and specificity for diagnosing severe stenosis or occlusion at the origin of the celiac or superior mesenteric artery, but similar to ultrasound, it has limited value in diagnosing nonocclusive mesenteric ischemia and distal occlusion [27]. Scan time is prolonged compared with CT which may result in a delay in management, and access to MRI is also limited in many centers. MRA has the advantage of avoidance of iodinated contrast medium and lack of ionizing radiation. The use of gadolinium contrast media should be in line with the recommendations of the American College of Radiology manual on contrast media, and caution is advised in patients with renal failure. Non-contrast MRI can be used in cases where both iodinated and gadolinium-based contrast media are contraindicated, but it has a lower sensitivity and specificity [27].

In the Management of Acute Intestinal Ischemia, Surgery Has Been the Treatment of Choice: Is There a Role for Endovascular Intervention?

Summary of Evidence Endovascular revascularization can be considered in patients with acute intestinal ischemia without clinical evidence of peritonitis but with radiological evidence of advanced ischemia and recent onset of symptoms and with a low threshold for converting to open surgery if required (limited evidence).

Supporting Evidence The gold standard treatment of acute intestinal ischemia is revascularization of the affected bowel and restoration of normal perfusion. Traditionally surgery was the only option [28]. Open or endovascular revascularization is performed as rapidly as possible prior to bowel resection. Preoperative clinical evaluation determines whether the patient has peritonitis or not, with laparotomy indicated if there is peritonitis [29]. A palliative approach may be considered in those with advanced extensive bowel infarction.

Immediate supportive management includes nasogastric drainage, intravenous rehydration, and anticoagulation with or without antiplatelet therapy. The traditional treatment for mesenteric embolus is open surgical embolectomy. Mesenteric artery thrombosis is treated with mesenteric bypass. In hemodynamically stable patients with recent sudden onset of abdominal pain and without clinical or radiological signs of advanced ischemia or peritonitis, endovascular intervention can be considered. Endovascular options include pharmacologic or mechanical thrombectomy and balloon angioplasty with arterial stent placement. Conversion to open surgical exploration may be required if the patient deteriorates clinically.

The use of endovascular treatment in acute intestinal ischemia is increasing [30, 31]. Patients with acute intestinal ischemia often have multiple comorbidities, and consequently minimally invasive endovascular treatment is becoming more appealing. No randomized control trials exist comparing the two treatments, making it difficult to compare outcomes, as there are many confounders.

A retrospective review of the Swedish vascular registry has reported that endovascular treatment has better 30-day and 1-year mortality rates than open surgery. However, these findings are limited by the fact that sicker patients go directly to surgery and endovascular failures are also treated with open surgery [31]. Beaulieu performed a retrospective review of the National Inpatient Sample Database in the USA between 2005 and 2009 for patients who had intervention for acute intestinal ischemia. Endovascular intervention increased from 11.9% in 2005 to 30% in 2009. Endovascular treatment was associated with decreased mortality, shorter length of stay, and lower rates of bowel resection compared to the surgical group [30]. A number of other smaller retrospective studies have also found improved outcomes with endovascular revascularization [32–34].

Acute mesenteric venous thrombosis is diagnosed typically on the portal venous phase of CT. Initial supportive management includes nasogastric tube insertion and intravenous hydration.

Systemic anticoagulation is the main treatment, limiting thrombus propagation, allowing recanalization, and improving survival [35]. Modified endovascular interventional techniques include thrombolysis and thrombectomy via percutaneous transhepatic, transjugular, or transjugular portosystemic shunt access into the portal vein. Transarterial thrombolysis via the SMA has also been described. There are no large randomized control trials to guide decision-making regarding catheter-based techniques [29]. Surgical laparotomy is recommended if there are signs of intestinal necrosis or perforation.

Take-Home Tables

Table 24.1 summarizes the conditions causing intestinal ischemia, and Table 24.2 highlights the specificity and sensitivity of CT for the diagnosis of acute intestinal ischemia.

Imaging Case Studies

Case 1

Figure 24.1a–c presents a 66-year-old patient with acute onset severe abdominal pain and a history of atrial fibrillation.

Case 2

In Fig. 24.2a, b, a 93-year-old patient presents with a 1 week history of worsening abdominal pain, vomiting, diarrhea, and fever.

Suggested Imaging Protocols

- CT angiography should be performed if there is clinical suspicion of acute intestinal ischemia. The use of a multidetector array scanner is preferred. Acquisition should be performed with a nominal section thickness of 3 mm or less. The scan should be reconstructed with overlapping sections at a maximum increment

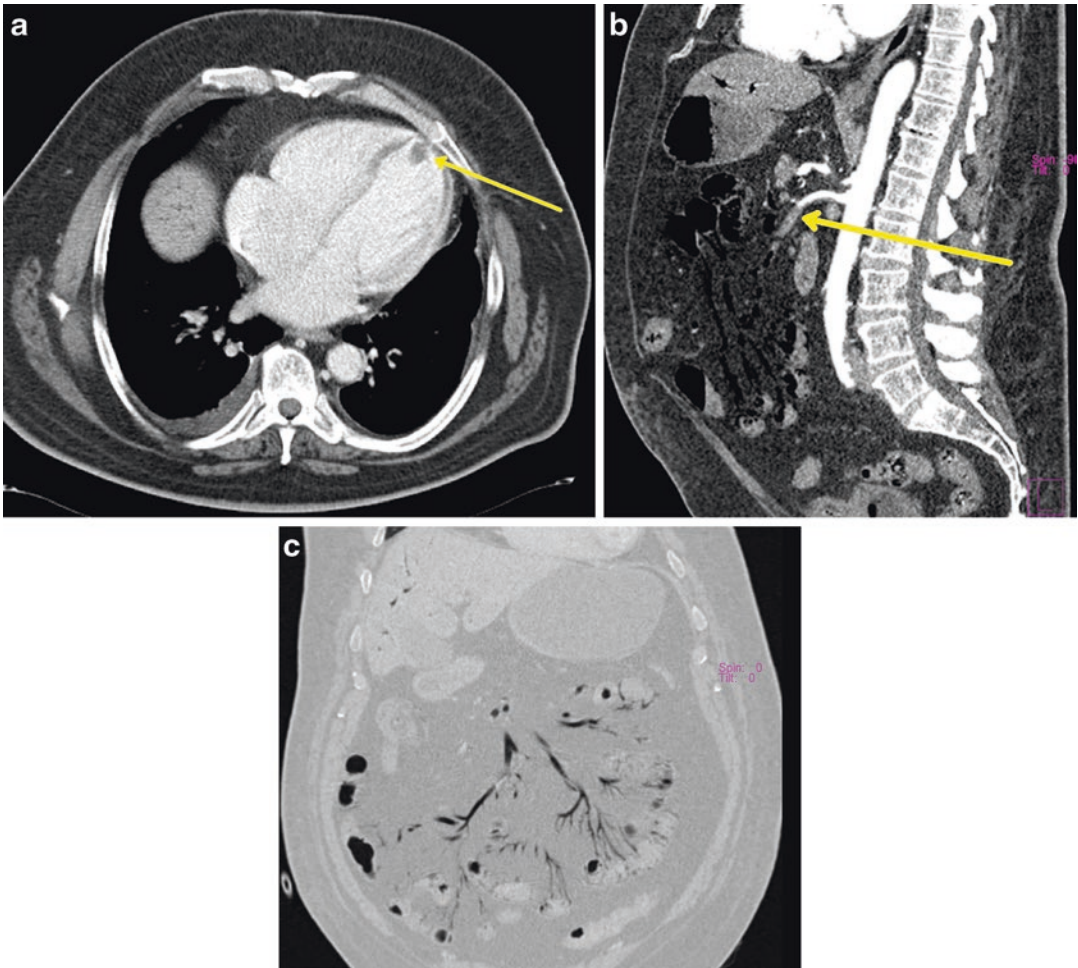


Fig. 24.1 (a–c) A 66-year-old patient presented with acute onset severe abdominal pain with a background history of atrial fibrillation. Blood tests revealed white cell count $17 \times 10^9/L$, INR 1.3, and serum lactate 13 mmol/L. Axial arterial phase CT image at the level of

the left ventricle shows thrombus within the apex of the left ventricle (a). Sagittal arterial phase CT image shows occlusive embolus in the SMA (b), and coronal CT image on lung windows shows intrahepatic portal venous gas, with gas also within the tributaries of the SMV (c)

of 50% of the effective section thickness to enhance the quality of two-dimensional and three-dimensional reconstruction images and prevent artifact [36].

- Use of a mechanical injector and a saline flush is advised to administer nonionic contrast medium (350 mg/mL) to achieve a minimum injection rate of 3 mL/s for a total of 150 mL of contrast medium. Bolus tracking software that monitors passage of contrast material through the descending aorta is recommended, with the trigger threshold set at 100 HU aortic

enhancement (i.e., trigger pulled when CT value increases by 100 HU) [37].

- Images should be acquired in at least two phases if there is clinical suspicion of intestinal ischemia: early arterial phase (immediately after bolus tracking or at 15–20 s post injection) and portal venous phase (50–60 s after bolus tracking or 70–80 s post injection). An unenhanced helical CT acquisition may be useful prior to acquiring the CT angiogram as it may demonstrate mural hemorrhage and delineate arterial calcification. These benefits may offset

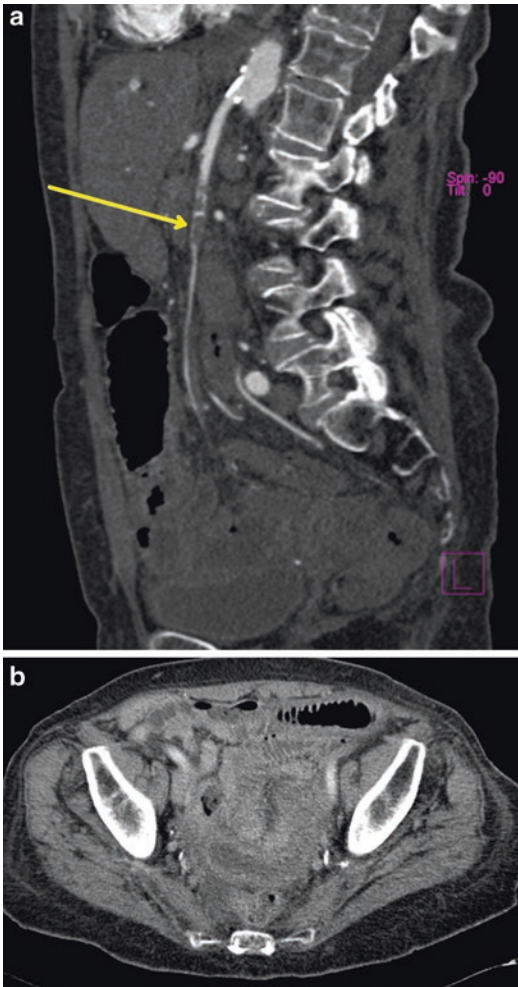


Fig. 24.2 (a, b) A 93-year-old patient presented with a 1-week history of worsening abdominal pain, vomiting, diarrhea, and fever. Blood testing revealed white cell count $15 \times 10^9/L$, CRP 170 mg/dL. Sagittal arterial phase CT image shows occlusive thrombus in the SMA (a). Axial arterial phase CT image of the pelvis shows mural thickening of the hypoenhancing small bowel wall, fat stranding, and free fluid (b)

the disadvantage of radiation exposure associated with this supplementary scanning.

- Low attenuation oral contrast medium, e.g., water, can be used as it allows better visualization of the enhancing bowel wall. Alternatively negative oral contrast can be omitted to avoid delaying treatment.
- Postprocessing of the CT to provide multiplanar reformations and/or three-dimensional renderings is mandatory.

Future Research

- Has the widespread use of multidetector CT resulted in earlier diagnosis of intestinal ischemia and therefore improved outcomes?
- No randomized control trials exist comparing outcomes of surgical intervention to endovascular revascularization in patients with acute intestinal ischemia.

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Acute Urinary Tract Conditions in Adults: Evidence-Based Emergency Imaging

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Key Points

- Non-contrast computed tomography (NCCT) is the best imaging test for identification of urinary tract stones (strong evidence).
- Ultrasound may be used to diagnose hydronephrosis and guide management in the emergent setting (moderate evidence).
- Uncomplicated lower urinary tract infections are primarily diagnosed clinically. Imaging may be performed if the clinical diagnosis is uncertain or if other diseases or complications are suspected. Contrast-enhanced computed tomography (CECT) is the imaging test of choice (limited evidence).
- Imaging is not routinely indicated for upper urinary tract infections unless a complication (e.g., pyelonephritis or renal abscess) is suspected. CECT is the preferred imaging test to diagnose

complications of an upper urinary tract infection (moderate evidence).

- Ultrasound and magnetic resonance imaging (MRI) are considered first-line imaging modalities for suspected renal colic or complications of urinary tract infections in pregnant patients (ultrasound or non-contrast MRI) or in patients with iodinated contrast allergies (moderate evidence).

Definition and Pathophysiology

This chapter discusses imaging decisions for adults that present with acute renal symptoms, which can be caused by obstructive and nonobstructive calcifications and infections. Nephroliths, or renal stones, are solid crystals or concretions from minerals or chemicals in the urine formed in the kidney that can cause blood in the urine (hematuria) and can pass into the ureters, bladder, and urethra causing pain. Pain from renal stones (also known as renal colic) is spasmodic pain usually felt in the back radiating to the groin. Risk factors for renal stone formation are dehydration, high intake of animal protein, sodium, refined sugar, oxalate, underlying

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metabolic conditions including renal tubular acidosis and medullary sponge kidney, and human immunodeficiency virus (HIV) medications [1–5].

Urinary tract infections (UTIs) can be divided into upper tract infections (kidneys and ureters) and lower tract infections (urinary bladder and urethra). Acute pyelonephritis (APN) is inflammation of the renal parenchyma, calices, and pelvis, most commonly due to bacterial infections. Symptoms include fever and flank pain at the costovertebral angles. A severe form of pyelonephritis with gas forming in the renal tissues is emphysematous pyelonephritis. This severe infection has a higher prevalence in uncontrolled diabetics. If an infection in the kidney persists, it can form a cavity of necrotic cells and inflammatory response in the renal tissue or a renal abscess. Patients with diabetes are also at an increased risk for renal abscess formation. UTI with ureteral obstruction is termed pyonephrosis. Cystitis is inflammation of the urinary bladder, most commonly from a bacterial source and can cause painful urination, urge to urinate, hesitation during urination, and foul smelling/cloudy urine. An infection with air within the bladder wall is termed emphysematous cystitis. Like emphysematous pyelonephritis, emphysematous cystitis is more prevalent in diabetics. Risk factors for urinary tract infections include female sex, diaphragm use for birth control, chronic prostatitis in older males, urinary catheterization, diabetes, vesicoureteral reflux, and spinal cord injuries [6–8]. Most upper urinary tract infections start as lower UTIs, cystitis, and prostatitis [9].

Epidemiology

A study of renal stone prevalence in the United States found an overall prevalence of stone disease of 8.8% [10]. Males have a 1.3 times higher odds of developing renal stones than women [10]. Non-Hispanic whites have the highest prevalence of renal stone disease, 10.3% [10]. Prevalence in Hispanics is 6.4% and 4.3% in African Americans [10]. The prevalence of renal stones in normal weight patients is 6.1%, but this

increases to 9.2% in overweight patients and 11.2% in obese patients. Patients with diabetes have 1.55 times higher odds of developing renal stones than nondiabetics [10]. It is estimated that UTIs cause 7 million physician office visits a year, 1 million emergency room visits a year, and 100,000 hospitalizations a year in the United States [11]. UTIs are more common in females than males, and it is estimated that 40–50% of women will experience a UTI that requires treatment in their lifetime [12–15]. The prevalence and incidence of emphysematous cystitis is unknown [16] but is estimated to be 15–17 cases per 10,000 females and 3–4 cases per 10,000 males per year [17].

Overall Cost to Society

The direct costs of renal stones were estimated to be an extra \$3494 per patient in working-age adults compared to a similar population without nephrolithiasis [18]. According to Saigal et al., an estimated 1.3 million working-age adults receive treatment for renal stones per year [18]. This calculates to approximately \$4.5 billion in direct costs annually in the employed population alone [18]. Saigal et al. also estimated renal stones caused approximately 3.1 million lost workdays per year, using private insurance data [18]. Using a conservative estimate of \$250 per day of work for employers, the indirect costs of renal stones are approximately \$775 million per year [19, 20]. Direct and indirect costs annually for community-acquired UTIs are estimated to be \$659 million and \$936 million, respectively, for a total of approximately \$1.6 billion [21, 22]. The estimated annual cost of nosocomial UTIs in the United States ranges from \$424 to \$451 million [23].

Goals of Imaging

The goal of imaging in patients presenting with flank pain or renal colic is to determine if a renal stone is present, if it is causing upstream obstruction, and if the size of the stone is amenable to medical management or requires surgical

intervention. For urinary tract infections, the goal of imaging is to determine if the infection is present in the kidney parenchyma, has an abscess formed requiring percutaneous drainage, and is the infection emphysematous, which has a higher morbidity and mortality rate.

Methodology

A comprehensive Medline search (United States National Library of Medicine database) for original articles published between 1966 and September 2014 using the Ovid and PubMed search engines was performed using a combination of the following key terms: *renal stone, nephrolithiasis, urinary tract infection, cystitis, emphysematous cystitis, pyelonephritis, pyonephrosis, emphysematous pyelonephritis, renal abscess, radiography, KUB, ultrasound, computed tomography, magnetic resonance imaging, evidence-based medicine, epidemiology, and cost*. Only articles using the English language and human studies were used. The articles were reviewed and selected based on methods, outcomes, and diagnostic accuracy. Additional relevant articles were selected from the references of reviewed articles and published guidelines.

Discussion of Issues

What Is the Imaging Modality of Choice for Suspicion of Urinary Stone Disease?

Summary of the Evidence Presently, non-contrast computed tomography (NCCT) is considered the diagnostic test of choice for patients with presenting with renal colic (strong evidence) [20]. NCCT is highly accurate for the identification of uroliths, for detecting evidence of ureteral obstruction, and for the identification of other potential etiologies of flank pain [24]. The major disadvantage of NCCT is radiation exposure to the patient [25, 26]. In patients with known urolithiasis and/or a presentation classic for renal colic, the combination of abdomen and pelvis

radiography (kidneys ureters bladder, KUB) and ultrasound (US) may be an acceptable and much lower radiation alternative for the diagnosis of clinically significant ureteroliths (moderate evidence) [27, 28]. MRI is an excellent tool for the evaluation of hydronephrosis though is limited in its ability to detect small uroliths (moderate evidence) [29].

Supporting Evidence

Radiography

Radiography may suggest a renal stone if a calcification is identified in the expected location of the urinary system on the side of the pain. However, not all stones are radiopaque on radiographs [30]. Additionally, some radiopaque objects visible on radiographs may represent phleboliths or other vascular calcifications. Also, the sensitivity of the KUB for urinary stones can vary due to many factors, such as stone composition, location, size, body habitus, and overlying bowel contents [30]. The sensitivity of radiography, when compared to NCCT, for urinary stones >5 mm in the proximal ureter is 72%, but the sensitivity for a stone of any size in any location in the urinary tract drops to 29% [31]. Another study compared abdominal radiographs to NCCT and found the sensitivity for urinary stones on KUB to be 59% with a specificity of 71% [32].

Radiography exposes patients to less ionizing radiation as compared to CT. The effective radiation dose from a single abdominal radiograph is approximately 0.6 mSv as compared to 10–12 mSv for conventional NCCT of the abdomen and pelvis and 2 mSv for low-dose NCCT of the abdomen and pelvis [33].

Ultrasound

Ultrasound (US) can be useful for the evaluation of renal colic while not exposing patients to ionizing radiation. US may be able to demonstrate a stone, as well as findings of obstructive uropathy.

When evaluating flank pain, US has a sensitivity of 61–90% compared to NCCT for the detection of stones in the ureters [28, 34]. Looking for a twinkle artifact on color Doppler imaging [35, 36] may improve the ability to detect urinary stones

[27, 28]. The twinkle artifact is an intense multi-colored signal behind a stone when color Doppler is applied to the stone [28]. However, the sensitivity of US compared to NCCT for detecting urinary stones is relatively low 24–57%, especially for small stones [37, 38].

For the diagnosis of urinary obstruction in patients with acute flank pain, US has been found to have a sensitivity and specificity of up to 100% and 90%, respectively [38]. The US findings of obstructive uropathy include hydronephrosis, ureterectasis, and perinephric fluid [38]. However, US may still be limited within the first 2 h of presentation because enough time may not have elapsed for these findings to have developed [39]. Initial evaluation with ultrasound was found to result in lower cumulative radiation exposure than initial evaluation with CT without significant difference in repeat emergency department visits, high-risk diagnoses with complications, or serious adverse events [40].

A combination of abdominal radiography and US can be used as a technique for evaluation of urinary stones for patients with renal colic and has a lower ionizing radiation dose and cost as compared to NCCT [41]. A prospective study of 66 patients using a KUB/US combination found a sensitivity of 79% (93% for NCCT) for detecting ureteral stones [38]. Because all missed cases had spontaneous ureterolith passage, the authors concluded that a NCCT after a negative KUB/US would not add useful information, and they suggested a NCCT should be obtained in patients that do not respond to conservative management or when surgical intervention is anticipated [38].

The advantages of US during the investigation of renal colic include lack of ionizing radiation and ability to demonstrate some urinary stones. The disadvantages include need for skilled personnel, inability to accurately measure stone size, and inability to differentiate dilatation without obstruction from true obstruction [42, 43].

Computed Tomography

NCCT currently is the gold standard for diagnosis of urinary stones [44]. Urinary stone location on NCCT has also been correlated with rates of spontaneous stone passage with more proximal

urinary stones having an increased need for intervention [45]. An advantage of NCCT images is the ability to reformat acquired axial images into other planes (e.g., sagittal and coronal). Two studies found reviewing coronal reformations with the axial dataset can increase urolith detection [46, 47]. Coronal reformations also enhanced estimation of maximal stone size [47].

Because of the increased risk of radiation exposure, especially in young patients, reduced dose CT protocols have been developed [48–57]. One evidence-based study concluded that a low-dose protocol should be used if NCCT is ordered to evaluate urinary stones [58]. Dose reduction techniques include lower kVp, lower tube current, use of automated tube current modulation, and use of iterative reconstruction [50]. Limiting the scan range to include only the kidneys, ureters, and bladder also lowers dose [59]. Low-dose protocols can reduce mean radiation dose to 1.9 mGy, as compared to 9.9 mGy for a conventional protocol, without loss of diagnostic accuracy [50].

A meta-analysis of diagnostic performance of low-dose (<3 mSv) CT for detecting urinary stones found a pooled sensitivity and specificity of 97% and 95%, respectively [60]. Additionally, the measurements of uroliths on low-dose CT were demonstrated to be equal to standard-dose CT [61]. The sensitivity of urinary stone detection decreases with stone size, and the sensitivity for smaller stones is further impeded with increasing dose reduction [62]. However, using dose reduction of approximately 50% with iterative reconstructive techniques for the detection of urinary stones was not inferior to full-dose scans reconstructed with filtered back projection [63].

Delayed phase images on contrast-enhanced CT (CECT) after intravenous contrast administration can assist in differentiating between a urolith and a phlebolith adjacent to the ureter [64, 65]. NCCT can also demonstrate secondary signs of a recently passed urinary stone including ureteral dilatation and perinephric edema [66, 67]. NCCT is also useful for diagnosing other causes of flank pain, such as appendicitis and diverticulitis [67–70]. Even if a CECT is performed, the sensitivity for detecting all urinary stones is 81% and >95% for all stones ≥ 3 mm [71].

Characterization of urinary stone composition with dual-energy CT can be useful; however, the optimized energy levels for imaging and post-processing have not yet been determined [72–77]. Virtual unenhanced images from dual-energy CT are reasonably accurate in subtracting excreted contrast material from the renal collecting systems and can be used to diagnose urinary stones >2.9 mm with good reliability [78]. However, dual-energy CT virtual unenhanced images are not accurate enough to currently replace true unenhanced images [79].

Magnetic Resonance Imaging

MRI may be used as an alternative to low-dose NCCT in certain patient populations: pregnant women (non-contrast MRI), young individuals, and individuals with multiple prior CT examinations [29]. While MRI is good at diagnosing hydronephrosis and perinephric edema, its detection of the actual urinary stone is much less accurate as compared to NCCT [80].

Magnetic resonance urography (MRU) was found in one study to have 100% sensitivity for obstruction, and the site of obstruction was found in 80% of the cases. Round signal voids on the MRU corresponded to urinary stones on correlative intravenous urogram (IVU) in 12 of 18 cases [81]. Another study of obstructive uropathy with 13 cases of ureteroliths demonstrated that MRU correctly identified the site of obstruction in all but one case (one ureterolith moved between the MRU and confirmatory imaging). The ureteral stones were seen as signal voids against a background of bright urine on T2-weighted images in 46% of the cases [82]. More recent data found that MR-visible urinary stones measured 1.1 cm on average (range 0.15–3.3 cm) and stones not visible at MR measured an average of 0.46 cm (range 0.1–0.9 cm) [83]. Blood oxygen level-dependent MRI used increased oxygen content in the renal cortex and medulla to detect acute unilateral renal obstruction [84]. Changes in renal perfusion and diffusion during acute ureteral obstruction can be found using diffusion-weighted imaging (DWI) [85]. Excretory MRU was found to be more sensitive for ureterolith detection

than T2-weighted MRU; however, the former is limited is not recommended for pregnant patients due to the use of gadolinium [86].

What Is the Imaging Modality of Choice for Clinical Concern for a Lower Urinary Tract Infection?

Summary of Evidence Uncomplicated lower urinary tract infections are primarily diagnosed clinically, using patient symptoms and urinalysis (UA) [87], and diagnostic imaging is usually reserved for patients with recurrent infections, failed treatment, or patients with severe symptoms (moderate evidence) [88]. There are no diagnostic imaging examinations indicated in simple cases of acute community-acquired cystitis [89]. Imaging may play an earlier role in diagnosis of lower UTIs if the clinical situation and UA are uncertain or if other diseases, such as urinary stones, are suspected [88]. Additionally, in immunocompromised or diabetic patients, early imaging may be beneficial [88, 90]. Because lower urinary tract infections are usually not diagnosed with imaging, little recent evidence-based literature has focused on lower UTIs. Currently CT scan, especially CECT if renal stones are not suspected, is the diagnostic test of choice for complicated UTI (moderate evidence) [91]. CECT is also the diagnostic test of choice for emphysematous cystitis [92].

Supporting Evidence

Radiography

Very few peer-reviewed scientific articles could be found describing the sensitivity, specificity, accuracy, or use of radiography in the diagnosis of uncomplicated lower UTIs in adults. Previously, intravenous urograms (IVUs) were widely used to evaluate urinary tract symptoms; however, studies found that IVU could be avoided and replaced with ultrasound and radiography [93]. One study found that 91% of IVUs were negative in uncomplicated UTIs [94]. Another study indicated that US alone is almost as good as IVU in women because of the lower incidence

of urinary stone disease [95]. For emphysematous cystitis, radiography can often be diagnostic demonstrating curvilinear or mottled areas of increased lucency in the region of the urinary bladder [96]. One study analyzing all articles written in English between 1956 and 2006 on emphysematous cystitis found that 84% of the cases were diagnosed with radiography [92]. However, radiography lacks sensitivity, estimated at approximately 50% by one study [97], and it lacks specificity [96], as air shadows of adjacent bowel can cause difficulty in diagnosis [98]. Intravenous urography was found to insensitive for the diagnosis of emphysematous cystitis [99].

Ultrasound

Very few peer-reviewed scientific articles could be found describing the sensitivity, specificity, accuracy, or use of US in the diagnosis of uncomplicated lower UTIs in adults. Ultrasound can be useful in evaluating patients with a poorly emptying bladder, a population at risk for recurrent lower UTIs. US can assess bladder wall thickness and post-void residual volumes [93]. US can diagnose emphysematous cystitis without ionizing radiation exposure, but has been documented to have a low sensitivity and may be better used to follow patients showing clinical improvement [96]. Findings on ultrasound in emphysematous cystitis include bladder wall thickening and small echogenic foci within the bladder wall and lumen with dirty posterior acoustic shadowing and reverberation artifact. These intraluminal foci are due to air and can be mobile and shift with changes in posture [100–102].

Computed Tomography

Very few peer-reviewed scientific articles could be found describing the sensitivity, specificity, accuracy, or use of CT in the diagnosis of uncomplicated lower UTI in adults. CT can be used to differentiate a lower UTI from an upper UTI if symptoms are questionable and management would be changed [91]. CECT findings of cystitis include irregular thickening and enhancement of the bladder wall [91]. CT is considered the best test for diagnosis of emphysematous cystitis because it is more sensitive [103] and specific

than radiography [96]. CT can define the extent, location, and any complications more precisely [104]. If there is a contraindication to intravenous contrast, a NCCT can be obtained to evaluate for emphysematous cystitis [99]. Additionally, CT can diagnose alternative causes for air within the urinary bladder, including vesicocolic fistula, intra-abdominal abscess, adjacent neoplastic disease, ascending infection, scrotal abscess, and the presence of emphysematous pyelonephritis [92, 96, 99, 105, 106].

Magnetic Resonance Imaging

Very few peer-reviewed scientific articles could be found describing the sensitivity, specificity, accuracy, or use of MRI in the diagnosis of uncomplicated lower UTIs in adults. MRI can be used as an alternative if an iodinated contrast allergy exists; however, due to higher expense, cost restraints, less common availability, and longer scan times compared to CT, it is not a routinely diagnostic test for lower UTIs [91, 107, 108]. Therefore, MRI is usually reserved for problem-solving or when other imaging modalities have not provided an answer or are unsuitable [91]. Another limitation of MRI is signal voids created by gas from infections that can cause difficulty in interpretation [91, 108], and no studies have investigated MRI and emphysematous cystitis.

What Is the Imaging Modality of Choice for Clinical Concern for an Upper Urinary Tract Infection?

Summary of Evidence Imaging is not felt to be routinely indicated in urinary tract infections unless severe symptoms are present, there was no clinical response to antibiotics, or the patient is immunocompromised or diabetic [90]. However, more recently it has been suggested that early imaging in acute pyelonephritis (APN) is cost-effective and imaging should be obtained for all APN patients who required hospital admission [109]. Presently, CECT is the gold standard imaging modality for diagnosis and assessment of APN and its complications (moderate evidence) [110].

Abdominal radiography may be useful as a screening exam for evidence of gas in emphysematous pyelonephritis. US can be an initial screening modality, particularly in pregnant patients, and is used for guiding interventions (limited evidence). MRI is mainly indicated for pregnant patients and for individuals allergic to iodinated contrast material (limited evidence) [110].

Supporting Evidence

Radiography

Radiography, especially intravenous urography (IVU), has been replaced by other modalities, like CT, in the setting of acute upper urinary tract infections because up to 91% of IVUs will be negative in uncomplicated disease [94]. In the low percentage of IVUs that are positive in the setting of acute upper UTIs, enlargement of the kidneys, delayed contrast excretion with persistent or striated appearance of contrast in the renal parenchyma, and compression of the collecting systems are findings [88, 111, 112]. Mass-like appearance is a rare finding [111]. IVU is not sensitive for complications of APN including renal abscess and perinephric collections [113]. Additionally, IVU has a lower sensitivity for detecting renal abscess [114].

Abdominal radiography may still be useful in detecting crescent-shaped gas collections [112] overlying the renal parenchyma in up to 85% of cases of emphysematous pyelonephritis [115]. Calcifications associated with renal tuberculosis infections (putty kidney) can also be seen on abdominal radiographs in the appropriate clinical settings [110]. Fluoroscopy can be used to guide placement of a percutaneous nephrostomy (PCN) tubes for pyonephrosis, which is a medical emergency [111].

Ultrasound

While US is less sensitive than CT, findings of APN on US include ill-defined areas of decreased or increased echogenicity caused by edema and hemorrhage [107]. Secondary signs include renal enlargement, loss of corticomedullary differentiation, and compression of renal sinus fat [111]. Doppler and power Doppler US can improve

sensitivity of hypoperfused parenchymal abnormalities [112].

Mitterberger et al. investigated 100 patients with clinical symptoms of APN and compared contrast pulse-sequence technique ultrasound (use of nonlinear fundamental frequencies and higher-order harmonics allowing high imaging frequencies, up to 14 MHz, to construct real-time perfusion images with high-contrast agent-to-tissue specificity and spatial resolution) to CT. Their study found contrast pulse-sequence US had a sensitivity of 98%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 89% compared to CT as the gold standard [116].

Renal abscess on US can appear as an anechoic or hypoechoic complex mass with increased transmission of sound waves [112]. Mobile echoes in the abscess, septations, loculations, fluid-fluid levels, and fluid-solid interfaces can be seen internally. Dirty shadowing of sound waves is indicative of air in an abscess [113, 117]. The addition of Doppler imaging can also detect renal abscesses and with low velocity scales detect perfusion defects that represent foci of acute renal inflammation, also known as nephritis [118]. US can also be used to guide procedures, such as abscess drainages [113].

In the setting of upper UTIs, US may be used to detect hydronephrosis, hydroureter, and perinephric fluid collections [91]. Furthermore, US is less costly than other cross-sectional imaging modalities and does not use ionizing radiation [114]. Ultrasound can be used to guide procedures for treatment of renal abscess and pyonephrosis [110, 111]. The lack of ionizing radiation can be useful in pregnant patients, and ultrasound is usually considered the first imaging modality of choice for upper UTIs in pregnant patients. However, physiologic pelviciectasis can confound findings of actual obstruction [113].

US can be operator-dependent, limited by in patients with a large body habitus, and is less sensitive than CT for evaluating potential complications of upper tract UTIs [114]. Majd et al. reported a sensitivity and specificity of 74.3 and 56.7% for ultrasound diagnosis of acute pyelonephritis [108]. A study comparing US to CT where

renal abscesses were detected found ultrasound to be normal in 52.1% of patients where abscesses were found on CT [119]. Stojadinovic et al. compared the detection of renal abscess on CT and US and reported that CT reduced the risk missing a renal abscess by 37 times [120].

Debris causing echogenic material in a dilated collecting system on US has a 100% positive predictive value for the diagnosis of pyonephrosis [117]. Gas-forming organisms can cause echoes in the dilated collecting system as well [121]. However, in some circumstances, the shadowing from air can appear similar to shadowing from an obstructing stone, and a radiograph or CT may be needed for differentiation [88].

Computed Tomography

Computed tomography (CT) is considered to be superior to IVU [122] and US [123] in detecting parenchymal abnormalities, delineating disease, and detecting perinephric collections [124], especially multiphase CECT [91]. Yoo et al. found that CT was 81% sensitive for APN as compared to a 33% sensitivity for US [125]. NCCT can be useful for detection of calculi, blood products from hemorrhage, and calcifications in the renal parenchyma that can be obscured on CECT [90, 112]. The nephrographic phase, when the renal cortex and medullary pyramids enhance equally, is the superior phase for detection of APN abnormalities [90]. APN classically appears as a striated nephrogram with ill-defined streaks or triangular areas of decreased enhancement from the papilla to the cortical surface [90, 111, 112], which may be singular or multifocal and unilateral or bilateral [113]. Piccoli et al. found APN was bilateral in 12.6% of cases and multifocal in 79.8% of cases [126]. Delayed scans in the excretory phase may be useful in distinguishing inflammation from tumor by showing delayed enhancement in inflamed areas of previously hypoenhancing regions [112]. It is important to note that in more severe cases of APN, the striated nephrogram appearance can persist for weeks [88, 112].

CT can easily demonstrate other signs of APN, including focal or diffuse swelling of the kidney, inflammatory stranding in the perinephric fat, thickening of Gerota's fascia, and effacement

of renal sinus fat [90, 111, 112]. Especially in diffuse APN, poor enhancement and poor excretion of contrast can be seen [111] and are usually directly proportional to the severity of the infection [113]. Additionally, CT has also been used by Kim et al. to develop a predicative score for patients with APN that may have poor outcomes despite treatment. Six of nine of the criteria are findings found on CT (abscess, pyonephrosis with or without stone, pelvicalyceal air, poor global excretion of contrast, obliteration of the renal sinus, and global renal enlargement); the other three are clinical or laboratory findings (tachycardia or hypotension, persistent fever or pyuria, and diabetes) [127].

CT is the most accurate modality for diagnosis, assessment of extent, and follow-up of abscesses [90, 113, 122, 123]. Piccoli et al. found renal abscesses in 39.5% cases of APN [126]; however, Rollino et al. found 23.5% of patients with APN had renal abscesses [119]. On NCCT, renal abscess appears as a hypoattenuating lesion [112]. After contrast administration, a mature abscess can demonstrate a thick, irregular capsule that can enhance in up to 50% of cases [112, 123]. Renal abscesses can coalesce, spread through the renal parenchyma, and break into the perinephric space [128]. CT can also clearly demonstrate gas in an abscess [112], but this is an uncommon finding [129].

The modality of choice for emphysematous pyelonephritis is CT [111, 112, 130, 131]. Gas can appear linear or as multiple small bubbles that dissect along the planes of the renal parenchyma [124]. Other findings of emphysematous pyelonephritis on CT are large locules of gas, gas-fluid levels, and parenchymal destruction [113]. CT also provides the option of guided drainage as treatment [124].

CT is considered the test of choice for obstruction and detecting pyonephrosis as it can more readily find an underlying cause [90, 112, 124]. Despite NCCT being the gold standard for detection of renal stones, CECT, which is more desirable for detection of infection, has an accuracy of 97% in the detection of ureteral calculi [132]. However, distinguishing pyonephrosis from uninfected hydronephrosis can be difficult [128, 133].

CT findings of pyonephrosis include pelvic and ureteral wall thickening, perinephric fat stranding, renal enlargement, and a striated nephrogram. However, these findings can also be seen in noninfected urinary obstruction [90, 128, 134], but tend to be more severe in pyonephrosis [124, 134]. Specifically, the sensitivity of pelvic wall thickening for pyonephrosis is 76% [134]. Gas within the collecting system, absent of recent instrumentation, is the most accurate indicator of infected fluid [134], but is only occasionally encountered [111, 112].

Magnetic Resonance Imaging

Like CT, MR allows for multiphase dynamic post-contrast imaging which provides additional information for lesion characterization [135]. MRI provides good anatomic information of the kidney, renal pelvis, ureter, and surrounding perinephric tissues [108, 136].

APN appears as areas of low signal intensity on T1-weighted images and increased signal intensity on T2-weighted images with loss of corticomedullary differentiation due to the inflammatory edema [107, 108]. Browne et al. found MRI to be a radiation-free alternative to the diagnosis of APN along with the ability to determine renal function and evaluate the arterial supply and venous drainage of the kidneys [91]. Newer studies have evaluated the use of diffusion-weighted images (DWI) in the diagnosis of APN because such images do not require intravenous contrast material and can be acquired rapidly. De Pascale et al. compared DWI to contrast-enhanced MRI and found DWI had a sensitivity of 95.2%, specificity of 94.9%, positive predictive value of 96.9%, negative predictive value of 92.3%, and accuracy of 94.6% [137]. Faletti et al. found a 94.3% agreement between DWI and contrast-enhanced MRI [138]. Compared to CT, Rathod et al. found that DWI had a higher sensitivity for APN (95.3%) as compared to NCCT (66.7%) and CECT (88.1%) [139].

Renal abscesses on MRI have low and often heterogeneous low T1-weighted signal intensity with increased, heterogeneous T2-weighted signal. The intensity of T1-weighted and

T2-weighted signal depends on the amount of protein, fluid, and cellular debris present [107]. If debris is found, a fluid-fluid level can be present [107]. Martina et al. found renal abscess in 32.5% of cases of APN [140]. DWI and the apparent diffusion coefficient (ADC) values on DWI can be helpful in renal abscess detection. Rathod et al. found that APN had significantly lower ADC values than normal tissue, and renal abscesses had significantly lower ADC values than APN [139].

Pyonephrosis is suggested on MRI if fluid-debris levels are found in the collecting system [141]. Investigations have been proposed to determine if DWI can differentiate hydronephrosis from pyonephrosis. While both are hyperintense on T2-weighted imaging, Chan et al. found pyonephrosis had hyperintense signal on DWI, while hydronephrosis was hypointense [142].

Take-Home Table

Table 25.1 summarizes the sensitivity and specificity of various imaging modalities for the detection of kidney stones, obstructive uropathy, and pyelonephritis.

Imaging Case Studies

Case 1

Figure 25.1a–d presents renal colic: a 35-year-old female with left flank pain.

Case 2

Figure 25.2a–c presents physiologic hydronephrosis of pregnancy: a 22-year-old female in the second trimester of pregnancy with right flank pain.

Case 3

Figure 25.3 presents a 52-year-old diabetic male with urinary tract infection.

Table 25.1 Diagnostic performance for detection of kidney stones, obstructive uropathy, and pyelonephritis

	Sensitivity	Specificity	Reference	Evidence
Kidney stones				
Non-contrast CT	97%	95%	[59]	Strong
Ultrasound	24–57%	79–85%	[37, 38]	Moderate
Radiography	29–72%	71%	[31, 32]	Moderate
Obstructive uropathy				
Combined ultrasound and radiography ^a	79%	90%	[38]	Moderate
Pyelonephritis				
Ultrasound	33–74%	57%	[107, 124]	Moderate
Contrast-enhanced CT	81%	NA	[124]	Moderate

^aLow radiation dose alternative to non-contrast CT with non-contrast considered the reference standard

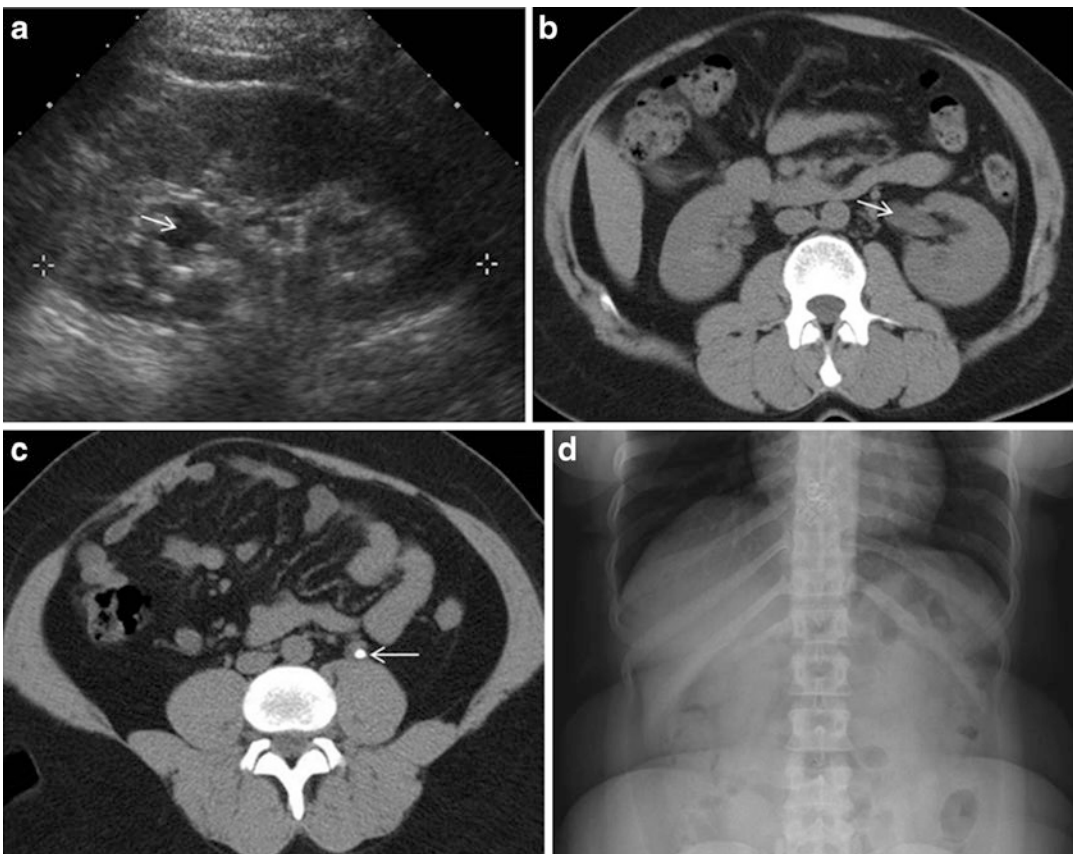


Fig. 25.1 (a)–(d) A 35-year-old female with left flank pain. (a) Initial ultrasound demonstrates mild left hydronephrosis (*arrow*). The mid and distal left ureter was obscured by bowel gas and could not be evaluated. The patient's symptoms did not improve, and she then underwent non-contrast CT to further evaluate for a ureteral calculus. (b) Non-contrast axial CT image at the level of the kidneys demon-

strates mild left hydronephrosis (*arrow*). (c) Non-contrast axial CT image at the level of the mid abdomen demonstrates a 5 mm stone (*arrow*) in the mid left ureter. (d) Abdominal radiograph obtained at the same time as the CT scan does not demonstrate the stone illustrating that not all stones seen at CT are visible on radiographs due to stone composition, stone size, and patient body habitus

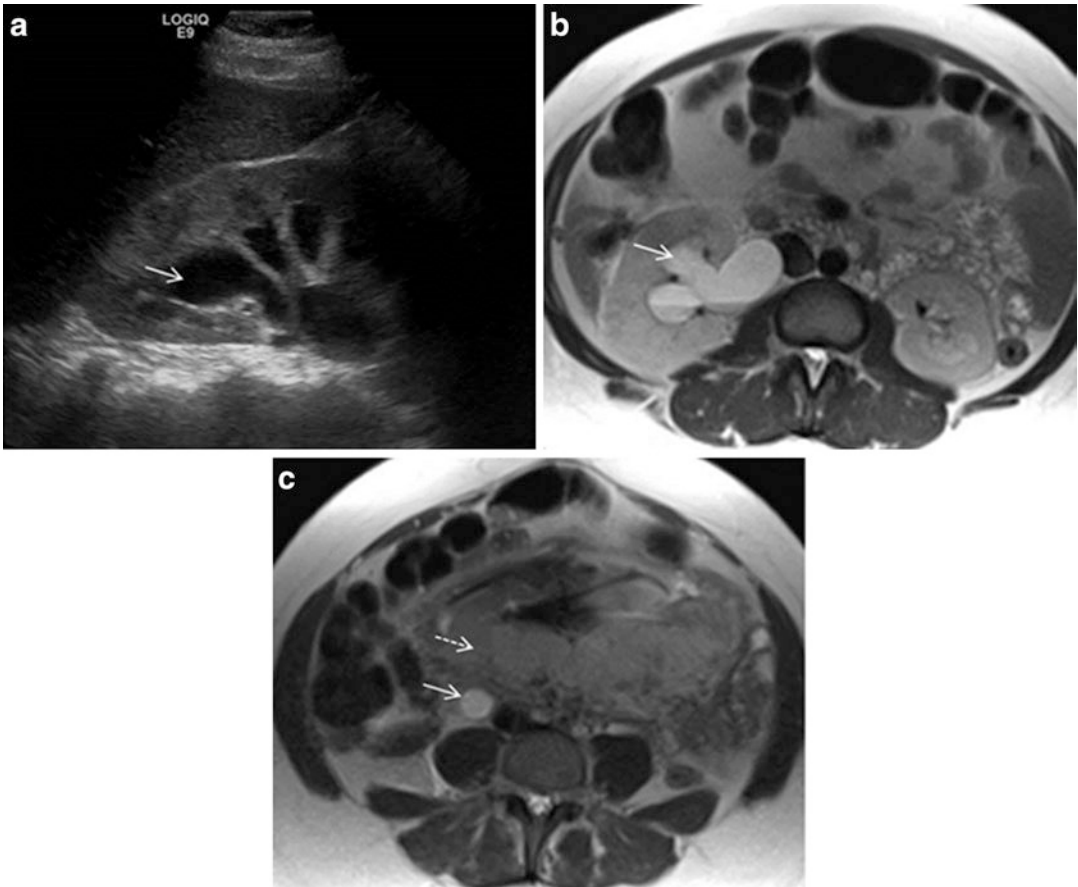


Fig. 25.2 (a)–(c) Physiologic hydronephrosis of pregnancy: a 22-year-old female in the second trimester of pregnancy with right flank pain. (a) Initial ultrasound image demonstrates moderately dilated right renal calyces (arrow) and right renal pelvis indicating moderate right hydronephrosis. The patient then underwent a non-contrast MRI study (b and c) to determine the etiology of

her right-sided hydronephrosis. (b) Axial T2-weighted MR image demonstrates moderate to severe right hydronephrosis (arrow). (c) Axial T2-weighted image demonstrates a moderately dilated right ureter (solid arrow) which is compressed by the gravid uterus (dashed arrow) reflecting physiologic hydronephrosis of pregnancy

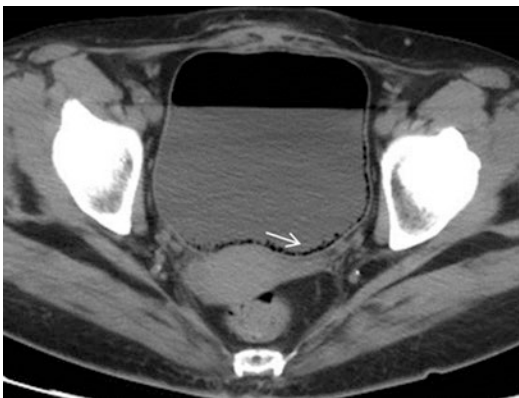


Fig. 25.3 A 52-year-old diabetic male with urinary tract infection. Axial contrast-enhanced CT image demonstrates air in the bladder wall (white arrow), compatible with emphysematous cystitis

Case 4

Figure 25.4a, b presents pyelonephritis: a 36-year-old female with urinary tract infection and right flank pain.

Case 5

Figure 25.5 presents a 45-year-old diabetic male with flank pain.

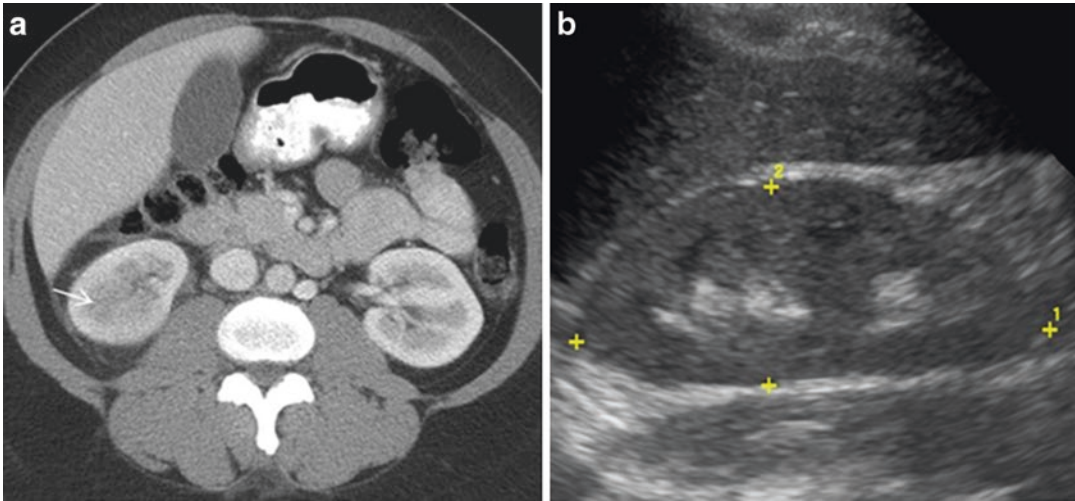


Fig. 25.4 (a) and (b) Pyelonephritis. A 36-year-old female with urinary tract infection and right flank pain. (a) Axial contrast-enhanced CT image demonstrates ill-defined hypoenhancement in the lower pole right kidney (arrow) with perinephric edema reflecting pyelonephritis.

(b) Renal ultrasound of the same kidney demonstrates a normal ultrasonographic appearance of the lower pole right kidney illustrating the relatively low sensitivity of ultrasound as compared to contrast-enhanced CT for the diagnosis of pyelonephritis

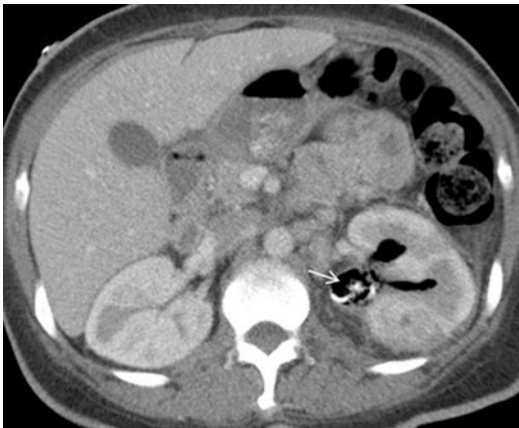


Fig. 25.5 A 45-year-old diabetic male with flank pain. Axial contrast-enhanced CT image demonstrates air in the left renal collecting system compatible with emphysematous pyelonephritis (arrow)

Suggested Imaging Protocols

- To evaluate for renal and/or ureteral stones:
- Low-dose non-contrast CT (renal stone protocol): coverage from 2 cm above kidneys to the symphysis pubis; collimation 2.5 mm; interval 1.25 mm; kVp 120; mA patient weight (lbs.) \times 0.7; viewing on window width and

level of 500 and 50; include coronal and sagittal reformatted images.

- To evaluate for renal parenchymal infection:
- Pre- and post-contrast-enhanced CT: non-contrast scan from 2 cm above kidneys to 2 cm below kidneys; collimation 2.5 mm; interval 2.5 mm; kVp 120; auto mA with min/max (100/575); viewing on window width and level of 500 and 50; post-contrast scan (nephrographic phase) 65 s after injection; coverage from 2 cm above kidneys to the symphysis pubis; delay 65 s; collimation 2.5 mm; interval 1.25 mm; kVp 120; auto mA with min/max (100/575); delayed scan post-contrast (pyelographic phase) 120 s after injection; coverage from 2 cm above the kidney to 2 cm below the kidney; collimation 2.5 mm; interval 1.25 mm; kVp 120; auto mA with min/max (100/575); include coronal and sagittal reformatted images.
- Ultrasound: indicated to evaluate for hydronephrosis; can also detect some kidney stones; can also detect renal parenchymal infection in some cases.
- Radiography: indicated to detect renal and ureteral stones, though accuracy varies based on stone size, stone composition, and patient body habitus.

- Magnetic resonance imaging: non-contrast MR imaging can be performed to evaluate for the site of ureteral obstruction and for parenchymal infection in pregnant patients. This can include pre-scan furosemide 20 mg IV and glucagon 0.5 mg IM, coronal T2-weighted turbo spin-echo images with breath holding, axial diffusion imaging, axial T2-weighted turbo spin echo in breath-hold, axial T2 with fat saturation using respiratory triggering, and coronal T2-weighted images with long TE.

Future Research

- Further CT radiation dose reduction techniques
- Role of contrast-enhanced ultrasound in the detection of pyelonephritis
- Noninvasive renal stone composition determination using dual-energy CT techniques
- MRI as a radiation-free alternative for the diagnosis of obstructive uropathy

Summary

- The best imaging test to identify renal and ureteral stones is low-dose non-contrast CT.
- Ultrasound is a radiation-free alternative for diagnosing hydronephrosis in the emergent setting. Some renal stones will be visible on ultrasound.
- In patients with recurrent lower tract urinary tract infections, with failed treatment, or who have severe symptoms, contrast-enhanced CT should be the imaging modality for diagnosing complications.
- Contrast-enhanced CT should be obtained in patients with upper urinary tract infections that require hospitalization, when there is no clinical response to antibiotics or the patient is immunocompromised or has diabetes mellitus. Contrast-enhanced CT is the best test to evaluate for pyelonephritis or renal abscess.
- Ultrasound and non-contrast MRI are the imaging modalities of choice for pregnant patients or patients with iodinated contrast allergies.

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Acute Abdominal Pain in Pregnant Patients: Evidence-Based Emergency Imaging

26

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Key Points

Imaging in pregnancy must focus on safe and efficient diagnosis of abnormalities in the mother while taking into account fetal well-being, especially exposure to ionizing radiation and intravenous contrast agents.

- Symptoms and clinical findings of appendicitis, cholecystitis, pyelonephritis, and other acute abdominal conditions are not always typical on physical exam during pregnancy. However, maternal and fetal morbidity is often higher, especially if there is delay in diagnosis.
- Most imaging pathways in acute abdominal pain during pregnancy start with sonographic evaluation, but when sonography is equivocal, MRI or CT can be considered second line depending on the pre-test probability (moderate evidence).

- Fetal MRI is safe at 3.0 Tesla or less during second and third trimesters (moderate evidence).
- The use of MRI in first trimester should be restricted to maternal indications for which information provided is clinically important (limited evidence).

List of Abbreviations

ACOG	American Congress of Obstetricians and Gynecologists
ACR	American College of Radiology
ALARA	As low as reasonably achievable
CT	Computed tomography
LLQ	Left lower quadrant
LUQ	Left upper quadrant
MRI	Magnetic resonance imaging
NPV	Negative predictive value
OB/GYN	Obstetrics and gynecology
PPV	Positive predictive value
RLQ	Right lower quadrant
RUQ	Right upper quadrant
SAR	Specific absorption rate
SOGC	Society of Obstetricians and Gynecologists
US	Ultrasound

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Definitions and Pathophysiology

Imaging of patients with acute abdomen during pregnancy presents many challenges. In pregnancy, there are many physiologic changes that occur and become more pronounced as the pregnancy progresses. Intra-abdominal organs may be displaced from their usual position, and physiologic changes associated with pregnancy can mimic pathology in some cases. Also, clinical symptoms at presentation may be atypical, leading to delays in diagnosis.

Epidemiology

Throughout pregnancy, an acute abdomen can be due to obstetric and gynecologic (OB/GYN) causes, or it can be non-OB/GYN causes. Non-OB/GYN acute abdomen presents in approximately 1 in 500–630 pregnancies [1]. Diagnosing these causes of acute abdomen in pregnant women can be challenging because the clinical presentation can be atypical or confusing, at times mimicking normal symptoms of pregnancy. Radiologic evaluation may be necessary, but safety issues such as ionizing radiation to the mother and fetus must be considered.

Overall Cost to Society

As an imaging modality in pregnant patients with acute abdominal pain, sonography is inexpensive compared to MRI and also incrementally less than CT. Sonography is less expensive but has known diagnostic limitations and may perform poorly depending on the pregnant body habitus. The cost of delayed diagnosis includes maternal and fetal morbidity and mortality including increased length of stay in hospital [2]. MRI and CT may provide a more definitive diagnosis, but are more expensive and associated with risks to the mother and fetus, including radiation (CT) and intravenous contrast (MRI and CT).

The exact risk of fetal radiation exposure is unclear and likely depends on dose as well as the stage of development during pregnancy when exposure occurs. It is estimated that a 10–20 mSv fetal exposure may increase the risk of leukemia by 1 in 2000 children exposed to radiation in utero [3]. The background risk of developing this disease is 1 in 3000. Although this can be expressed as a 1.5- to 2.0-fold increased risk of developing cancer, the cost of aborting all fetuses exposed to ionizing radiation would mean that one case of leukemia would be prevented for 1999 normal fetuses aborted [3].

Goals of Imaging

Imaging in pregnancy focuses on timely diagnosis of clinically significant abdominal and pelvic pathology. Efforts are directed at optimizing maternal outcomes, as the best chance for fetal survival is maternal survival.

The ALARA (as low as reasonably achievable) principle should be followed when considering optimal imaging for pregnant patients. Most imaging algorithms for assessing pregnant patients begin with ultrasound, due to a combination of lack of ionizing radiation, fairly ubiquitous imaging access, lower cost, and generally adequate sensitivity and specificity for diagnosing most common acute abdominal abnormalities in pregnancy. However in equivocal cases or when symptoms are discordant, MRI or CT scan should be considered for further evaluation [4].

According to the 2014 SOGC practice guidelines, the use of MRI in first trimester should be restricted to maternal indications for which the information is considered clinically imperative. Of note, exposure to unenhanced, magnetic resonance imaging during the first trimester has not been associated with any long-term sequelae (SOGC level of evidence III-C, limited evidence) (Fig. 26.1) [5]. During the second and third trimesters, fetal magnetic resonance imaging is safe

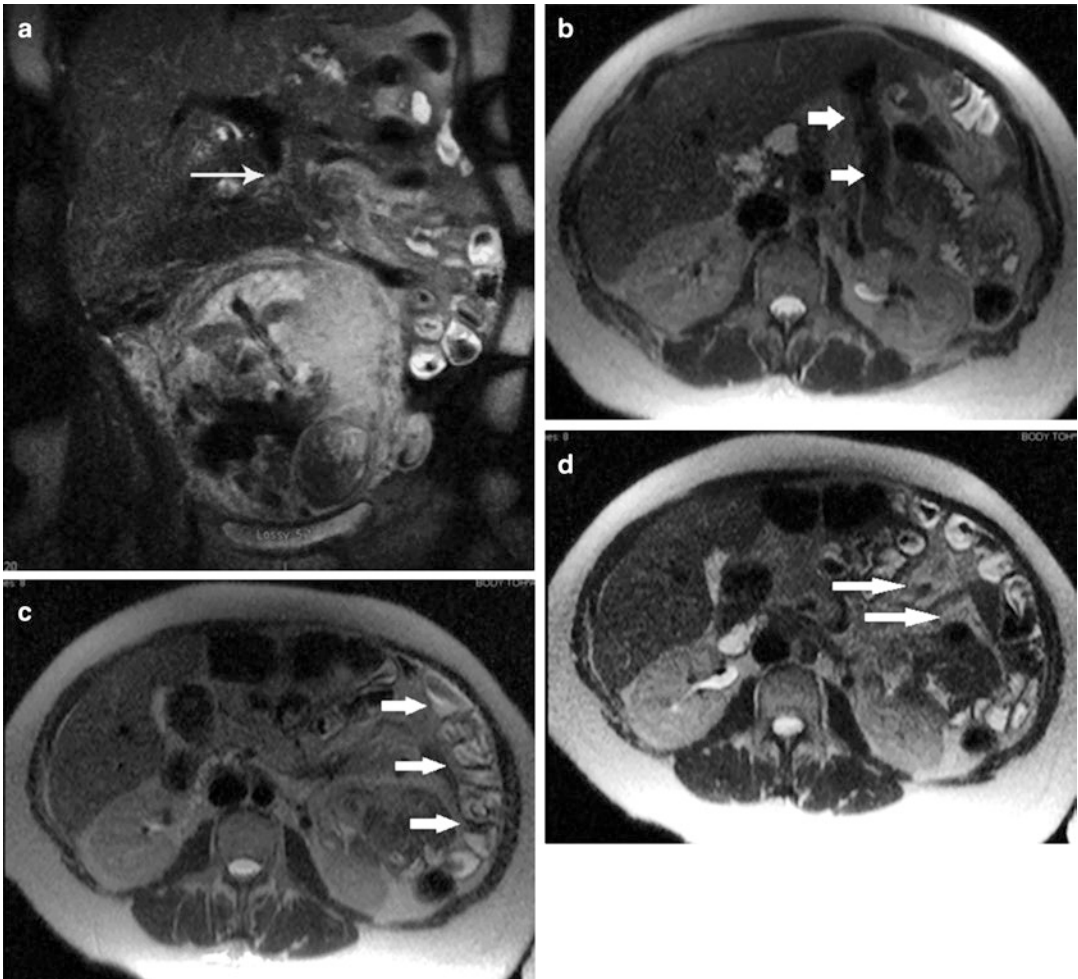


Fig. 26.1 (a)–(d). 29 year old presenting to the emergency department with intermittent, worsening abdominal pain. She had a history of Roux en Y gastric bypass for weight loss 2 years earlier and had achieved significant weight loss prior to pregnancy. MRI was performed without intravenous contrast demonstrating an internal hernia.

Note the beak sign of SMV as it gets twisted (*arrow in a*). There is an unusual loop of bowel travelling anterior to posterior (*arrowheads in b*). Too many bowel loops on left (*arrows on image c*) and there is slight edema in the small bowel mesentery (*small arrows in d*)

up to 3.0 Tesla (SOGC level of evidence II-2, moderate evidence) (Fig. 26.1) [5].

Methodology

“Acute abdominal pain in the pregnant patient.” A literature search was performed of English language articles from 2005 to February 2015, using the MEDLINE database as well as EMBASE and the Cochrane Library. Search terms included the various MeSH terms including diagnostic imag-

ing, appendicitis, bowel obstruction, renal calculi, renal colic, pyelonephritis, gallstones, ectopic pregnancy, abruption, safety, and ovarian torsion combined with the term pregnancy, as well as the MeSH terms computed tomography, ultrasound, sonography, MRCP, and magnetic resonance imaging. Inclusion criteria incorporated systematic reviews, meta-analysis, prospective studies, and retrospective studies related to acute abdomen in pregnancy. Review articles and society position papers related to staging systems on these topics were also sought.

Discussion of Issues

These will be divided into issues which are non-obstetric in nature and then will cover those related specifically to pregnancy.

What Is the Imaging Modality of Choice for Evaluation of the Acute Abdomen in Pregnancy for Non-obstetric Causes?

Right Lower Quadrant Pain: Rule Out Appendicitis

Summary of Evidence The incidence of acute appendicitis in pregnancy is approximately 1 in 1500–1700 pregnancies [6, 7]. Imaging pathways supported by ACR and several obstetrical societies including ACOG and SOGC favor the use of ultrasound as the first imaging modality in most cases (strong evidence), followed by MRI (moderate evidence) [5, 8, 9]. However, the use of CT should not be excluded when maternal safety and health are at stake (insufficient evidence) [5].

Supporting Evidence The diagnosis of appendicitis may be more challenging in pregnant women due to the displacement of the normal location of the appendix by the enlarging uterus. Patients who are pregnant and develop appendicitis are more likely to present with ruptured appendicitis compared to nonpregnant patients, thus increasing risk of maternal morbidity and fetal loss. Performing laparoscopic surgery in cases of negative appendicitis is also associated with a slight increase in premature delivery, and thus the risks and benefits of imaging and intervention must be carefully weighed [10–12].

In pregnant patients with right lower quadrant pain, the ACR recommends starting with an abdominal ultrasound, including graded compression, to look for the appendix. This was given a rating of eight out of nine for appropriateness [6]. Reported sensitivity and specificity of graded compression sonography for appendicitis in pregnancy patients vary depending on stage of pregnancy, patient body habitus, and degree of displacement of the normal position of the appen-

dix by the gravid uterus. Published sensitivity of sonography varies significantly, with older studies reporting sensitivities as high as 85–100% [13, 14], while newer studies which compared ultrasound directly to other cross-sectional imaging modalities reported much lower sensitivities, in the range of 20–36% [14]. Specificity is high with a range of 92–96% [15].

Following an equivocal ultrasound result, MRI without intravenous contrast is the next most commonly recommended imaging. In a study by Pedrosa et al., of pregnant patients with suspected appendicitis, a normal appendix was identified in only 2% of pregnant patients with ultrasound versus 87% on MRI with oral contrast [16].

A meta-analysis by Blumenfeld et al., in 2011, evaluated the use of MRI without intravenous contrast after equivocal ultrasound, for diagnosing acute appendicitis. They demonstrated a sensitivity of 90.5%, specificity of 98.6%, PPV of 90.4%, and NPV of 99.5% [17].

Another pooled analysis performed by Long et al. supported the diagnostic strength of unenhanced MRI for diagnosing appendicitis. The specificity was 98–100% and NPV 94–100%. Authors indicated that finding a normal appendix on MRI was highly accurate in excluding appendicitis (Table 26.2) [18].

When considering CT for diagnosing acute abdominal pathology in pregnancy (including ischemic bowel, bowel obstruction, complications of Crohn's disease, or nondiagnostic findings on MRI and ultrasound), the ALARA principle should be used. Oral and rectal contrasts are rarely required but could be considered on a case-by-case basis. In a meta-analysis by Basaran et al., sensitivity and specificity of CT with intravenous contrast in pregnancy have been reported to be 86% and 97%, respectively [19–21]. Negative predictive value is up to 99% [22].

Cost-Effectiveness Analysis

A study by Katsenberg reviewed cost-effectiveness of various diagnostic modalities used when ultrasound is equivalent for diagnosing appendicitis. The study found MRI to be more cost-effective compared to CT and diagnos-

tic laparotomy, costing \$6767 per quality-adjusted life-year gained. Despite the small increased rates of childhood cancer, CT is more cost-effective than diagnostic laparotomy when MRI is not available [2].

Right Upper Quadrant Pain from Hepatobiliary Causes

Summary of Evidence As in nonpregnant patients, sonography is the imaging modality of choice for assessing the gallbladder for calculi. This is given a recommendation of nine out of nine by the ACR appropriateness guidelines (strong evidence) [6]. MRCP is the next preferred test in cases of inconclusive US (insufficient evidence) [6].

Supporting Evidence Cholelithiasis is present in 12% of pregnant women, but symptomatic in only 0.1–0.3% [23]. Other considerations of RUQ pain in pregnant women include HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome, fatty liver of pregnancy, as well as Budd-Chiari syndrome (which pregnant women are at increased risk for due to their hypercoagulable state). In addition, other considerations of hepatobiliary abnormalities which are not necessarily related to pregnancy itself need to be considered. This includes acute hepatitis, pancreatitis, and primary sclerosing cholangitis [24]. Finally, in pregnant patients presenting with RUQ pain, the diagnosis of acute appendicitis should still be considered, since the cecum is progressively displaced cranially by the gravid uterus and, thus, acute appendicitis, particularly in the third trimester, can present with symptoms referred to the right upper quadrant [25].

ACR appropriateness criteria rated ultrasound as nine out of nine in pregnant women with fever and leukocytosis [26]. Ultrasound in pregnant and nonpregnant patients has high positive and negative predictive values (92.2% and 95.2%, respectively) for diagnosing cholecystitis [27]. However sensitivity of ultrasound in the detection of common bile duct stones is lower, with some publications quoting sensitivity of only 20–38% [28].

MRCP is considered eight out of nine for pregnant patients with right upper quadrant pain according to the ACR appropriateness criteria [26]. This is considered the preferred test to follow an inconclusive US. It is useful to evaluate the entire biliary system and to assess other causes of acute abdominal pain without exposing the patient to ionizing radiation [25].

According to the meta-analysis in nonpregnant patients by Kiewiet et al., the summary sensitivity for MRI is 85% (95% CI: 66%, 95%) and specificity is 81% (95% CI: 69%, 90%) with similar diagnostic performance expected in the earlier stages of pregnancy [29].

Acute Bowel Pathology: Bowel Obstruction

Summary of Evidence Intestinal obstructions complicate between 1 in 1500 and 3000 pregnancies. Maternal and fetal mortality rates have been noted to be as high as 6% and 25%, respectively [30, 31]. ACR appropriateness guidelines give MRI a recommendation of 4/9 for assessing small bowel obstruction, but specifically indicate that this is the most appropriate imaging for pregnant women, in addition to children (moderate evidence) [32]. According to the SOGC 2014 recommendations for imaging in pregnancy, gadolinium contrast agents may be used in pregnant women when the benefits outweigh the potential risks (SOGC level of evidence III-C, limited evidence) [5]. As with appendicitis, use of CT for suspected bowel obstruction, or ischemic bowel, should not be excluded when maternal safety and health are at stake (SOGC level of evidence III-C, limited evidence) [5].

Supporting Evidence Most bowel obstruction is related to adhesions, though volvulus, hernias, and other causes have been reported. Crohn's disease should also be considered in the differential diagnosis, particularly if the patient has a prior history of this diagnosis. In patients post Roux-en-Y gastric bypass, there is an increased risk of internal hernia (including Petersen-type hernia and jejuno-jejunal anastomosis hernias) [33, 34].

MRI should be considered for evaluation of the location of the transition point and cause of

obstruction, particularly in clinically stable patients with signs of partial or incomplete obstruction. T2-weighted images including HASTE or True FISP may be used for anatomic evaluation. Fat-saturated T2-weighted images also depict free fluid and edema around bowel loops [34, 35]. Specific absorption rate (SAR) limits should be observed in all cases of MRI when used in pregnancy. These SAR limits are determined for each pulse sequence to ensure that the increase in body temperature is less than 0.5 °C [36]. Gadolinium-containing intravenous contrast agents are considered category C medications by the US Food and Drug Administration and are generally not recommended in pregnancy [37]. However the SOGC recommends using gadolinium contrast materials in pregnant women when the benefits outweigh the risks [5]. This was given a SOGC level III-C grading recommendation (limited evidence) (Table 26.1) [5].

In comparison, according to publications by Bourjeily and Atwell, there have been no documented cases of neonatal hypothyroidism from the use of water-soluble iodinated contrast agents used for CT. Given that all newborns are already screened for congenital hypothyroidism at the time of their birth, no extra attention is necessary if a fetus is exposed to CT-iodinated contrast agents in utero [38, 39].

There are situations after birth where new mothers require urgent MR imaging. In these cases, SOGC guidelines indicate that the use of gadolinium in a lactating patient is safe and lactation can continue without any need to stop for any period of time [5]. This was based on a study published by Chen which indicates that only 0.1% of intravenously injected gadolinium is excreted via the mother's milk and, of that, only 1% is absorbed by the lactating baby [37].

Flank Pain: Renal Colic

Summary of Evidence Sonography is the preferred imaging modality to assess the kidneys, ureters, and bladder during pregnancy. This is supported by ACR, ACOG, and SOGC recommendations (strong evidence) [5, 6, 10]. No clinically significant biological effects have been reported with in utero exposure to sonography.

Table 26.1 Canadian task force on preventive health care (SOGC) gradation of levels of evidence

Level	Quality of evidence assessment
I	Evidence obtained from at least one randomized controlled trial
II-1	Evidence is from well-designed controlled trials but without randomization
II-2	Evidence is from well-designed cohort or case-control studies, preferably from >1 research group
II-3	Evidence is obtained from comparisons between times and places with or without the intervention. Dramatic results in uncontrolled experiments
III	Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees
Grade	Classification of recommendations
A	Good/strong evidence to recommend the clinical/preventive action
B	Fair/moderate evidence to recommend the clinical/preventive action
C	Current evidence is conflicting. No recommendation for or against the use of a clinical/preventive action. Other factors may influence decision-making
D	Fair/moderate evidence to recommend against the clinical preventive action
E	Good/strong evidence to recommend against the clinical preventive action
L	Insufficient evidence to make a recommendation.

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However, Doppler US can produce high-intensity energy and should be used judiciously. As a second-line option, non-contrast MR urography (MRU) is a safe and viable option (limited evidence).

Supporting Evidence 1 in 3300 pregnancies is affected by ureteral calculi [40]. Most calculi pass on their own, but up to 30% may cause some degree of renal obstruction, leading to increased risks of complications including superimposed infection and premature labor [41]. Anatomical changes in the renal collecting system in pregnancy include dilatation of the renal calyces and ureters due to the compression by the pregnant

uterus in addition to the effect of progesterone on the ureteral smooth muscle. These findings are more commonly seen on the right side during the late second and early third trimesters of pregnancy, and the appearance can mimic true hydronephrosis from pathologic obstruction [42].

Sonographic evaluation for ureteric calculi is complicated by overlapping features of physiologic dilation of the renal collecting system of pregnancy which is seen in 60 to over 90% of pregnant patients, more often in the third trimester due to compression of the ureter by the enlarging, gravid uterus. The absence of ureteric jets is not especially helpful for differentiating calculi from physiologic obstruction since 15% of asymptomatic pregnant women have been shown not to have ureteric jets [43].

Resistive index (RI) calculation (peak systolic velocity of intrarenal blood flow minus the end-diastolic velocity divided by the peak systolic velocity) has shown some promise in pregnancy with a value of 0.7 to have moderate sensitivity and specificity (77% and 83%). Also, a change in RI of >0.06 has also been shown to be associated with acute obstruction [44]. However, these techniques are not specifically recommended by ACR, ACOG, or SOGC. Computed tomography has a higher sensitivity (93% vs. 79%) and NPV (71% vs. 46%) for the detection of calculi when compared to sonography. The combination of calculi plus obstructive signs has sensitivity and specificity of 100% for CT and of 100% and 90%, respectively, for US. The 11 calculi which were not detected by US in this study all passed spontaneously (10 were <5 mm) [45]. Both techniques showed similar extrarenal pathology. Computed tomography is the most accurate technique for the detection of ureteral calculi. However, the combination of radiography and US is an alternative to nonenhanced CT with good practical value, even if the sensitivity and specificity are somewhat lower.

As second-line imaging, MR urography (MRU) is a safe and viable option. In MRU during pregnancy, the pyelocalyceal system and the ureters are visualized using heavily T2-weighted images. Currently, MRU, not CT urography, is the preferred imaging test in children and pregnant patients with dilated collecting systems

based on the ALARA principle which aims to minimize the use of ionizing radiation in these patient populations. However, few studies have assessed PPV, NPV, and accuracy of MRU, nor have comparison studies been performed comparing accuracy of MRU to CT urography [20].

Pathologic obstruction of the ureter is characterized by an abrupt caliber change of the ureter, enlargement of the kidney, and, in optimal circumstances, visualization of the obstructing calculus in the ureter. In comparison physiologic dilation typically seen associated with pregnancy occurs in the mid ureter with gradual tapering. MR is relatively insensitive for the detection of calcium-containing structures, including calculi; thus the diagnosis of ureteral calculi often relies on detecting secondary signs of obstruction [46]. Some of these secondary signs visible on MRI include the presence of a standing column of urine below the level of the pelvic brim, an abrupt ending of the ureter (implying an obstructing calculus at this point), and the presence of perinephric or peri-ureteral edema [46].

Although the protocol for MRU in pregnancy varies between institutions, it is performed without intravenous contrast. Sequences typically include using coronal and axial half Fourier single-shot turbo spin-echo sequence (HASTE). T2-turbo spin-echo sequences with fat suppression may provide more detailed T2-weighted information and detect filling defects in the ureters. T1-weighted images with in- and out-of-phase imaging may help detect blood (bright on T1-weighted images) or fat-containing lesions [47].

Trauma

Summary of Evidence

1. Trauma is the leading non-OB/GYN cause of maternal death, and all efforts are directed to maximize maternal outcomes in order to provide best chances for fetal survival. In patients who are hemodynamically unstable, urgent surgical intervention is warranted, often bypassing any cross-sectional imaging. In clinically stable pregnant patients, the type of imaging chosen depends on location of injury and severity [48].

2. Sonography can be used initially if the mother is clinically stable, and fetal viability can be assessed, but a negative US in the setting of high clinical suspicion does not exclude traumatic injury. In addition, a negative US does not exclude placental abruption. When serious injuries are suspected, then contrast-enhanced CT is warranted (moderate evidence) [49].
3. CT is warranted to evaluate for trauma, and the risks of iodinated contrast and ionizing radiation are outweighed by the benefit of having a timely, accurate diagnosis to direct medical and surgical care (moderate evidence) [50].
4. Trauma patients may undergo repeat CT scans depending on their injuries and hospital course which may expose the fetus to higher doses of ionizing radiation. Fetal doses below 50–100 mGy are not a reason for termination, and a standard CT of the abdomen and pelvis is in the range of 25 mGy [8, 9]. With repeat exposure to CT scans, consultation with a radiation physicist and genetic counselor should be considered.

Supporting Evidence Trauma affects 7% of pregnant women, with the highest incidence occurring in the third trimester, most frequently due to MVC, followed in frequency by assault and falls [23, 48, 49]. The rate of fetal loss from trauma is dependent on severity of the trauma and area of injury. Obstetric complications from trauma include placental abruption, uterine rupture, direct injury of the fetus, and maternal demise leading to fetal demise. Non-obstetric trauma includes all other abdominal organs; however, splenic rupture is the most commonly organ injured, leading to free intraperitoneal blood [51]. In a study by Brown et al., sensitivity of ultrasound for detecting blunt abdominal trauma was 80%, and specificity was 100% [52]. However, when high-energy trauma is reported, a negative ultrasound should not preclude additional imaging when clinical symptoms warrant it.

In the setting of trauma when CT is being considered for diagnostic purposes, intravenous iodinated contrast agents are necessary for detec-

tion of solid organ injury. Maternal and fetal risks related to CT imaging include exposure to ionizing radiation and to iodinated contrast. Potential effects of ionizing radiation to the fetus are teratogenic and carcinogenic. Neither effect is considered significant at a standard CT abdomen and pelvic dose of 25–30 mGy, and the small risk incurred from ionizing radiation is outweighed by the benefit of a definitive diagnosis provided by the CT study which could avoid potential maternal and fetal morbidity and mortality from delayed or missed diagnosis [5, 50].

Neonatal hypothyroidism has been associated with some iodinated agents taken during pregnancy. However, given the doses used for a single CT, the risks are considered very low [50]. Breastfeeding can continue after administration of iodinated contrast agents [53].

What Is the Imaging Modality of Choice for Evaluation of the Acute Abdomen in Pregnancy for Obstetric Causes?

Ectopic Pregnancy

Summary of Evidence Ectopic pregnancy affects 1–2% of pregnancies and presents with abdominal pain in the first trimester. It is a leading cause of pregnancy-related morbidity and mortality [54]. Ultrasound is the recommended modality to assess a suspected ectopic pregnancy, in addition to any other cause of first trimester bleeding (strong evidence). The use of sonography has been given an appropriateness criteria rating of nine out of nine by the ACR (strong evidence) [55]. However, non-contrast-enhanced MRI can also be used for this diagnosis, particularly when ultrasound findings are equivocal. The ACR appropriateness rating is six out of nine (moderate evidence) [55].

Supporting Evidence During sonographic evaluation, the presence of a yolk sac within a gestational sac in the endometrium is the first definitive sign of an intrauterine pregnancy. Other specific imaging findings which are helpful for identifying an intrauterine pregnancy include the pres-

ence of a “double decidual sign.” This finding has been found to be nearly 100% specific (though only 64% sensitive) for early intrauterine pregnancy [56].

Assessment of the adnexal regions is still recommended when an intrauterine gestation is identified. This is done to rule out other abnormalities that may be the cause of pain including rupture of a corpus luteum cyst, ovarian torsion, or, very rarely, a heterotopic ectopic pregnancy, which occurs in 1:10,000 cases [57]. A heterotopic pregnancy is defined as one gestational sac within the endometrial cavity, and a concomitant gestation elsewhere, usually in the adnexa. This occurs more commonly in women who are using assisted fertility techniques [57].

Abruption

Summary of Evidence Ultrasound should be used to evaluate for suspected placental abruption but is limited in sensitivity; a negative ultrasound does not exclude the presence of placental abruption (limited evidence). The role of CT remains controversial: although placental abruption can be identified by CT, the overall performance has not been compared to US (insufficient evidence). Given the risk of ionizing radiation, CT is not the recommended test to diagnose placental abruption. The accuracy of MRI to diagnose placental abruption has not been assessed in studies (insufficient evidence).

Supportive Evidence Placental abruption, in which the placenta separates from the uterus usually due to shear forces, occurs in 1% of pregnancies and can lead to fetal death in 20–60% [58, 59]. Placental abruption is the most common injury to the uterus after blunt trauma, occurring in 30–50% with major trauma [48, 60]. This diagnosis is the leading cause of vaginal bleeding in the second half of pregnancy, affecting 15–30% with third trimester bleeding, and is a significant cause of morbidity and mortality to the fetus. The larger the abruption, the worse the fetal outcomes, with abruption involving more than 50% of the placenta frequently associated with fetal death [48, 61]. When the mother is hemodynamically stable, ultrasound is used to assess for pla-

cental abruption. However, the sensitivity is limited, with 50–80% of cases undetected by sonogram, i.e., false negative [62, 63]. The evidence supporting the accuracy of CT in diagnosing placental abruption is weak, with studies limited by small sample size or the lack of a reference standard [58, 64]. Although the sensitivity for CT was found to be 100% for both readers in one study [58], the sensitivity was 42% based on the original dictated report, and the false-positive rate was as high as 20%, suggesting that directing the readers’ attention to the possibility of placental abruption increased their awareness of looking for the condition but also resulted in overcalling. Due to ionizing radiation, CT should not be used to diagnose placental abruption. However, in instances when CT is obtained in a pregnant patient, the radiologist should be aware of the appearance of placental abruption. No studies have been performed to assess the comparative accuracy of ultrasound to CT, nor have studies been performed to assess the accuracy of MRI for diagnosing placental abruption.

Ovarian Torsion

Summary of Evidence Sonography is the imaging modality of choice to make this diagnosis [65], and the ACR appropriateness guidelines recommend transabdominal and transvaginal ultrasound to diagnose this condition as well as other causes of acute gynecologic pain in pregnant women (strong evidence) [9]. These recommendations are given a rating of nine out of nine. However, MRI can also be used for this diagnosis, particularly when ultrasound findings are equivocal (strong evidence). The ACR appropriateness rating is six out of nine [9].

Supportive Evidence Ovarian torsion is considered a surgical emergency requiring untwisting when possible. Oophorectomy may be required if the diagnosis is delayed. Up to 20% of ovarian torsion cases occur during pregnancy, and this is an important differential diagnostic consideration of the acute abdomen. Imaging findings of torsion, regardless of the modality used, include an enlarged ovary, more centrally located in the pelvis, with associated thickening of the fallopian

tube. Often on sonography a swirling of vessels in the adnexal area can be identified particularly on cine clips [66]. These imaging findings help to differentiate torsion from other nonsurgical diagnoses such as pelvic inflammatory disease [67].

T2-weighted images are most commonly used to assess for suspected ovarian torsion when using MRI [68]. On T2-weighted images, the acutely torsed ovary is typically enlarged and edematous, which is reflected by some degree of higher signal intensity in the stromal tissue. Ovarian follicles are arranged peripherally and may contain hemorrhage which is readily detected by MRI. Most hemorrhagic ovarian follicles or cysts are imaged in the subacute phase of extracellular hemoglobin when they are hyperintense on T1 weighting and can be high or intermediate to low signal intensity on T2-weighted images. Old blood products are comprised of hemosiderin and are hypointense on T1W and T2W [68].

Take-Home Tables and Figure

Table 26.1 lists the SOGC gradation of levels of evidence, and Table 26.2 summarizes the sensitivity and specificity of US and MRI for diagnosing acute abdomen in pregnancy. Figure 26.1 is an imaging algorithm for pregnant patients present with acute abdominal symptoms.

Take-Home Points

In pregnant patients presenting with acute abdomen from any cause, abdominal US is the usual first imaging modality recommended, followed by non-contrast-enhanced MRI. These imaging modalities have excellent safety profiles for both the mother and fetus. However, there are cases where CT should be considered, especially if other imaging is inconclusive or unavailable. Also, for pregnant patients with suspected serious traumatic thoracic or abdominopelvic injuries, further evaluation with CT is warranted:

- Efficient triage of pregnant patients with abdominal pain in all three trimesters is

needed to reduce risk of morbidity and mortality of the mother and fetus.

- When considering any imaging, especially when considering CT, the principle of ALARA should be followed while still allowing a technically diagnostic imaging study to be performed.
- Written consent should be obtained when imaging pregnant women with CT or MRI [23].

Imaging Case Studies

Case 1

Figure 26.2a–d discusses a 29-year-old woman with a history of Roux-en-Y gastric bypass who presents to the ER with intermittent, worsening abdominal pain

Case 2

Figure 26.3a–d discusses a 24-year-old woman, 15 weeks pregnant, with right upper quadrant pain

Case 3

Figure 26.4a, b discusses a 33-year-old woman, 29 weeks pregnant, who has upper and lower abdominal pain following a motor vehicle accident at 70 km/h

Case 4

In Fig. 26.5, a 30-year-old woman, 16 weeks pregnant, presents with right upper quadrant pain

Suggested Imaging Protocols

- (a) Sonography is recommended by ACOG and ACR appropriateness criteria when assessing pregnant patients with abdominal pain from obstetric and non-obstetric causes. The use

Table 26.2 Summary of sensitivity and specificity for US and MRI for diagnosing acute abdomen in pregnancy

Disease	Modality	Sensitivity	Specificity	Predictive Values	Comments
Appendicitis	US	Wide range reported in the literature	92–95%		Depends on stage of pregnancy, patient body habitus, etc.
	MRI	90.5%	98.6%	PPV = 90.4% NPV = 94–100%	
Acute cholecystitis	CT	86%	97%	NPV = 99%	
	US	92%	95%		
	MRCP	81%	85%		
Renal colic	US	79–90%			
	CT	93–100%	>98%		
	MRI	–	–	–	Insufficient evidence
Trauma (hemodynamically stable)	US	80%	100%	–	Brown et al. [46]

US ultrasound, CT computed tomography, MRI magnetic resonance imaging, MRCP magnetic resonance cholangiopancreatography, PPV positive predictive value, NPV negative predictive value

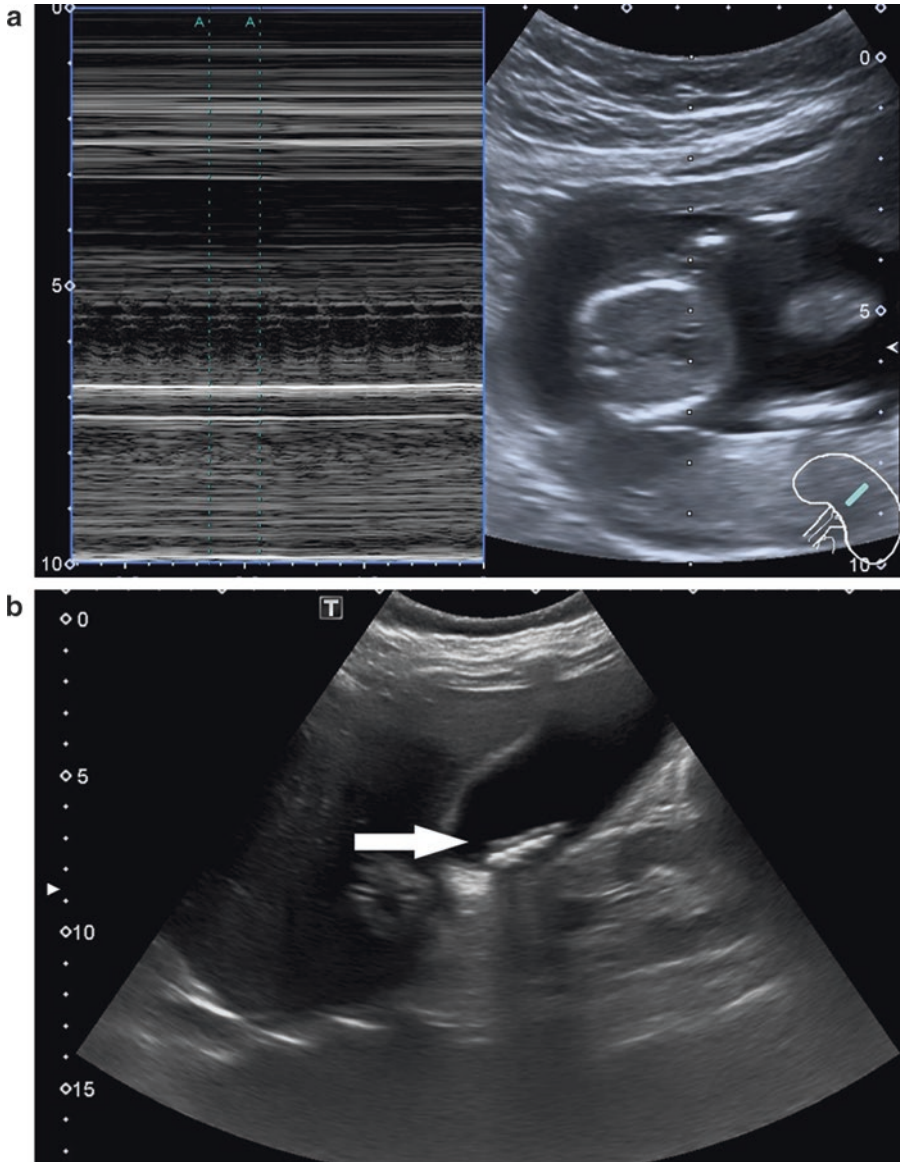


Fig. 26.2 (a)–(b) 24 year old woman, 15 weeks pregnant () presents with right upper quadrant. Sonographically, there were gallstones in the gallbladder (arrows in b) and

a sonographic Murphy’s sign. However, there was no significant gallbladder wall thickening

of graded compression, whereby increasing pressure is placed on the abdomen to displace overlying bowel loops out of the field of view, is specifically recommended by the ACR appropriateness criteria particularly in cases of suspected appendicitis [9, 10].

(b) MRI is often considered the second-line imaging in pregnancy when sonographic findings are equivocal in non-trauma cases:

- Written consent should be obtained prior to performing MRI in a pregnant patient. Of note, no long-term sequelae have

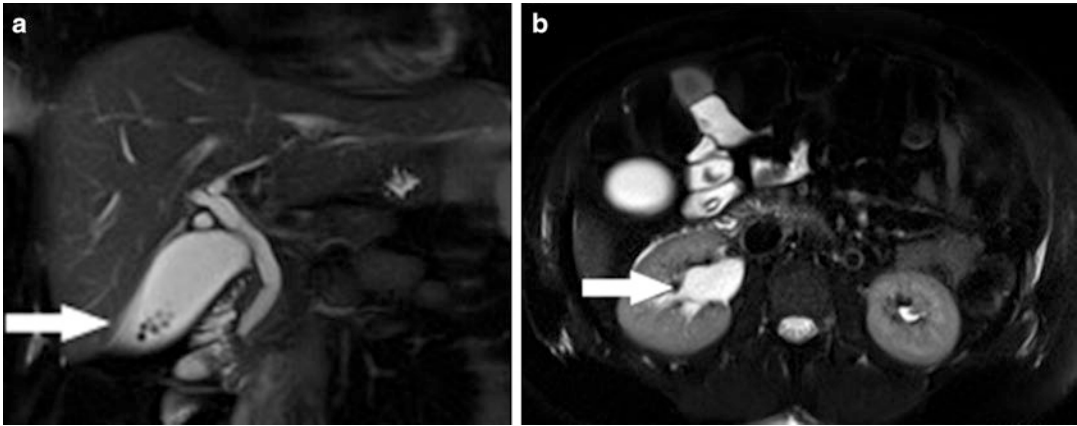


Fig. 26.3 (a)–(b) The pain worsened the next day, thus a MRI was performed. On the T2 weighted images, there was visualization of the gallstones (arrow in a) and some distension of the gallbladder but no CBD calculi and no pericholecystic fluid or significant gallbladder wall thick-

ening. Incidental note was made of physiologic dilation of the right renal collecting system (arrow in b) which persisted throughout the pregnancy but resolved after delivery

been identified in cases of inadvertent MRI exposure in first trimester [5]. Imaging should be tailored to the area of concern and should be overseen by a radiologist to obtain only those sequences which are required to make the diagnosis. One of the goals is to reduce the SAR (specific absorption rate) of deposited energy and heat in the patient and fetus.

- Multi-planar, single-shot fast spin-echo T2-weighted images are most commonly used initially to get an overview of the area of concern.
- Fast spin-echo T2-weighted fat-suppressed images of the abdomen are used to identify edema and free fluid.
- Unenhanced T1-weighted images, in- and opposed-phase images, can be used to look for intracellular fat. T1-weighted fat-saturated images can be used to look for

blood products as well as lesions containing fat (e.g., dermoid).

- Axial bright blood vascular sequences (without saturation bands above or below) can help differentiate blood vessels from the appendix.
 - MRCP can be used in cases of pancreaticobiliary abnormalities
- (c) CT should be considered when maternal symptoms warrant further imaging and sonography is inconclusive or nondiagnostic and in the trauma setting. CT is a significant consideration in cases of acute ischemic bowel where intravenous contrast is required (especially since gadolinium contrast agents in MRI are considered class C drugs). When CT is being considered, the area of concern should be adequately collimated to reduce the cranio-caudal extent of scanning when possible. Intravenous contrast may be used as needed.

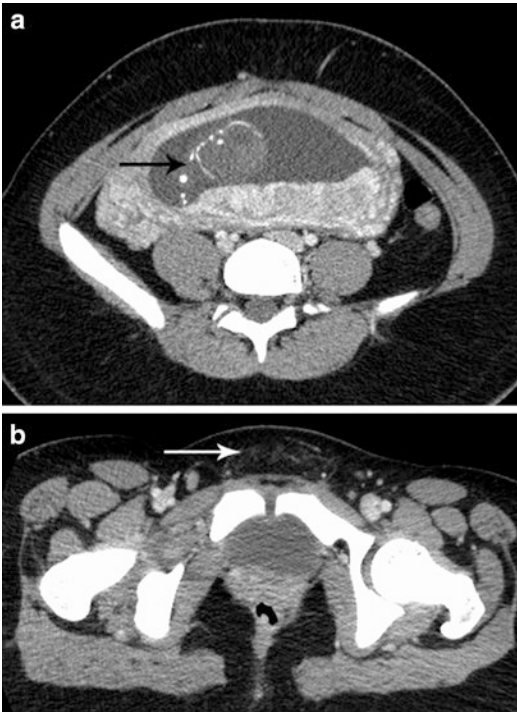


Fig. 26.4 (a)–(b) 33 year old, 29 weeks pregnant (*arrow in a*) was in a motor vehicle accident at 70 km/h. She presented with upper and lower abdominal pain. She was hemodynamically stable and although the initial sonogram in the emergency department did not show free fluid, she underwent CT to exclude occult solid organ injury. All solid organs were intact. Only some bruising was noted over the lower, anterior pelvis from the seatbelt (*arrows in b*). The patient was observed in hospital for 24 hours and then discharged home in good condition

Future Research

- Long-term safety of exposure to MRI and gadolinium-based contrast materials in utero
- Radiation risks to fetus from intrauterine exposure to ionizing radiation
- Positive predictive value and negative predictive value of MR urography in assessing renal and ureteric calculi in pregnancy

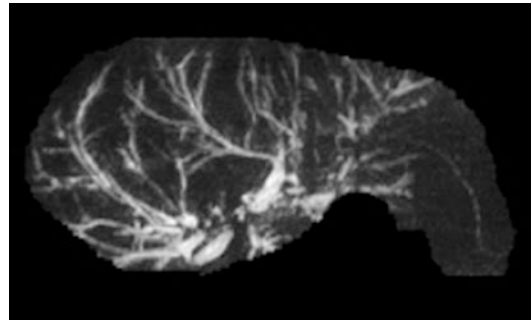


Fig. 26.5 30 year old woman presented with right upper quadrant pain but no discrete abnormality seen on ultrasound (not shown). However, on the MRCP images, note was made of several focal areas of narrowing with interspersed beading of the intrahepatic bile ducts. This was a first presentation of primary sclerosing cholangitis. 6 months post-partum, the patient was also diagnosed with Crohn's disease

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Acute Pelvic Pain in Premenopausal Women, Children and Infants: Evidence- Based Emergency Imaging

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Key Points

- Ultrasound (US) is the recommended initial imaging tool for pregnant and nonpregnant women and girls presenting with acute pelvic pain and in which a gynecological etiology is suspected (strong evidence).
- Transvaginal ultrasound is the single best diagnostic modality for the detection of ectopic pregnancy (strong evidence).
- In menstruating women and adolescents, pregnancy (orthotopic or ectopic) should

always be considered as a cause of abdominopelvic discomfort/pain (moderate evidence).

- Doppler US is useful in the diagnosis of ovarian torsion but cannot rule out or rule in this diagnosis (moderate evidence).
- If US is nondiagnostic and the clinical picture remains uncertain, magnetic resonance imaging (MRI) can be performed as the next imaging test and problem-solving tool, particularly in pregnant patients (moderate evidence).
- If US is indeterminate and the clinical picture remains uncertain, and MRI not available, CT can be considered as an alternative imaging test in nonpregnant women (moderate evidence).

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Definitions and Pathophysiology

Acute lower abdominal and pelvic pain in premenopausal women has a wide range of etiologies including gastrointestinal, urological, obstetrical, and gynecological causes. In girls and female adolescents, acute pelvic or lower abdominal pain is mainly associated with gastrointestinal disorders, but may be secondary to a wide range of gynecological disorders [1, 2]. In adolescents, a gynecological process is more commonly the cause for acute pain than appendicitis. Klein et al. diagnosed pelvic inflammation or a gynecological process (including pregnancy) in 20% of girls over 12 years of age with acute pain, whereas appendicitis was only found in 4% [3]. Gynecological disease (adnexitis or ovarian cysts) was identified in 12% of children, adolescents, and young adults following negative appendectomy for a preoperative diagnosis of appendicitis in the study by Puig et al. [4]. Specifically, in younger patients, it is difficult to localize the pain during both history and physical examination, making it a diagnostic challenge.

Acute pelvic pain is defined as that lasting less than 3 months [5]. Gynecological or obstetric symptoms are often nonspecific, and the clinical presentations of the various conditions overlap and can vary. In adolescents and premenopausal women, a gynecological or obstetrical etiology should always be considered, and it is crucial before diagnostic workup to determine whether the patient is pregnant or not as this will influence the imaging workup [6, 7]. Many of the potential conditions (such as gastroenteritis, appendicitis, diverticulitis, ureteric colic, etc.) are discussed in other chapters of this book. In this chapter, we focus on five common gynecological conditions [ovarian torsion, hemorrhagic or ruptured ovarian cysts, ectopic pregnancy, endometriosis, and pelvic inflammatory disease (PID)], which can present as acute pelvic pain, some of which may be potentially life-threatening and potentially impact fertility.

Ectopic pregnancy should be suspected in any pregnant woman presenting with acute pelvic pain [8]. The classic triad for ectopic pregnancy after the confirmation of pregnancy at a specific

β -hCG discriminatory level is pelvic pain, vaginal bleeding, and an adnexal mass. Most ectopic pregnancies are located in the fallopian tube, and of these, 75–80% are ampullary, 10% are isthmic, 5% are fimbrial, and 2–4% are found in the interstitial portion [9]. The most common underlying cause of ectopic pregnancy is salpingitis due to previous pelvic infections, and in one surgical study, almost 50% of patients had clinical history or histological findings of acute salpingitis [10]. Other causes include altered ciliary motility in the oviduct due to hormonal imbalances or tobacco abuse, altered tubal architecture from pelvic masses, adhesions from prior tubal surgeries, and abnormal embryonic development. These processes result in fallopian tubes having decreased luminal diameters or altered architecture resulting in the fertilized oocyte, or embryo, having difficulty navigating the length of the tube to the intrauterine cavity. The comparatively smaller spermatozoa can travel distally resulting in fertilization, and if the delay in passage of the fertilized oocyte or embryo exceeds 7 days of gestational age, then implantation occurs in the fallopian tube rather than in the uterus.

Pelvic inflammatory disease (PID) is often associated with *Chlamydia trachomatis* and/or *Neisseria gonorrhoeae* infections [11, 12]. The hallmark of diagnosis is pelvic tenderness combined with inflammation of the lower genital tract, from the cervix to the peritoneal cavity [11, 13]. Recently, Lis et al. presented a meta-analysis including ten studies published between 1987 and 2012, showing that *Mycoplasma genitalium* infections are associated with an increased risk of PID (pooled OR 2.14, 95% CI, 1.31–3.49) [14]. Other microorganisms of the vaginal flora including anaerobes, streptococci, staphylococci, *Escherichia coli*, and *Haemophilus influenzae* may also be involved in the etiology of PID [11, 15, 16]. The infection spreads from the vagina to the fallopian tubes and leads to pelvic pain, vaginal discharge or dyspareunia, endometritis, salpingitis, parametritis, oophoritis, tubo-ovarian abscess, and/or pelvic peritonitis [12]. The clinical diagnosis of PID is based on the finding of pelvic organ tenderness, as indicated by cervical motion tenderness, adnexal tenderness,

or uterine compression tenderness on bimanual examination, in conjunction with signs of lower genital tract inflammation [11]. A palpable adnexal mass may be seen in PID complicated by tubo-ovarian abscess.

Ovarian cysts are generally benign and naturally resolve without treatment. These cysts cause little, if any, symptoms, especially if they are small. Functional (follicular and corpus luteal) ovarian cysts can be complicated by acute intracystic hemorrhage or intraperitoneal rupture and lead to acute pelvic pain [8]. The ovary becomes increasingly vascular about 2–4 days after ovulation, and with neovascularization, blood from the vascular theca zone can fill the cavity of the cyst. The cyst usually reabsorbs the blood, but, if the extent of bleeding is large or the cyst ruptures, hemoperitoneum can result [17]. Enlarging ovarian follicles can produce a colicky pain or dull unilateral tenderness in the lower abdomen or pelvis. Ruptured cysts may manifest as hypovolemia and hemodynamic instability.

Adnexal torsion is defined as a complete or partial rotation of the ovary and/or fallopian tube including the vascular pedicle [18]. Torsion may occur throughout life, from prenatally to postmenopause, with a peak occurrence during the reproductive years [18]. In women, the normal ovarian size varies, but some suggest an upper length limit of 4 cm and a volume of 20 mL [17]. For children over age 1 year, this is less well established, but some suggest a length of 5 cm for torsion [18]. While ovarian torsion is the twisting of an ovary on its ligamentous supports, which may result in a compromised blood supply, the term adnexal torsion describes a twisting of either the ovary or fallopian tube, or both. Concomitant torsion of an ovary and the ipsilateral fallopian tube occurs in up to 67% of patients with adnexal torsion [17, 19, 20]. It may lead to initial compromise of lymphatic and venous drainage, later to arterial occlusion and thrombosis, resulting in a hemorrhagic infarction. Adnexal torsion may be misdiagnosed as appendicitis [21]. Adnexal torsion presents with intermittent acute abdominal pain and is almost always associated with an enlarged ovary or a mass, with the greatest risk when the mass measures between 8 and 12 cm

[22]. There is an increased incidence for adnexal torsion in patients undergoing in vitro fertilization as the ovarian follicles become hyperstimulated and enlarged. Pregnancy may also predispose a patient to adnexal torsion with the enlarging uterus extending out of the pelvis (around 10–12 weeks) into the abdominal cavity, displacing the ovaries anteriorly. Ovarian tumors account for 50–60% of torsion cases, with mature cystic teratomas (dermoid tumors) most frequently involved.

Endometriosis is defined as the presence of functional endometrium-like tissue outside the uterine cavity [23]. It may be associated with infertility and dysmenorrhea, dyspareunia, dysuria, or dyschezia. Although it is a chronic disease, it may lead to acute symptoms, when the ectopic endometrial tissue responds to hormonal changes during the menstrual cycle [24]. The appearance of endometriosis ranges from small peritoneal lesions to large ovarian endometriotic cysts and extensive fibrosis and adhesions leading to significant distortion of pelvic anatomy. The three primary types of endometriosis are superficial peritoneal lesions, ovarian endometriomas, and deep infiltrating endometriosis [25]. About 3–12 years may pass between symptom onset and a definitive diagnosis [26–28]. The spectrum of symptom severity in endometriosis is wide and includes severe abdominal or pelvic pain or an acute abdomen.

Epidemiology

According to the US National Center of Health Statistics, the number of patients presenting with acute abdominal pain (including lower abdominal and/or pelvic pain) increased by 31.8%, from 5.3 million in 1999–2000 to 7.0 million in 2007–2008 [29]. In women, acute pelvic pain is the main cause of emergency consultations for gynecological conditions [30].

Ectopic pregnancy occurs in 1–2 out of 200 pregnancies and is the leading cause of maternal death in the first trimester [8, 31]. If an intrauterine pregnancy is present, the likelihood of an ectopic pregnancy is dramatically decreased, noting

that heterotopic pregnancies (concurrent intra-uterine and extrauterine pregnancies) are extremely rare, occurring in 1:2100 to 1:30,000 of spontaneous pregnancies [9]. In adolescents and young women, the incidence is 0.5% of pregnancies. However, the incidence of heterotopic pregnancy can be as high as 2.9% in the assisted reproduction population [9, 32]. In the study by Menon et al. of symptomatic women, the incidence of ectopic pregnancies was significantly lower in women under 20 years of age (9.7%) compared with those aged 20 years and older (21.7%) [33]. Zane et al. estimated a total number of 10,221–77,129 ectopic pregnancy cases per year in the USA [34]. In the UK, nearly 32,000 ectopic pregnancies are diagnosed every year, resulting in an incidence of about 11 per 1000 pregnancies [31].

Pelvic inflammatory disease is one of the most common causes of acute pelvic pain in sexually active women and is the most frequent gynecologic cause of emergency department (ED) visits, with the number of visits approaching 350,000 per year in the USA [35]. As many as 70% of adolescents with PID are diagnosed in the ED, and nearly 1 million patients with PID are diagnosed annually in the USA, resulting in 275,000 hospitalizations [5, 8, 36]. Factors associated with PID are related to sexual behavior (young age, multiple partners, recent new partners in the previous 3 months, and past history of sexually transmitted disease) and interruption of the cervical barrier (e.g., termination of pregnancy, insertion of an intrauterine device within the past 6 weeks, hysterosalpingography, and intrauterine insemination) [12]. Multiple studies have shown that 19–55% of women who present with pelvic pain have PID [1, 5, 8, 11, 14, 17, 30, 37–45].

Adnexal torsion may occur at any age, even prenatally, but most commonly happens in the first two decades of life [28]. Some authors reported a peak incidence after menarche, others in pregnant women [17, 46, 47]. Adnexal torsion is reported to account for up to 2.7% of all cases of acute abdominal pain in children and is the fifth most common gynecologic emergency with a reported incidence of 3% in one series [20, 48, 49]. At large institutions, 3–5 cases of adnexal torsion are seen per year [20, 50, 51]. It represents a real medical and surgical emergency.

Concomitant fallopian tube torsion has been shown to occur in up to 67% of cases of ovarian torsion [18]. Adnexal torsion has even been described in the neonatal and antenatal period [51]. There is a predisposing factor found for torsion in women 64–82% of the time, and this is similar in children [52]. The most frequently encountered ovarian lesions causing torsion in both adults and children are typically benign, with cystic teratomas (31%) and hemorrhagic or follicular cysts (23–33%) being the most common [52].

Functional (follicular and corpus luteal) ovarian cysts are thought to be a common cause of acute pelvic pain when associated with acute intracystic hemorrhage or intraperitoneal rupture. The exact incidence of hemorrhagic or ruptured ovarian cysts in premenopausal females is uncertain.

Endometriosis is a relatively common disease affecting 0.5–15% of women, in general, and 25–80% of women with pelvic pain and/or infertility. The true prevalence of endometriosis remains unclear [53]. For adolescents, a prevalence of 25–38% of those with acute pelvic pain is reported. If the pain is persistent, the prevalence increases to 70–79% [54–56].

Overall Cost to Society

Trent and colleagues calculated the costs per episode of medical care for PID in adolescents in the emergency department to be an average of \$1382 in 2009 [57]. In a study from the early 1990s, using insurance data, Washington and colleagues estimated that direct costs of PID, PID-associated ectopic pregnancy, and infertility amount to \$2.73 billion in 1990, with hospitalization costs amounting for 75% of this total [58]. These authors made an assumption of a ratio of 2:1 for physician offices compared to hospital outpatient and emergency department visits. Direct costs of hospitalization were estimated at \$1850.40 in this study, but no specific figures are available for emergency department visits [58]. Later in the 1990s, Rein and colleagues used insurance claims data to estimate the lifetime cost (\$1167) of a case of PID with

the majority (\$843) of these costs for acute PID care [59]. The same authors estimated that nearly three quarters of cases (73%) would not accrue costs beyond those of treatment of the acute episode of PID.

An estimated 96 million *C. trachomatis* and *N. gonorrhoeae* infections occur globally among women each year, and about 15% of untreated infections lead to PID, the global burden of PID and the cost to society are substantial [11]. Yeh et al. calculated the costs of major complications of PID based on a cohort of 100,000 women aged 20–24 years, in which 8550 ectopic pregnancies, 16,800 cases of infertility, and 18,600 cases of chronic pelvic pain were projected to occur [60]. They found an average per-person lifetime cost of US\$2150. The incidence of PID is thought to be decreasing, but it will remain a significant cause for acute and chronic pelvic pain and reproductive sequelae [61].

With the prevalence of endometriosis estimated at 6–10% of women in the reproductive age group, direct healthcare costs for managing endometriosis, as well as indirect costs to patients, employers, and society due to loss of employment and productivity, are substantial [62]. In this systematic review from 2016, total direct costs in the USA were estimated to be \$12,118 per patient per year, compared to other countries, which ranged from \$1109 per patient per year in Canada to \$8820 per patient per year in Austria [62]. These figures are in agreement with previous systematic reviews reporting on the economic consequences of endometriosis and related symptoms [28, 63]. Assuming a prevalence of 10% (the rate most frequently reported in the literature), direct healthcare costs for endometriosis were estimated at more than \$17 million and indirect costs of lost productivity at nearly \$5 million in the USA. [28, 63]. A major contributor to those costs is delays in reaching the correct diagnoses. Cost estimates for acute episodes are not currently available.

Estimated direct costs for treatment of ectopic pregnancy were summarized in a recent literature review by Ebner et al. [64]. Total direct costs for cases managed surgically ranged between \$2695 in France to \$6840 in the USA, while for

medically managed (methotrexate) cases, total direct costs ranged from \$818 in the USA to \$4066 in the Netherlands [64].

For other specific causes of acute pelvic pain in women, a reduction of costs is suggested if diagnosis occurs earlier [65, 66], although no evidence was found for this assumption nor an estimation of the amount of healthcare costs raised by these problems.

Goals of Imaging

In cases of acute lower abdominal or pelvic pain, confirmation or exclusion of gonadal causes in girls and adolescents is mandatory, since it may constitute a surgical emergency. Clinical presentation is often nonspecific and may overlap with symptoms of other abdominal pathologies such as appendicitis. In adolescents and premenopausal women, diagnosis of extrauterine pregnancy is critical to avoid catastrophic complications. Many of the diagnoses considered for acute pelvic pain require confirmatory testing. History, physical examination, and laboratory testing narrow the differential diagnosis and guide the physician to choose the proper imaging test. Life- and/or fertility-threatening conditions are the first to be considered until they can be confidentially excluded. Regardless of what testing is performed, limiting radiation exposure is paramount, particularly for infants and children, radiosensitive tissues, and for the developing fetus in potentially pregnant patients.

Methodology

The diagnostic performance of radiographic examinations in patients with pelvic pain caused by gynecological pathologies was evaluated based on a systematic literature review using PubMed, Scopus, the Cochrane Library, and the Appropriateness Criteria® of the American College of Radiology. All searches were performed in July 2015 without any time restrictions. The search strategy used the following statements: *lower abdominal OR pelvic pain, women, clinical examination, epidemiology,*

imaging (including *MRI, ultrasound, computed tomography, scintigraphy*, and acronyms of these terms), *diagnosis*, as well as combinations of these search strings. Animal studies and publications of languages other than English or German were excluded.

Discussion of Issues

What Initial Imaging Tests Are Appropriate in Infants, Girls, Adolescent Girls, and Premenopausal Women Presenting with Acute Pelvic Pain?

Summary of Evidence When a menstruating patient presents with symptoms of acute pelvic pain, knowledge of pregnancy status is of utmost importance. In order to locate the pregnancy, ultrasound (US) is the imaging tool of choice (strong evidence). Because of its wide availability, low cost, and diagnostic versatility, US is also recommended for the (initial) assessment of other disorders of obstetrical and gynecological etiology (moderate evidence). When US is indeterminate, magnetic resonance imaging (MRI) or computed tomography (CT) [if MRI is not available] should be considered (moderate evidence).

Supporting Evidence The American College of Radiology Appropriateness Criteria (ACRAC)[®] 2015 update for the clinical condition “Acute pelvic pain in the reproductive age group” recommends both transvaginal and transabdominal US as first choice imaging modality in all women in which a gynecological etiology is suspected (variant 1, serum β -hCG positive, and variant 2, serum β -hCG negative) as well as in pregnant women in which other causes are presumed (variant 4) [7]. The appropriateness rating applied for all of these variants was 9/9 (usually appropriate). In women and sexually active adolescents and girls, transvaginal US allows detailed visualization of the uterus, adnexa, ovaries, and thickened fallopian tubes. Transabdominal US is complementary to the endovaginal examination because it provides

a more global view of the pelvic contents. Transabdominal US also evaluates the pelvis and lower abdomen and can detect appendicitis, in some cases, nephrolithiasis, ovarian cysts, tumors, and tubo-ovarian abscess. In addition, duplex and color or power Doppler imaging can be used to assess vascularity of the ovaries and the adnexal structures, providing information that can be helpful in narrowing the field of differential considerations. While the ACRAC rating for pulsed Doppler US ranges between 7 and 9/9 (usually appropriate) to evaluate for gynecological and non-gynecological etiology, the ACRAC advises that Doppler imaging should be avoided in the setting of developing intrauterine pregnancy and be performed in pregnant patients only when absolutely necessary [7].

A systematic review of 14 studies including more than 12,000 pregnant patients computed a positive likelihood ratio of 111 for ectopic pregnancy if an adnexal mass was present in the absence of intrauterine pregnancy on transvaginal US [67]. A number of studies show that US examinations are also very useful for the detection of other gynecological conditions in the ED setting [7] (see Issue II) and even the initial study in symptoms of gastrointestinal or urological disorders [68–71] (see relevant chapters in this book).

In serum β -hCG-positive patients with suspected gynecological etiologies and a negative or inconclusive US, the ACRAC guidelines recommend MRI as the next imaging test, giving it an appropriateness rating of 6/9 (may be appropriate). When available, MRI is preferable to CT because it lacks ionizing radiation. The MRI is usually performed without contrast material, as a problem-solving tool, particularly in pregnant patients. Gadolinium can cross the placenta, and while no studies have demonstrated adverse effects to fetuses at clinically recommended doses have been used, the ACRAC advise caution with contrast-enhanced MRI, using it only when necessary to critically change a diagnosis. In pregnant patients, the ACRAC recommend against the use of CT as the next line test for gynecological etiologies, giving it a rating of 1/9

(usually not appropriate). Contrast-enhanced MRI is also not recommended, with a score of 1/9 (usually not appropriate).

For serum β -hCG-positive patients, with suspected non-gynecological etiologies, the ACRAC guidelines recommend non-contrast MRI as the next imaging test, giving it an appropriateness rating of 8/9 (usually appropriate). For serum β -hCG-positive patients, with suspected non-gynecological etiologies, when MRI is not available, the ACRAC give CT with contrast material a rating of 4/9 (may be appropriate) and CT without contrast material a rating of 3/9 (usually not appropriate). Some have suggested low-dose non-contrast CT in these pregnant patients to reduce radiation exposure, but CT is best avoided during pregnancy when possible. In these patients, contrast-enhanced MRI receives a low recommendation, with an appropriateness rating of 2/9 (usually not appropriate).

In serum β -hCG-negative patients with suspected gynecological etiologies and a negative or inconclusive US, the ACRAC guidelines recommend MRI with and without contrast as the next imaging test, giving it an appropriateness rating of 6/9 (may be appropriate). For nonpregnant patients with suspected gynecological disease, and a negative or inconclusive US, non-contrast MRI and CT are indicated as the next most appropriate tests, both receiving lower ratings of 4/9 (may be appropriate).

For serum β -hCG-negative patients with suspected non-gynecological pathology, the ACRAC guidelines recommend a contrast-enhanced CT of the abdomen and pelvis as the first-line test, with an appropriateness rating of 8/9 (usually appropriate). Similarly, a large study of more than 1000 adult patients with nontraumatic acute abdominal pain presenting at different EDs concludes that in the imaging evaluation of adults, a conditional strategy with CT after negative or inconclusive US results shows the highest overall sensitivity, with only 6% missed urgent conditions, and the lowest overall exposure to radiation [72]. Transabdominal US with Doppler receives an appropriateness rating of 7/9 (usually appro-

priate). Non-contrast CT may also be appropriate (rated as 6/9), as is contrast-enhanced MRI in the evaluation of nonpregnant women with suspected non-gynecological disease. Transvaginal US receives a lower rating for the evaluation of these non-gynecological disorders at 4/9 (may be appropriate).

Special Case: Infants, Children, and Adolescents

There are a few considerations in the pediatric population that require different imaging decision-making from women. First, ionizing radiation protection culture often results in substitution of MRI for CT in the ED setting and in follow-up imaging. The adolescent may have similar pathology to the adult women, but the use of radiation optimization protocols such as the Image Gently or Image Wisely sites is recommended (www.imagegently.org; www.imagewisely.org). Second, the premenarchal children typically do not undergo transvaginal US. Yet, they will have similar diagnoses with the exception of pregnancy and unlikely PID that include ovarian torsion (15% of all cases occur in children), ovarian cysts with or without hemorrhage, and tumors. Further, there are unique indications in the ED setting that the pediatric population may present with that include foreign body, child abuse, and congenital Mullerian anomalies (vaginal obstruction). The Mullerian anomalies will be discussed in a separate section.

In the pediatric emergency setting, MRI is increasingly used as the second-line emergency diagnostic imaging test after an inconclusive or negative transabdominal US. Contrast-enhanced MRI of the pelvis provides excellent tissue contrast without radiation exposure in the evaluation of suspected ovarian torsion in children and pregnant patients [18, 73]. Magnetic resonance imaging may also demonstrate the early stages of ovarian edema and hemorrhagic infarction in cases where US is inconclusive [74]. Contrast-enhanced MRI may also help characterize tubo-ovarian abscess and differentiate it from malignancy and endometriosis [75].

What Are the Best Imaging Techniques for the Diagnosis of Acute Pelvic Pain in the Emergency Department?

Summary of Evidence CT is the preferred imaging technique for identifying causes of acute pelvic pain in the gastrointestinal and urinary tract showing high sensitivity and specificity (strong evidence). CT is suggested as second-line imaging tool in female, serum β -hCG-negative patients with equivocal US findings and symptoms suggestive of gynecological etiologies, although MRI may also be used, specifically if an infectious etiology is suspected (moderate evidence). In the pregnant patient, MRI is preferred to CT if US findings are indeterminate (limited evidence). Apart from that, the decision whether to use CT or MRI after inconclusive US findings should be based on the suspected etiology of acute pelvic pain.

Supporting Evidence The recently updated ACR Appropriateness Criteria[®] 2015 for the clinical condition “Acute pelvic pain in the reproductive age group” recommend CT with an appropriateness rating of 9/9 (usually appropriate) for the evaluation of the gastrointestinal and urinary tract in nonpregnant women presenting with acute pelvic pain (variant 4) [7].

Ectopic Pregnancy

As ectopic pregnancy is a life-threatening condition, a rapid diagnosis is crucial. It is suspected if transabdominal US does not show an intrauterine gestational sac and the patient’s β -hCG level is greater than 6500 IU/L or if transvaginal US does not show an intrauterine gestational sac and the patient’s β -hCG level is 1500 IU/L or greater [76].

Summary of Evidence Combined transvaginal US and serial quantitative β -hCG testing are very sensitive and specific in the evaluation of ectopic pregnancy (strong evidence). Pregnancy and ectopic pregnancy are both best imaged by sonography (strong evidence). Abdominal ultrasound is performed initially, and if this is nondiagnostic for pregnancy or ectopic pregnancy, transvaginal sonography improves diagnostic accuracy (mod-

erate evidence). In cases where US is nondiagnostic or equivocal, MRI is the next indicated imaging test (moderate evidence).

Supporting Evidence Combined transvaginal US and serial quantitative β -hCG are 96–99% sensitive and 84–97% specific for diagnosing ectopic pregnancy [77–80]. The systematic review by Crochet et al. computed a positive likelihood ratio of 111 for ectopic pregnancy if an adnexal mass was present in the absence of intrauterine pregnancy on transvaginal US [67]. In the same meta-analysis, they found that existing studies do not establish a single serum hCG level to be diagnostic of ectopic pregnancy; therefore transvaginal US is considered the single best diagnostic modality in this regard. Clinical factors affecting the accuracy of US include low hCG levels, significant bleeding, and lacking evidence of a yolk or embryo [81].

Ultrasound findings most predictive of ectopic pregnancy are extrauterine cardiac activity, a gestational sac, a mass, and fluid in the pouch of Douglas, although these signs are only seen in 8–26% of cases [9, 80]. An extrauterine gestational sac containing a yolk sac, with or without an embryonic pole, is also a relatively specific finding. More commonly, an echogenic tubal ring and complex adnexal mass separate from the ovary are found with ectopic pregnancy and need to be distinguished from a corpus luteum cyst in the ovary, which is more common than an ectopic pregnancy. On color Doppler imaging, flow surrounding an adnexal mass, or the “ring of fire,” can be present with an ectopic pregnancy or corpus luteum. Color Doppler imaging may be helpful to detect an ectopic pregnancy that is surrounded by loops of bowel [9]. The visualization of an intrauterine sac is the strongest evidence against ectopic pregnancy, although concomitant intrauterine and ectopic pregnancy can occur, especially in women with assisted reproduction, but they are extremely rare [76].

Magnetic resonance imaging has been utilized in the evaluation of suspected ectopic pregnancy in very early gestational age cases or where the US was inconclusive. Direct signs of ectopic pregnancy (a gestational sac) had a sensitivity of 91%, a specificity of 100%, and a pos-

itive predictive value of 100% in a small retrospective study by Takahashi et al. [82]. In the same study, the diagnostic accuracy increased from 92% to 100% when the diagnostic criteria required at least two indirect signs or the direct sign [83]. The characteristic feature of a gestation saclike structure with a “three-ring” appearance on T2-weighted images with marked enhancement in the tubal wall was described in 80% of cases in a more recent small retrospective study in 24 patients [84].

When the combination of serum beta-hCG level and US findings is nondiagnostic, another option to be considered, depending on the presenting patient’s individual risk, is repeated beta-hCG level testing or surgical consultation [78].

Pelvic Inflammatory Disease

Historically, PID is diagnosed clinically with imaging findings (US or MRI) used to confirm clinical suspicions [75]. Despite its relative frequency, PID is a diagnostic dilemma with mild nonspecific symptoms that overlap those of other abdominal and pelvic processes, which may not direct the clinician toward the correct diagnosis. As a consequence, CT of the abdomen and pelvis may inadvertently be performed as the initial diagnostic imaging examination. US should be the first diagnostic imaging examination to be performed in cases of suspected PID [7]. However, acute uncomplicated PID may be difficult to detect with US only [83]. Therefore, reported sensitivity rates have a relatively wide range (Table 27.1).

Summary of Evidence Early manifestations of or uncomplicated PID may be difficult to detect with US only (moderate evidence). US is moderately sensitive and highly specific in the diagnosis of tubo-ovarian abscess (strong evidence). Transvaginal US is more sensitive than transabdominal US in the evaluation of PID and tubo-ovarian abscess (limited evidence). For the depiction and management planning of pelvic abscesses, advanced cross-sectional imaging with contrast-enhanced CT or MRI is often required (moderate evidence). Comparison studies between US, CT, and MRI are not available (limited evidence).

Table 27.1 Sensitivity and specificity of ultrasound in the evaluation of obstetrical/gynecological conditions in women and children presenting with acute pelvic pain

	Sensitivity (%)	Specificity (%)
Ectopic pregnancy	96–99	84–97
Pelvic inflammatory disease (PID)	56–100	78–80
Hemorrhagic/ruptured ovarian cyst	80–90	98
Adnexal/ovarian torsion	75–100	93
Endometriosis	75–95	83–100
Tubo-ovarian abscess	56–93	86–98
Torsion		
Tissue edema	21	100
Absent flow	52	91
Absent arterial flow	76	99
Absent/abnormal venous flow	93–100	97

For ectopic pregnancy diagnosis, the US performance is by transvaginal and reported in conjunction with the appropriate hCG levels

Data from references [7, 77–79, 89, 102, 105, 109, 114–117]

Supporting Evidence Ultrasound features in hydrosalpinx include dilated fluid-filled fallopian tubes, with folds and incomplete septations [9]. On transverse section, short linear projections protruding into the lumen can cause a cogwheel appearance. Small echogenic foci may be seen in the tubal wall, representing flattened endosalpingeal folds secondary to distension of the tube giving a “beads-on-a-string” appearance. Indentations present on opposite sides in the longitudinal scanning plane have been described as the “waist sign.” Color or power Doppler transvaginal US can be used to detect more subtle abnormalities of PID, which include uterine enlargement and indistinctness, endometrial thickening with or without endometrial fluid, larger than normal ovarian volumes due to thickening of the ovarian stroma and reactive polycystic change, and complex free fluid with internal echoes [85]. Transrectal US may also be used to demonstrate rectal involvement in endometriosis, but it has not been shown to be superior to transvaginal US [86].

Bulas et al. studied the diagnostic performance of transabdominal and transvaginal sonography prospectively in 84 patients aged 12–21 years with

the clinical diagnosis of acute PID [87]. Transvaginal sonography demonstrated superior resolution of 25 dilated fallopian tubes. However, 31 transabdominal and transvaginal US studies were normal despite patients fulfilling strict clinical criteria for PID. The severity level of PID, as diagnosed by transabdominal sonography, was changed in 28 cases, with medical therapy altered in 23 cases because of additional transvaginal sonographic findings. Transvaginal sonography provided superior anatomic information in patients with PID, demonstrating abnormalities not seen at transabdominal sonography in 71% of cases [87].

US is also indicated to evaluate for complications of PID. A tubo-ovarian abscess, a potentially life-threatening complication of PID, can be detected by means of transvaginal US with a sensitivity of 56–93% and a specificity of 86–98% [7]. Transvaginal US is superior to transabdominal ultrasound in identifying thickened, fluid-filled fallopian tubes. Since the sonographic findings for a tubo-ovarian abscess are nonspecific, the presence of a mass in the expected location of the ovaries or in the cul-de-sac together with an elevated white cell count and erythrocyte sedimentation helps to establish the diagnosis [88]. In a recent small prospective study including 17 patients with laparoscopically confirmed salpingitis, all 13 cases with moderate or severe salpingitis were diagnosed with US, compared with one of four cases of mild salpingitis [83].

On MRI, fat-suppressed T2-weighted images are very sensitive for the detection of inflammation [8, 89, 90]. On MRI, both hydrosalpinx and pyosalpinx appear as dilated, fluid-filled tubular structures, and cannot be reliably differentiated from each other, although a pyosalpinx usually has thicker walls and may have layering T1 signal secondary to proteinaceous debris. A tubo-ovarian abscess appears as a multilocular cystic structure or a heterogeneous mass with solid and cystic components. The abscess wall and adjacent inflammatory changes enhance avidly with gadolinium-based contrast. Contrast-enhanced MRI may also help characterize tubo-ovarian abscess and differentiate it from malignancy and endometriosis [75].

CT plays also an expanding role in the evaluation of PID due to its wide availability and often vague and nonspecific nature of disease symptom-

atology. It is performed mainly in patients with equivocal US findings [7]. CT should be performed with oral and intravenous (IV) contrast, as unopacified bowel loops may be confused with abscesses [8]. In addition, early manifestations of PID can be better appreciated on CT than on US [91]. The most common general CT findings of PID described in the literature are thickening of the uterosacral ligaments, obliteration of fascial planes, free fluid in the cul-de-sac, loss of definition of the uterine border, pelvic fat infiltration or haziness and pelvic edema, reactive lymph node enlargement, and signs of peritonitis [75]. On CT, enhancing, thickened fallopian tubes containing complex fluid and debris are characteristic of pyosalpinx. A tubo-ovarian abscess appears as a thick-walled, complex fluid collection with septations, a fluid-debris level, and occasionally gas [9]. Pelvic fat haziness is one of the most sensitive findings of acute PID and is seen in as many as 65% of patients, but it has very low specificity [75]. The combination of the two findings of hepatic capsular enhancement on the late arterial phase images and fallopian tube thickening of more than 5 mm has a sensitivity of 71.9%, a specificity of 81.3%, and an accuracy of 76.6% [92]. The specificity of the tubal thickening sign alone has been reported to be as high as 95% [93].

Hemorrhagic or Ruptured Ovarian Cysts

Hemorrhagic cysts usually result from hemorrhage within a corpus luteum or other functional cyst and often present as an acute abdomen in females of childbearing age. Hemorrhagic cysts typically resolve within 8 weeks. Relevant history should include when the patient's last menstrual period occurred. Abdominal pain can occur with ovulation of a follicular cyst mid menstrual cycle, known as mittelschmerz, "mid (cycle) pain." Enlarging ovarian follicles often produce a colicky or dull unilateral tenderness in the lower abdomen or pelvic region. Rarely, patients with hemorrhagic cysts present with hypovolemia and hemodynamic instability. The triad of symptoms includes a delay in menses, followed by spotting, unilateral pelvic pain, and a small, tender, adnexal mass [22]. On physical examination, corpus luteal cysts can mimic ectopic pregnancy.

Summary of Evidence US of the pelvis (a combination of transabdominal and transvaginal approaches to visualize the cyst) is recommended as the first-line imaging test to evaluate large cysts in the pelvis of nonpregnant females of reproductive age (strong evidence). The US findings of fibrin strands and a retracting clot in ovarian cysts have a high diagnostic accuracy for hemorrhage (moderate evidence). Clinically detected simple cysts less than 5 cm in size in females of reproductive age don't require follow-up (strong evidence). Clinically detected simple cysts greater than 5 and ≤ 7 cm in size in females of reproductive age will require annual follow-up (strong evidence).

Supporting Evidence The characteristic appearance of a hemorrhagic cyst on US is a complex cystic mass with lacelike reticular echoes (also known as fishnet, cobweb, or spiderweb) due to fibrin strands or a solid-appearing component with concave margins representing clot [9, 94]. Classic features on US include no internal vascularity by color Doppler, but there may be circumferential flow in the cyst wall. These features allow a confident diagnosis of a hemorrhagic ovarian cyst [94].

A study assessing the likelihood ratio of US findings for the diagnosis of a hemorrhagic ovarian cyst found that in at least 90% of cysts, one or both of the following features are present: fibrin strands and a retracting clot [95]. The authors concluded that these are the paramount observations in allowing high confidence in the diagnosis of hemorrhagic ovarian cysts. Free fluid in the pelvis can be an indicator of cyst rupture but is nonspecific [8]. Generally, the diagnostic accuracy of US for the detection of hemorrhagic or ruptured ovarian cysts is high [7] (Table 27.1). In cases of cyst rupture, the ovary may be normal in size if rupture has decompressed any cysts. In these cases, a large amount of pelvic fluid is usually noted.

For nonpregnant females of childbearing age, the ACR appropriateness criteria for clinically suspected adnexal masses (variant 1, initial evaluation) recommend US (using a combination of transabdominal and transvaginal to visualize the lesion) of the pelvis with Doppler, giving an appropriateness rating of 9/9 (usually appropriate)

[96]. The next most appropriate test during the initial encounter in females of childbearing age with clinically suspected adnexal mass is MRI with and without IV contrast, which is given a rating of 6/9 (may be appropriate), or MRI without contrast which has a rating of 5/9 (may be appropriate) [96]. Computed tomography with or without contrast material is not indicated in the initial evaluation, with a rating of 2/9 (usually not appropriate).

For nonpregnant females of childbearing age, the ACR appropriateness criteria for clinically suspected adnexal masses (variant 5, large simple cysts, greater than 5 cm diameter) recommend US (using a combination of transabdominal and transvaginal to visualize the lesion) of the pelvis with Doppler, giving an appropriateness rating of 9/9 (usually appropriate) [97]. If the hemorrhagic cyst is less than 3 cm in a woman of reproductive age, it is probably physiological and does not require follow-up according to the Society of Radiologists in Ultrasound (SRU) Consensus Conference Statement [94]. Hemorrhagic cysts less than 5 cm in women of reproductive age don't require any follow-up [94]. These recommendations also align with the advice from the Choosing Wisely initiative of the American Board of Internal Medicine foundation and the ACR (www.choosingwisely.org). If the cyst is greater than 5 cm, it should be described in the report, and short-term follow-up with US is recommended at 6–12 weeks to ensure resolution [94]. While short-term follow-up imaging in the follicular phase, on days 3–10 of the menstrual cycle, is optimal, this is sometimes difficult to coordinate in clinical practice, with annual follow-up recommended for persistent cysts according to the SRU Consensus Conference Statement [94]. For cysts greater than 7 cm in size in nonpregnant reproductive age females, which may be difficult to evaluate with US, the SRU recommends further imaging with MRI or surgical consultation be considered [94]. The next diagnostic testing option in females of childbearing age with large simple cysts is MRI with contrast material, which receives a rating of 4/9 (may be appropriate). Non-contrast MRI and CT have ratings of 3/9 and 2/9 (usually not appropriate) [97].

Since women in early postmenopause occasionally ovulate and, therefore can develop complex cysts with the appearance of a classic hemorrhagic cyst, these cysts should be described in the imaging report with short-interval follow-up (6–12 weeks) with US recommended to ensure resolution [94].

For indeterminate or probably benign cysts (such as a single thin septation <3 mm or a small calcification in the wall), follow-up can be similar to that for simple cysts. For indeterminate cysts (without classic appearances for hemorrhagic cysts, dermoids, or endometriomas) in women of reproductive age or women in early postmenopause, follow-up US should be performed in 6–12 weeks. Resolution of the lesion confirms a hemorrhagic cyst. If the lesion persists and is unchanged, then a hemorrhagic cyst is unlikely, and continued follow-up with either US or MR imaging should then be considered. If these studies do not confirm an endometrioma or a dermoid, then consider surgical evaluation at this stage [94].

For indeterminate cysts with features suggestive of benign neoplasms (multiple thin septations or a solid nodule without detectable flow at Doppler US), or with cyst wall irregularity or tiny areas of focal thickening, more comprehensive evaluation is required, and for women of reproductive age, this entails a short-interval follow-up (6–12 weeks) with US or occasionally further characterization with MRI [94]. MRI may be particularly helpful to confirm the absence of MR contrast enhancement in sonographically solid-appearing areas that do not have demonstrable flow at Doppler US. A short-interval follow-up of 6–12 weeks with US should allow enough time for a physiologic cyst to resolve and should be performed during a different phase of the menstrual cycle, ideally between days 3 and 10 of the menstrual cycle, so that new cyst development does not complicate things. Larger cysts take more time to resolve. If the lesion persists, and continues to have indeterminate findings at US or MRI, surgical evaluation should then be considered. Although size cannot reliably distinguish between benign and malignant etiologies, once

the cyst exceeds 10 cm in size, it has a 13% chance of being malignant [94].

For adnexal cysts with frankly malignant features, such as thick septations (>3 mm), solid elements with flow at Doppler US, and focal areas of wall thickening (>3 mm), particularly when seen in association with omental or peritoneal masses or a moderate or large amount of ascitic fluid in the pelvis [94], a cyst with a nodule that has internal blood flow has the highest likelihood of being malignant, and rather than follow-up imaging, they require surgical evaluation [98].

Adnexal/Ovarian Torsion

Adnexal torsion is a medical or surgical emergency and can occur with normal ovaries, particularly in adolescents. Postulated causes of normal adnexal torsion include mobile fallopian tubes or mesosalpinx, elongated pelvic ligaments, fallopian tube spasm, strenuous exercise, or abrupt changes in intra-abdominal pressure [17, 20, 51, 99]. Ovaries with any type of mass are predisposed to torsion, and benign lesions are most frequently implicated in both adults and children, with cystic teratomas (31%) and hemorrhagic or follicular cysts (23–33%) being the most common [52].

Summary of Evidence Ultrasound is the first-line modality in children and adolescents with abdominal and/or pelvic pain suspected to be of gynecological origin (limited evidence). In adult women, sonography is indicated as first imaging with acute pelvic pain, due to its excellent diagnostic accuracy in the evaluation of pregnancy (intrauterine or ectopic), ovarian cysts, and torsion (limited evidence). The most US common finding in ovarian torsion is an enlarged heterogeneous ovary (limited evidence). Ovarian enlargement and a lack of Doppler flow are the most sensitive and specific US signs in adnexal or ovarian torsion (moderate evidence). However, the presence of Doppler flow cannot be used to exclude ovarian/adnexal torsion as flow can be seen in up to a third of surgically proven cases (limited evidence). Therefore, close clinical correlation is mandatory, and if suspected, laparoscopy confirmation and treatment may be indicated.

Supporting Evidence Adnexal torsion is generally characterized by an enlarged, edematous ovary or ovarian complex consisting of an ovary and an associated adnexal mass. Common imaging findings are an adnexal mass, a displaced adnexal mass/enlarged ovary, and ascites—detectable with US nearly as reliably as with CT or MRI [96].

Chiou et al. reviewed surgically proven cases of adnexal torsion between 1990 and 2006 [96]. A correct preoperative diagnosis was made in 15 (71%) of 21 with initial sonography versus 5 (38%) of 13 cases with initial CT. A correct imaging diagnosis was made more frequently in premenopausal than in menopausal patients ($p = 0.02$). Common imaging findings were an adnexal mass (65% on sonography, 87% on CT, and 75% on MRI), a displaced adnexal mass/enlarged ovary (53% on sonography, 87% on CT, and 75% on MRI), and ascites (53% on sonography, 73% on CT, and 50% on MRI) [96].

The degree of ovarian volume asymmetry is important and should typically be at least 2:1 [7]. A retrospective study with surgically and pathologically proven ovarian torsions found in 100% of the patients an enlarged torsed ovary, with the median volume 12 times (range 4.4–27.3) that of the normal contralateral side [100].

The use of Doppler in this diagnosis is helpful, but its interpretation is controversial due to conflicting literature [7]. Findings on Doppler vary, including absent, decreased, or reversed ovarian artery flow, and may depend on the degree of obstruction and the chronicity [25]. Lack of Doppler flow enables fairly confident diagnosis, but the presence of arterial and venous Doppler signal has been documented in one-third of cases with surgically proven torsion [26, 27]. Arterial flow has been described in one-third of surgical cases of torsion [7, 96, 101]. Venous or arterial flow was present in the torsed ovary in 62% of a pediatric sonographic study [100]. Therefore the sensitivity of absent arterial flow is low at 40–73% [52]. More recently, a study has appeared in the literature demonstrating an abnormal flow pattern within the ovarian vein as the only Doppler finding in patients with early torsion, lending support

for Doppler findings associated with the diagnosis [28, 29]. In summary, indeterminate US Doppler results should not determine whether or not a patient undergoes laparoscopic examination if the clinical suspicion is high.

A twisted vascular pedicle (whirlpool sign) was found in up to 88% of twisted ovaries in earlier US studies [102, 103]. The sensitivity of sonography was 100%, and specificity was 93% in a small study of 28 girls, using an enlarged ovary as the criterion for abnormal (limited evidence). The volume of the enlarged ovaries ranged from 34 to 365 cm³ (mean 130 ± 99 cm³) [104].

Another feature suggestive of torsion is peripherally placed follicles in an enlarged ovary (in 74% of cases due to ovarian edema) with a small amount of pelvic free fluid; however this finding is not common and can also be seen in a polycystic ovary [7]. Other US signs include free fluid in the cul-de-sac (nonspecific) and a more medial position of the torsed ovary toward the uterus from twisting around the broad ligament [105].

Because adnexal/ovarian torsion often mimics the clinical presentation of appendicitis, diverticulitis, or renal colic, CT, rather than US, is often the first modality in which patients are imaged [106]. Alternatively, MRI can be used in inconclusive US findings, and many MRI features of adnexal torsion overlap with CT such as mal-location of the ovary, uterine deviation, adnexal fat infiltration, and the presence of free fluid. One advantage of MRI over CT in the diagnosis of adnexal torsion is its sensitivity in demonstrating blood products within the lesion [106].

Endometriosis

Endometriosis does not usually require emergent management, but women in whom the diagnosis has not yet been established can present with acute pelvic pain to the ED. Laparoscopy remains the gold standard for the evaluation of endometriosis, but it is invasive and it carries surgical risks. Therefore, diagnostic imaging tends to be performed, with its main purpose in the emergency setting being to exclude surgical or acute medical causes of acute pelvic pain, such as adnexal/ovarian torsion, ectopic pregnancy, or

PID/tubo-ovarian abscess, and for these reasons, US remains the first-line test.

Summary of Evidence Transvaginal US is the best initial imaging method for the evaluation of endometriosis (limited evidence). Outside the emergency setting, and for some less common imaging findings, MRI has higher sensitivity and diagnostic likelihood ratios for uterosacral ligament and vaginal endometriosis (limited evidence).

Supporting Evidence Serum biomarkers have been evaluated but have been found not to be clinically useful in the diagnosis of endometriosis [107]. Laparoscopy is the gold standard for the evaluation of endometriosis, but it is invasive and carries surgical risks. In a recent Cochrane systematic review, none of the evaluated imaging modalities (US, MRI, or CT) were able to detect overall pelvic endometriosis with enough accuracy that they would be suggested to replace surgery [108]. Therefore, imaging tends to be performed, with the goals of diagnosing other acute causes of pelvic pain.

Transvaginal US is the best initial imaging method for the evaluation of endometriosis [7]. This enables the diagnosis or exclusion of etiologies that require surgical or urgent medical management, such as adnexal torsion, ectopic pregnancy, and PID/tubo-ovarian abscess. A comparison between physical examination, transvaginal US, rectal endoscopic US, and MRI for the diagnosis of endometriosis in adult patients prior to surgery revealed that US and MRI perform similarly for the diagnosis of intestinal endometriosis; MRI, however, shows higher sensitivity for uterosacral ligament and vaginal endometriosis [109].

If endometriosis is suspected and US results are inconclusive, a workup using MRI may be recommended because MRI allows for more definitive characterization of suspected endometrial implants and endometriomas compared with CT [8]. MRI may help guide surgical approaches, especially for deep infiltrating endometriosis and other unusual sites of presentation [25]. It is superior to US in diagnosing rectosigmoid lesions and endometriosis of the bladder. Endometriosis is uncommon in children.

Special Case: Congenital Uterovaginal Abnormalities Including Congenital Vaginal Obstruction (Mayer-Rokitansky-Kuster-Hauser Syndrome)

The Mullerian fetal system forms two merging ducts that regress in the male and develop into the normal uterus, fallopian tubes, and upper two-thirds of the vagina. Mullerian ductal anomalies (MDA) are estimated to occur in 0.1–1.5% of women in the general population, and approximately 90% of these anomalies involve the uterus [110, 111], so vaginal obstruction is very rare. The etiology is not well known although there are associated congenital anomalies that include the skeletal and renal system.

The classification of MDA ranges from vaginal agenesis, the easiest to surgically repair (class 1), through various levels of uterine abnormalities as follows: class 2, unicornuate uterus; class 3, uterine didelphys; class 4, bicornuate uterus; class 5, septate uterus; class 6, arcuate uterus; and a group of unclassified defects. When there is vaginal agenesis with a Mullerian anomaly, this is referred to as the Mayer-Rokitansky-Kuster-Hauser (MRKH) syndrome.

Adolescent girls with MDA may present with acute pelvic pain and occasionally with an abdominal/pelvic mass due to vaginal obstruction. Because of the complexity of the embryology, obstruction may occur at different levels and in various degrees, including imperforate hymen, complete vaginal membrane, or atresia of the vagina and/or uterus [2, 110]. These conditions are usually encountered either in the neonatal period or in adolescence at the time of menarche [2].

Transabdominal US is the initial modality of choice for pediatric gynecologic patients. In teenagers with obstructive uterovaginal anomalies presenting to the ED with acute abdominopelvic pain, US is valuable in differentiating the frequent case of hemato(metro)colpos due to imperforate hymen or transverse vaginal septum from the rare case of hematometra due to cervical dysgenesis [112]. In indeterminate or complex cases, MRI provides more precise demonstration of

anatomic features in multiple planes and does not involve ionizing radiation [112, 113].

The neonate may also have vaginal obstruction and typically presents with a palpable abdominal mass. The maternal hormonal stimulation produce mucous and blood products, together with vaginal agenesis or obstruction to create this condition. Neonates may present with either hydrocolpos or hydrometrocolpos and should be evaluated for associated renal anomalies with US.

Because these presentations are uncommon, they are sometimes confused with ovarian cystic masses, the normal bladder, and perforated appendicitis at ultrasound and, sometimes, CT imaging.

There is a lack of diagnostic accuracy studies supporting these recommendations.

Take-Home Tables and Figure

Table 27.1 presents sensitivity and specificity of ultrasound in evaluating obstetrical/gynecological conditions in women and children with acute pelvic pain. Table 27.2 gives the differential diag-

Table 27.2 Differential considerations of acute pelvic pain in adolescent girls and premenopausal women

Gynecological: Adenomyosis, uterine fibroid, hemorrhagic or ruptured ovarian cyst, adnexal torsion, pelvic inflammatory disease (PID), spontaneous abortion, ectopic pregnancy, endometriosis, tubo-ovarian abscess, teratomas, cystadenomas

In *adolescent girls* additionally: congenital anomalies such as imperforated hymen, transvaginal septum

Pregnant women: Ectopic pregnancy, spontaneous abortion, corpus luteum hematoma, adnexal torsion, placental abruption (postpartum), ovarian vein thrombosis, endometritis (postpartum), uterine impaction

Gastrointestinal: Appendicitis, bowel obstruction, diverticulitis, gastritis, infectious enteritis, inflammatory bowel disease, inguinal hernia, irritable bowel syndrome, pelvic thrombophlebitis, perirectal abscess

Urological: Urinary tract calculi, pyelonephritis, cystitis

These diagnostic considerations also apply in the pediatric population except for pregnancy issues and uterine pathologies that tend to occur later in life (endometriosis, adenomyosis, and fibroids)

Data from references [5, 8, 118]

noses for acute pelvic pain in adolescent girls and premenopausal women. Figure 27.1 presents an algorithm to be used for the evaluation of acute pelvic pain in women.

Imaging Case Studies

Case 1

Figure 27.2a, b presents a 10-year-old girl with acute abdominal pain and urinary retention

Case 2

Figure 27.3 presents ovarian torsion in a 32-year-old female with acute pelvic pain

Case 3

In Fig. 27.4, a 27-year-old female with acute pelvic pain and a hemorrhagic ovarian cyst is presented

Suggested Imaging Protocols

Ultrasound

Ultrasound with Doppler—first transabdominal followed by transvaginal scanning—is the key screening tool and often the only examination needed. For adolescents and adults, a curved multifrequency probe is required. To evaluate the female reproductive tract, a full urinary bladder is essential. If the bladder is not adequately full, it may be useful to repeat the examination every 15 min or to place a Foley catheter and fill the bladder. Further evaluation with CT or MRI depends on the results of the sonograms, the clinical examination, and the acuity of the problem. For children, transabdominal US with Doppler is the key screening tool.

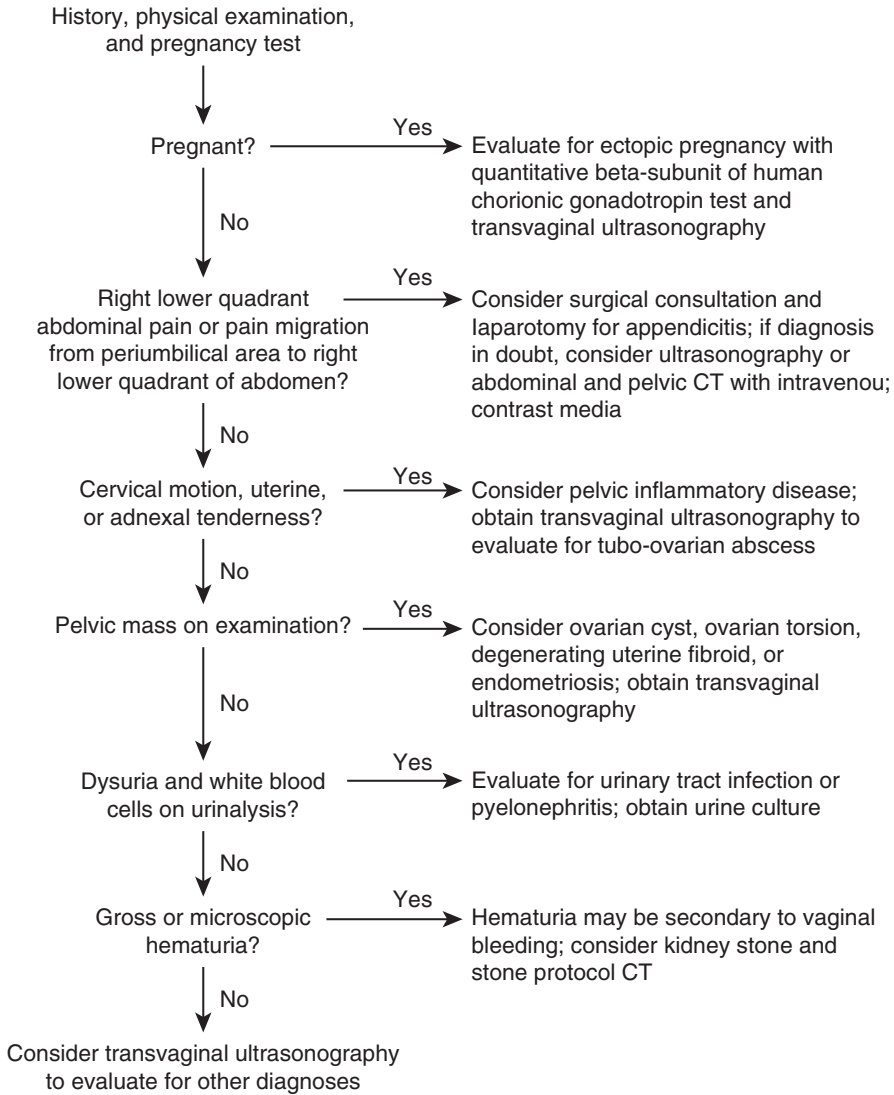


Fig. 27.1 Algorithm for the evaluation of acute pelvic pain in women (Used with permission of AAFP from Kruszka PS, Kruszka SJ. Evaluation of acute pelvic pain

in women. *Am Fam Physician* 2010;82:141–7. © American Academy of Family Physicians)

Multi-detector Computed Tomography

Intravenous contrast is essential to visualize infection or inflammation and abscess. Oral or rectal contrast may help to distinguish fluid-filled bowel loops in the pelvis.

Magnetic Resonance Imaging

Axial and coronal T1-spin echo, axial and sagittal T2 Fast Spin Echo (FSE) with fat saturation, coronal Short Tau Inversion Recovery (STIR) or Half-fourier Acquired Single shot Turbo spin Echo (HASTE), and axial and coronal T1 2D

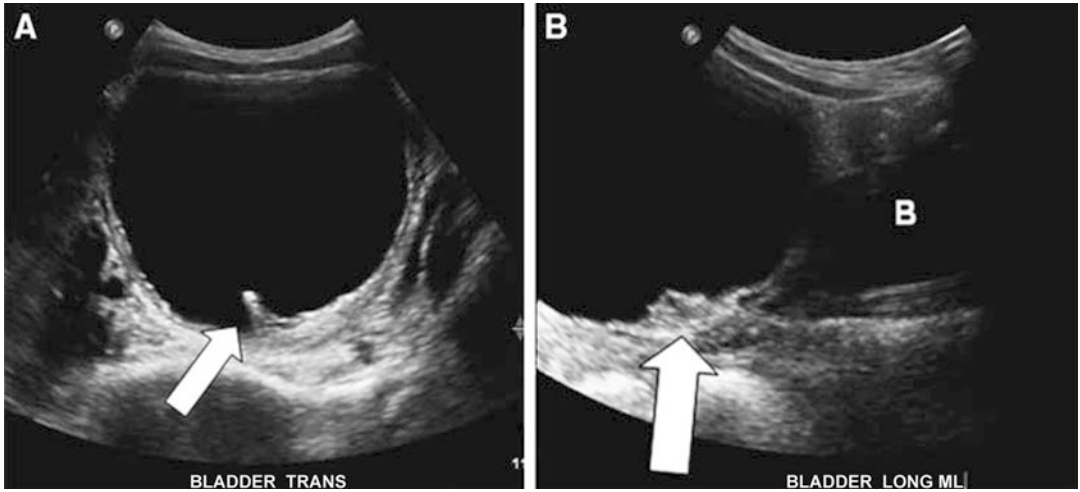


Fig. 27.2 (a) and (b). A 10-year-old girl presented with acute abdominal pain and urinary retention. At US, a very large simple cyst measuring up to 11 cm in transverse (a) and in long axis (b) could be seen. Note the wall of the cyst had a few focal thickened strands (white arrows). The bladder is visualized inferior to the cyst in b (bladder). At surgery, the ovary had torsed, was necrotic, and was

removed (Used with permission from Puig S. *Imaging of Female Children and Adolescents with Abdominopelvic Pain Caused by Gynecological Pathologies*. Medina LS et al., eds: *Evidence-Based Imaging: Improving the Quality of Imaging in Patient Care*. New York: Springer Science; 2011)

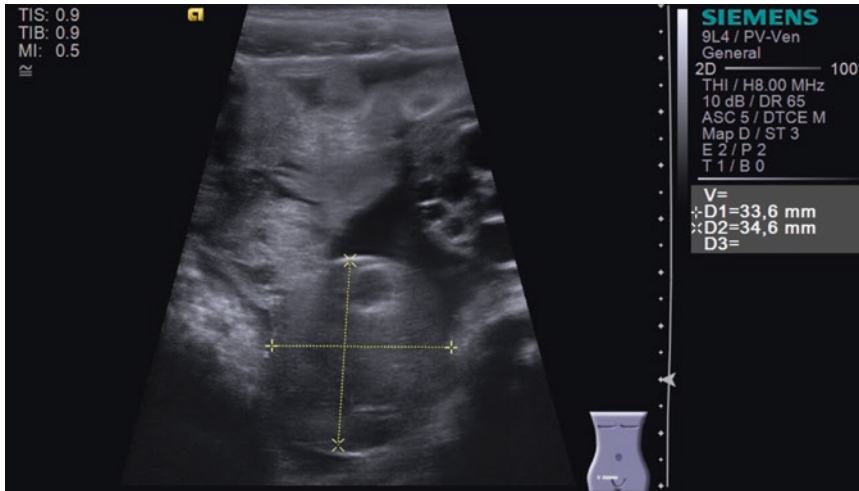


Fig. 27.3 Ovarian torsion in a 32-year-old female with acute pelvic pain. US in the axial plane shows an enlarged inhomogenous ovary without blood flow on color Doppler (not shown)

SPoiled Gradient Recalled echo (SPGR) with fat saturation before and after intravenous gadolinium (in patients with acceptable renal function). MRI can be used as an alternative to imaging with CT. It is not as sensitive for calcification but can provide functional data.

Future Research

- More and larger clinical follow-up studies are needed to better define the role and utility of imaging in the treatment of women and children presenting with acute pelvic pain in the ED.

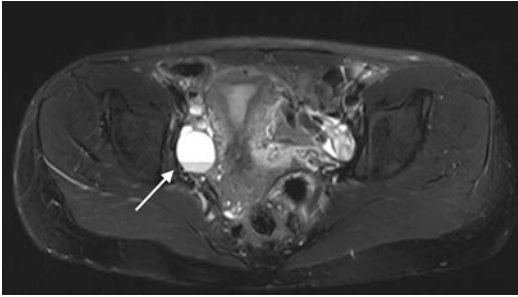


Fig. 27.4 Hemorrhagic ovarian cyst on the right (*white arrow*) in a 27-year-old female with acute pelvic pain. Axial MRI T2-fat-sat sequence depicts the hematocrit level within the cyst, indicating acute hemorrhage

- The use of limited, fast MR protocols should be investigated for their cost-effectiveness.
- The development of MR tables with continuous table movement similar to CT in conjunction with focused, fast MRI protocols will allow for increased use of MRI in infants and children without sedation.

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The Acute Scrotum in Adults and Children: Evidence-Based Emergency Imaging

28

Jennifer L. Cullmann and Stefan Puig

Key Points

- Of the etiologies for acute scrotal pain, testicular torsion is the only real emergency (strong evidence).
- Patients in whom there is a strong clinical suspicion for testicular torsion can be promptly referred for surgical exploration (moderate evidence).
- The first-line imaging tool of patients with suspected testicular torsion is color Doppler ultrasound with grayscale imaging, which is highly sensitive and specific (moderate evidence).
- Scintigraphy using technetium 99m to assess blood flow to the testes is a less commonly used imaging tool due to more available, less expensive, more rapid testing and less radiation with Doppler sonography (limited to moderate evidence).
- Successful manual detorsion of testicular torsion leads to reperfusion, which is

immediately visible with Doppler ultrasound. In cases of successful manual detorsion, surgical exploration with orchiopexy is still necessary (limited evidence).

Definition, Clinical Presentation, and Pathophysiology

Although the acute scrotum is defined as acute scrotal swelling with or without pain, most patients present with pain as their primary complaint. The most common differential diagnoses of the acute scrotum are torsion of the spermatic cord, torsion of the testicular appendages, and acute epididymitis or epididymo-orchitis (Table 28.1). Other diagnoses include strangulated hernia, segmental testicular infarction, trauma, testicular tumor, and idiopathic scrotal edema [1–3].

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Table 28.1 Potential causes of acute scrotal pain and swelling

Torsion	Trauma	Inflammation	Systemic disease	Other causes
Testicular torsion	Testicular rupture	Epididymitis	Henoch-Schönlein purpura	Incarcerated inguinal hernia
Torsion of the testicular appendages	Hematoma	Epididymo-orchitis	Lymphoma/leukemia	Scrotal edema
Testicular infarction	Hematocele	Abscess		Scrotal emphysema
				Appendicitis
				Testicular tumor

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Of the etiologies of acute scrotal pain, testicular torsion is the only real emergency [4–7]. It occurs when the testicle is abnormally mobile and twists on its vascular pedicle potentially resulting in testicular infarction. According to the mechanism, torsion of a testis can be divided into extravaginal (prenatal or neonatal) and the more common intravaginal (children and adults) torsion [8, 9]. The exact cause for extravaginal or neonatal torsion is unknown, and usually no anatomic defect can be identified to explain the torsion [10]. In patients with an intravaginal torsion, the most common anatomical anomaly identified is a narrow attachment of the tunica vaginalis from the spermatic cord to the testes secondary to high insertion of the tunica on the spermatic cord. This results in the “Bell-Clapper” deformity characterized by increased testicular mobility [10].

Immediate detorsion within a very narrow time window is necessary to provide a high testicle salvage rate, since irreversible ischemia may start after 6 h [8]. Dunne and O’Loughlin reported a series of 56 patients between 13 and 36 years of age, in which the average duration of pain in patients with viable testes was 9 h compared to 56 h of average duration of pain in those patients with nonviable testes [4]. Previous reports found 80% infarcted testes 10 h after pain onset, and after 24 h all testes were lost [4, 11]. Nearly 75% of patients need an orchiectomy if detorsion is delayed for more than 12 h [12]. However, anatomical variability may account for differences in the duration of viability of the torted testis [13].

Epidemiology

The incidence of spermatic cord torsion in patients presenting with an acute scrotum varies between 18% and 45%, depending on the age of patients [14–16]. The overall incidence is 1 in 4000 young males, with a peak age of 12–18 years [17, 18]. Testicular torsion is rare in patients older than 35 years [19]. Acute epididymitis is commonly the cause of acute scrotal pain in patients younger than age 18 and even more common in older patients [20]. Acute scrotal pain in prepubertal boys occurs most commonly from torsion of the testicular appendages, a process that may clinically mimic testicular torsion or epididymo-orchitis, but is managed conservatively with bed rest and pain relief [20, 21].

Overall Cost to Society

No data were found on the overall cost to society from the management of patients presenting with acute scrotum. In cases of testicular torsion, imaging of the scrotum will increase the costs, since surgery is required in those patients anyway. But this is counterbalanced by the imaging benefits for patients who do not need surgery [2].

Goals of Imaging

In cases of acute scrotal pain, the main goal in the emergency department (ED) is to confidently establish a surgical versus a nonsurgical diagno-

sis [22]. Testicular torsion requires emergency surgery. The clinical manifestations of other causes of acute scrotal pain such as epididymitis (epididymo-orchitis) or torsion of the testicular appendix resemble those of testicular torsion but are treated differently [21, 23–26]. In testicular torsion, manual detorsion may decrease the time of ischemia while surgical evaluation is being planned [8].

Methodology

This contribution is based on a systematic literature review using PubMed, Cochrane Library, and the National Guideline Clearinghouse for data relevant to the diagnostic performance and accuracy of both clinical and radiographic examinations in patients with acute scrotum. The search was performed without time limits and used the following terms: *acute scrotum, testicular torsion, epidemiology, clinical examination, imaging, ultrasound, scintigraphy, MRI, detorsion*, as well as acronyms and combinations of these terms. Animal studies and non-English and non-German studies were excluded.

Discussion of Issues

What Are the Clinical Findings That Raise the Suspicion of Testicular Torsion in Patients with Acute Scrotal Pain?

Summary of Evidence Clinical presentation and physical examination are nonspecific and include previous trauma, pain attacks, nausea, vomiting, elevation and transverse position of the testis, anterior rotation of epididymitis, and absence of the cremaster reflex. These findings have the highest sensitivity, specificity, positive and negative predictive values for testicular torsion, and the lowest for epididymitis (moderate evidence). The three key elements as predictors for testicular torsion are onset of pain less than 6 h, absence of cremasteric reflex, and diffuse testicular tenderness (limited evidence). The “blue dot sign” is only infrequently encountered (moderate evidence).

Supporting Evidence In the study that evaluated the three predictors for testicular torsion, out of the 141 patients, in the absence of any of these elements, none had testicular torsion. When these three elements were present, 87% were diagnosed with testicular torsion [24]. Other predictors of testicular torsion are a previous history of trauma and pain attacks, presence of nausea and vomiting, absence of urinary complaints, and a high position of testis [3, 6]. The “blue dot sign,” a pathognomonic finding described as a tender nodule with blue discoloration on the upper pole of the testis, is only infrequently encountered [6, 18, 20, 27]. Patients with testicular torsion typically present with abrupt scrotal pain, whereas those with epididymitis have a more gradual onset of pain [19]. Patients with torsion will have a normal urinalysis, whereas adults, but not children, with epididymitis will have an abnormal urinalysis [28].

What Is the Diagnostic Performance of the Different Imaging Studies?

Summary of Evidence Ultrasound with power Doppler has become the imaging modality of choice to diagnose or exclude torsion (moderate to strong evidence). It is a useful addition to the clinical examination, specifically to avoid unnecessary surgery (moderate evidence). Other imaging tools, such as the near-obsolete technetium 99m scintigraphy, are not superior to ultrasound (moderate evidence). If Doppler sonography is equivocal, magnetic resonance imaging (MRI) or scintigraphy can add diagnostic information but due to both higher costs and the relative delay to obtain these studies, particularly out of hours, their clinical value is limited (limited evidence).

Supporting Evidence

Ultrasound

In clinical practice, ultrasound is preferred over other imaging tools [20, 22, 29, 30]. Several cohort studies reported a sensitivity of at least 90% and a specificity of >95% to diagnose testicular torsion [31–42]. In combination with certain clinical conditions such as blunt trauma, specificity may reach 100% [38]. Ideally, both

pulsed and color Doppler ultrasound should be used. The real-time whirlpool sign on grayscale sonography in combination with the absence of flow in the distal spermatic cord, testis, and epididymitis was found to be the most specific and sensitive sign of torsion [43–45]. In general, the first ultrasound sign in patients with testicular torsion is hypo- or avascularity of the testicle with preserved homogeneous echotexture in the acute phase [26]. A false-negative finding might be due to flow in the capsule that is from a different arterial supply than the twisted spermatic cord [46].

Power Doppler ultrasound, which has been shown to be superior to color Doppler ultrasound in demonstrating slower flow better than [22] is especially useful to demonstrate intratesticular flow in prepubertal testes [19] and can be used in place of or as an adjunct to color Doppler ultrasound. Reported sensitivity rates for color Doppler ultrasound range from 96% to 100%, with a specificity of 84–95% [42, 47]. Caution is to be advised in the examination of prepubertal boys in which the study can be technically unsuccessful [19, 36].

A more common cause for acute scrotal pain than testicular torsion in adolescent boys and adults is epididymo-orchitis. Grayscale ultrasound combined with color Doppler imaging is the prime imaging means to make this diagnosis [48]. The most common cause of acute scrotal pain in children is torsion of an appendix testis [24], which can be difficult to identify with ultrasound. A size criterion of >5.6 mm alone may discriminate torsed from normal testicular appendages with low sensitivity but high specificity, obviating surgery in some cases [49]. Other uncommon causes of acute scrotal pain, diagnosed with ultrasound, are scrotal fat necrosis in overweight prepubescent boys [50], segmental testicular infarction in adult men [51, 52], and acute idiopathic scrotal edema, seen in both children and adults, and often a diagnosis of exclusion [53, 54].

Magnetic Resonance Imaging

Several studies show the value of MRI in detecting hypoperfused testes. After torsion of the testes,

the gadolinium enhancement and apparent diffusion coefficient (ADC) values in diffusion-weighted images are decreased [55, 56]. In case of inconclusive ultrasound and physical examination, MRI may be helpful. Watanabe et al. calculated a sensitivity of 93% and a specificity of 100% in 39 patients [57]. MRI can also visualize hemorrhagic necrosis in testicular torsion using contrast-enhances and blood-sensitive sequences.

However, due to the relative expense, less availability, and time-consuming examinations, including anesthesia in some children, MRI has decreased utility in the emergency setting [58–60].

Radionuclide Imaging

Scintigraphy has a high potential in differentiating ischemic from infectious disease [19, 34, 39, 61–64]. The specificity in the diagnosis of ischemia versus other photon-deficient lesions (such as infection) is slightly lower [20, 63]. Photon-deficient areas secondary to hydrocele, spermatocele, edematous appendix testis, and inguinal hernia can be mistaken for an avascular testis and therefore produce false positives [39, 63]. Also, the size of testes in infants and small children increases the risk of both false positives and false negatives [20]. For these reasons, and because of the longer preparation and exam performance time, lower availability, and higher costs relative to Doppler sonography, scintigraphy is no longer favored. Radionuclide scintigraphy also uses ionizing radiation and requires intravenous access while Doppler does not [8, 65].

In Cases of Testicular Torsion, Is Manual Reduction Required?

Summary of Evidence Manual detorsion of the testicle leads to immediate reperfusion of the affected testis and might be helpful to salvage the organ (limited evidence). If the ultrasound examination is performed by a physician with such experience, this procedure can be performed during the examination. However, it is successful in 30–100% of patients. The procedure must be

followed by bilateral orchiopexy to prevent future repeat testicular torsion (strong evidence).

Supporting Evidence Successful manual detorsion can lessen the surgical urgency of a twisted spermatic cord [8, 14, 66–68]. Most testes are torsed in the medial direction. Therefore, experienced clinicians/urologists can detorse these testes from the medial to the lateral side [8]. The subjective endpoint is the dramatic resolution of scrotal pain. One has to consider that the testis can be torsed up to 1080° [14]. A detorsed testis shows blood flow at ultrasound or scintigraphy immediately after the maneuver [14, 67, 68]. Adequate sedation and/or spermatic cord anesthesia should be administered, since the procedure is painful. Surgical exploration and orchiopexy remain necessary despite symptomatic improvement with manual detorsion [8, 14, 67]. Reported success rates in the literature vary from 30 to nearly 100% [66, 67].

Take-Home Table and Figure

Table 28.1 summarizes the causes of scrotal swelling and pain. Figure 28.1 presents an algorithm for patient workup for acute scrotum.

Imaging Case Studies

Case 1

Figure 28.2 presents a 12-year-old boy with 1 day of scrotal pain.

Case 2

Figure 28.3 presents a 7-year-old boy with scrotal pain for 1 day.

Case 3

In Fig. 28.4, a 38-year-old patient with scrotal pain is presented.

Suggested Diagnostic Protocols

Timely diagnosis and intervention are critical to decrease the risk of testicular loss [8, 14].

Ultrasound

Linear high-frequency transducer (7–12 MHz). Compare with opposite testis for blood flow and parenchymal homogeneity. If possible, try to visualize the twisted spermatic cord “whirlpool sign.” Spectral, color, and power Doppler should be used to evaluate the lack of blood flow within the testicular parenchyma. Doppler frequencies range from 3.5 to 10 MHz. Standoff pads can be used, if necessary, to improve imaging.

Manual Detorsion

Successful manual detorsion leads to immediate reperfusion of the testis. Since in most torsions the spermatic cord is twisted from lateral to medial, detorsion has to be performed from medial to lateral (the right testis counterclockwise, the left testis clockwise). Doppler is used both during the procedure and immediately afterward to assess testicular blood flow.

Future Research

- Accuracy of second-generation contrast media that might improve diagnosis, specifically in combination with modern ultrasound scanners with harmonic imaging.
- Prospective comparison of Doppler sonography with near-infrared spectroscopy, which is capable of noninvasively measuring a mixed venous and arterial hemoglobin tissue saturation of hemoglobin, which might allow noninvasive, bedside emergency diagnosis of testicular torsion.

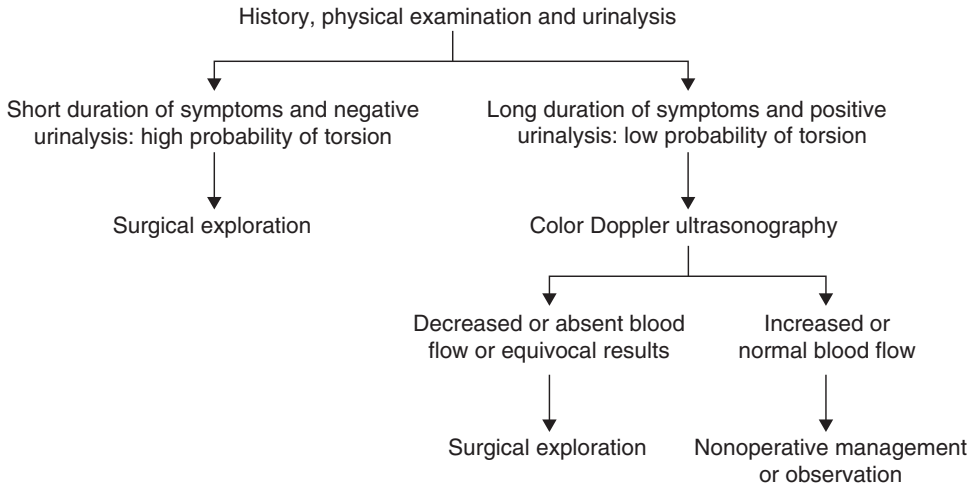


Fig. 28.1 Flowchart for patient workup. Acute scrotum can have a number of causes. Testicular torsion represents a surgical emergency because the likelihood of testicular salvage diminishes with the duration of torsion. (Adapted

with permission from Galejs LE, Kass EJ. Diagnosis and Treatment of the Acute Scrotum. American Family Physician Feb 15, 1999; 817, 59; 4. © American Academy of Family Physicians. All Rights Reserved)

Fig. 28.2 12-year-old boy with scrotal pain for 1 day. Torsion of the left testicle. Color Doppler ultrasound (left testis, long axis) shows a swollen heterogenous testicle without perfusion

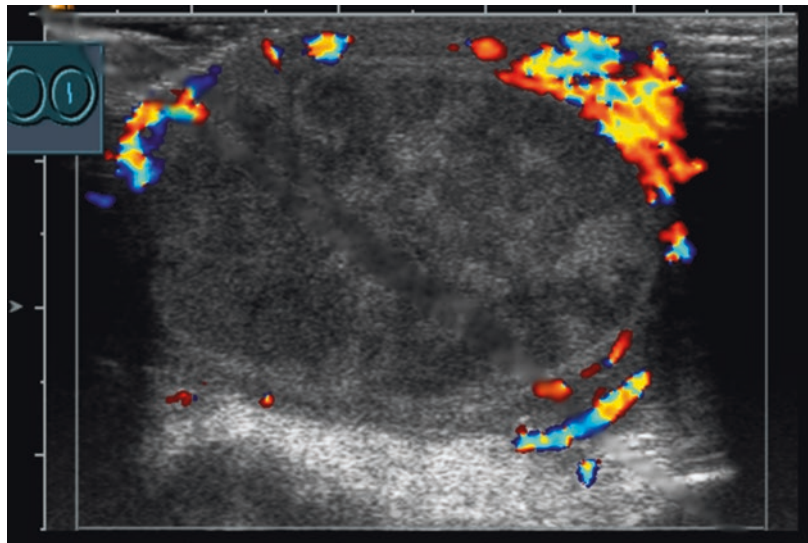


Fig. 28.3 Color Doppler ultrasound (short axis, at the level of the epididymis) in a 7-year-old boy with scrotal pain for 1 day. Enlarged heterogenous hyperechogenic epididymis on the left (arrow). Small hydrocele and scrotal edema

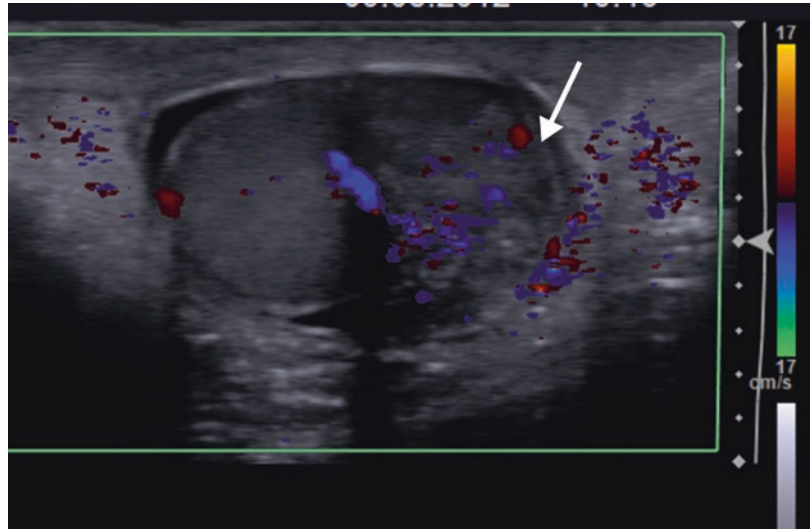
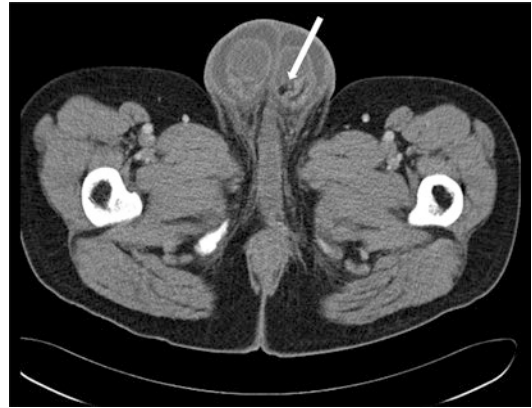


Fig. 28.4 Fournier gangrene. 38-year-old patient with scrotal pain. No improvement after medical therapy. Computed tomography shows an edema of the scrotum and fascial thickening with increased enhancement and gas gangrene (white arrow) on the left



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Part V

Musculoskeletal Imaging



Upper Extremity Injuries in Adults and Children: Evidence-Based Emergency Imaging

29

Kara Gaetke-Udager, Corrie M. Yablon, and Stefan Puig

Key Points

- Radiography is the initial imaging test of choice for upper extremity trauma (strong evidence).
- Wrist: Magnetic resonance imaging (MRI) has the best sensitivity and specificity to evaluate for *scaphoid fracture* and may be considered in the acute setting (strong evidence). Scaphoid fractures are often occult on radiographs, resulting in unnecessary immobilization (strong evidence). Bone scintigraphy is sensitive but not very specific for fracture; this can be useful for patients who cannot undergo MRI (moderate evidence). Computed tomography (CT) needs further study (insufficient evidence).

- Elbow: Radiographs are indicated as the first-line study in assessing for *elbow dislocation* (strong evidence). Vascular injury evaluation with CT angiography or conventional angiography must be considered if there is any suspicion of vascular injury (strong evidence); there is no evidence as to which of these methods is preferable. MRI provides excellent soft tissue evaluation in the acute or chronic setting (strong evidence). CT can be used in cases with complex fractures (moderate evidence).
- Shoulder: Radiographs are a necessary first-line study in the diagnosis of *glenohumeral dislocation* (strong evidence). MRI provides excellent soft tissue detail (strong evidence). MR arthrography is superior to MRI for evaluating labral, ligamentous, and cartilage injury (strong evidence). CT helps evaluate complex fractures (moderate evidence). CT arthrography can be useful in evaluating labral, ligamentous, and cartilage injury, although it is less useful for other soft tissue injuries compared to MR arthrography (moderate evidence).

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(continued)

- **Shoulder:** Radiographs are a necessary first-line study in acromioclavicular joint (ACJ) separation (strong evidence). When unilateral radiographs are negative or equivocal, bilateral views are necessary (strong evidence), and weighted views are recommended (moderate evidence). MRI provides excellent soft tissue detail and can be useful in distinguishing low- from high-grade injuries (strong evidence).

Definitions and Pathophysiology

Injuries of the upper extremity are common and occur most frequently at home, with recreational/sports-related injuries being the next most common setting [1]. Risk factors for upper extremity injuries in adults include advanced age, female gender, participation in athletics, and work that entails heavy machinery or other mechanism for high-energy trauma. In children, several independent risk factors have been identified: genetic constitution, birth weight, poor nutrition, low socioeconomic status, participation in sports, obesity, and repetitive stress [2].

Emergency department (ED) visits for upper extremity injuries are common, and imaging is a key component of diagnosis and management. This chapter focuses on the use of imaging to evaluate injuries to the upper extremities, specifically scaphoid fracture, elbow dislocation, glenohumeral dislocation, and AC joint separation. While other types of upper extremity injuries are more common, including finger lacerations and contusions [1], the use of imaging is not necessarily needed for such superficial injuries. In addition, many fractures, both in adults and children, can be easily diagnosed with radiographs without the need for further imaging evaluation [3]. We will focus on those injuries in which imaging evaluation might require multiple modalities and in which the use of some types of imaging is controversial.

Epidemiology

A data analysis of the US National Electronic Injury Surveillance System revealed that, as of 2009, there were about 3.5 million estimated injuries to the upper extremity treated at EDs in the United States [1]. This corresponds to an incidence of 1130 upper extremity injuries per 100,000 persons per year. By anatomic site, the majority were finger injuries (38.4%), followed by shoulder (16.8%), lower arm (15.3%), wrist (15.2%), elbow (10.5%), and upper arm (3.7%) injuries.

The most common type of upper extremity injury seen in an ED is a fracture [1, 3]. Wrist fractures account for 40% of all wrist injuries. About one third of elbow injuries and nearly one fourth of shoulder injuries are fractures. Dislocations of the elbow and shoulder comprise over 10% of injuries to those joints [1].

Overall Cost to Society

The estimated total compensable cost for upper extremity cumulative trauma in the United States was \$563 million based on data in 1992 [4]. There has been limited investigation into the cost of upper extremity trauma in the United States in recent years, with demand for more rigorous economic evaluation [5]. An investigation into the cost of trauma to the wrist, elbow, and shoulder in the Netherlands between 1986 and 2008 showed a total cost of 290 million euros, with wrist fractures overall being the most costly (83 million euros) [6].

Goals of Imaging

One of the primary goals of imaging in patients with upper extremity trauma is to identify acute injuries that require urgent attention, including closed reduction, or potential emergent surgical intervention. Another goal is appropriate triage of injuries that require clinical follow-up, including potential delayed/outpatient imaging studies such as MRI or CT.

Methodology

A comprehensive PubMed (US National Library of Medicine Database) search was performed for original articles published between 1966 and September 2015. The search strategy involved different combinations of the following terms: *scaphoid fracture, elbow dislocation, glenohumeral dislocation, acromioclavicular separation, Salter-Harris (or physeal) fractures, imaging, acute, radiography, MRI, CT, scintigraphy, and cost-effectiveness*. The search was limited to English language articles and human studies. Additional articles were identified by reviewing the references list of related articles. An initial review of articles' titles and abstracts were performed, followed by a review of the full text of selected articles.

Discussion of Issues

What Imaging Modalities Should Be Utilized to Diagnose Scaphoid Fractures?

Summary of Evidence Extensive research has been done to determine the optimal use of radiography, MRI, bone scintigraphy, and CT in diagnosing scaphoid fracture. Radiographs are typically the first-line study, but in at least 20% of cases, scaphoid fractures are radiographically occult (strong evidence). Standard practice is to apply a cast in those patients and repeat the clinical evaluation and radiographs in 10–14 days when resorption at the fracture line may make previously occult fractures visible. If the repeat radiographs are still normal or equivocal and the suspicion of scaphoid fracture continues to be strong, imaging with a second modality is indicated. A number of studies and several meta-analyses have shown that MRI has the best sensitivity and specificity for diagnosing fracture (strong evidence), and some groups recommend MRI on the day of injury to avoid unnecessary immobilization. Scintigraphy is very sensitive for fracture, and while not as specific as MRI, it is a reasonable alternative in patients who cannot

undergo MRI (moderate evidence). CT is widely available and has excellent sensitivity for cortical fractures, but trabecular fractures are sometimes missed, and more evidence is needed to warrant the routine use of CT in the acute setting.

Supporting Evidence The scaphoid is the most commonly fractured carpal bone, and the injury occurs most often in males 15–30 years old; the relative weakness of the radius in pediatric and elderly patients makes a buckle or Colles fracture, respectively, more common in these age groups [7]. The most common mechanism of injury is a fall on an outstretched hand [8]. Because the potential complications of a scaphoid fracture are serious, including nonunion, avascular necrosis, and arthritis, early diagnosis is crucial. While immobilization has commonly been used for nondisplaced fractures, with subsequent surgery as needed for nonunion, recent investigation has shown that early surgical management provides a favorable outcome to immobilization for acute nondisplaced and minimally displaced fractures, especially related to functional outcome and decreased disability [9].

After the initial clinical assessment, radiographs are usually the first-line imaging study to evaluate for fracture [10, 11]. However, fractures can be radiographically occult in one-fifth to one-third of cases [12, 13]. Because negative radiographic findings do not exclude a scaphoid fracture, up to 75% of patients with negative initial radiographs but suspicious clinical findings are unnecessarily immobilized [14]. Imaging follow-up for these patients varies greatly by institution, although a repeat set of radiographs after 10–14 days is most commonly performed [15].

MRI

A number of studies have focused on the use of MRI versus radiographs as short-term follow-up (within a week) to assess a clinically-suspected scaphoid fracture [13, 16–20]. Although MRI sometimes leads to false-positive diagnoses [21, 22], it has a high sensitivity for detection of occult fractures (Fig. 29.4) [13, 16–20], in some cases even when only two sequences (T1 coronal

and STIR coronal) are used [16]. In addition, MRI reveals other carpal fractures and soft tissue injuries that are not visible on radiographs [18, 19, 23]. Several reviews and meta-analyses have concluded that MRI is the imaging method of choice to evaluate scaphoid fracture [10, 22, 24], with an overall sensitivity of 96% and specificity of 99% [10].

Importantly, clinical management was changed for more than half of patients in one study who received an MRI after initial management based on radiographs [18]. One group showed that using MRI rather than repeat radiographs reduced immobilization time from 20 to 4 days and sick leave from 27 to 11 days; in-hospital costs were slightly reduced, while out-of-hospital costs were substantially reduced [25]. Another group showed that the costs of traditional work-up (i.e., initial radiographs, immobilization, and then repeat radiographs) were only about \$100 less than using MRI as an initial screening tool for patients with suspected scaphoid fracture [14]. Many of these patients eventually needed an MRI, thus further increasing the cost of this common diagnostic algorithm.

Scintigraphy

Because not all patients are able to undergo an MRI due to lack of availability, implanted metallic devices, and/or claustrophobia, bone scintigraphy is an alternative for those patients needing additional imaging evaluation for suspected scaphoid fracture. Scintigraphy shows increased radiotracer uptake at the fracture site, although this can lead to false-positive diagnoses in cases of bone contusion [26]. The sensitivity and specificity of scintigraphy have been reported as 97% and 89%, respectively [10]. However, several reviews that compared the utility of MRI and scintigraphy showed that MRI was superior for diagnosing scaphoid fractures as well as other soft tissue injury [27, 28].

CT

CT is widely available, has a fast acquisition time compared to MRI and scintigraphy, and has fewer patient restrictions compared with MRI. In addition, CT shows excellent osseous detail and, in

one small study, outperformed MRI in the identification of subtle cortical fractures [29]. However, CT has limited sensitivity for trabecular injury compared to MRI [29], and its overall sensitivity and specificity were 93% and 99%, respectively, in a large meta-analysis [10]. Another review concluded that while CT is cheaper and faster to obtain than MRI, CT should be used with caution due to its lower sensitivity.

What Imaging Modalities Are Appropriate to Evaluate Elbow Dislocation?

Summary of Evidence Radiographs are a necessary first step in the evaluation of elbow dislocation (strong evidence). There has been limited evaluation of the utility of CT in the acute setting, although CT is commonly used to evaluate complex fractures. MRI is the best modality for evaluating soft tissue injury, both in the acute and chronic setting, especially when surgical decision-making is based on the presence of ligamentous damage (strong evidence). Ultrasound offers the benefits of dynamic imaging and portability, but it is operator dependent and currently not widely used (limited evidence). A small but significant number of dislocations are associated with vascular injury, which is best assessed using either CT angiography or conventional angiography (strong evidence), depending on availability, with insufficient evidence to suggest one technique over the other.

Supporting Evidence The annual incidence of elbow dislocation in the United States is 5.2 per 100,000 person-years, with more than 40% of injuries occurring in patients 10–19 years of age, with a slight male predilection [30]. Elbow dislocations in adults are most commonly posterior [31]; anterior dislocations are rare and more commonly occur in children, while divergent dislocations, in which the distal humerus becomes interposed between the proximal radius and ulna, are also uncommon [32]. Most of the recent literature has focused on a mechanism of axial compression, supination, and valgus stress for

posterior dislocations, which most commonly results from a fall on an outstretched hand [31].

There are a few instances in which acute surgical management is necessary for elbow dislocation: open dislocation and compartment syndrome require emergent surgery, and elbows with unstable fractures might also need urgent surgical fixation [33]. Vascular injury also requires urgent intervention. As a general rule, non-emergent surgical intervention is needed in elbow dislocations with intra-articular fractures [34]. Those dislocations without fracture (simple dislocations) but with ligamentous instability are often surgically repaired, and some studies that evaluated the use of surgery in these patients showed good outcomes [35]. In elbow dislocations without ligamentous instability, an early, aggressive, range-of-motion rehabilitation protocol has been shown to be effective [33]. Imaging can aid in determining the presence and extent of these different types of associated injuries.

Radiographs

Patients with clinically suspected elbow dislocation should undergo radiographs as the first-line imaging study [36]. Two standard views (anterior-posterior and lateral) can be supplemented with specialty views such as medial or lateral oblique views, a radial head view, a coronoid view, various axillary views, and/or a gravity stress view. Dislocations result in a variety of fractures seen on radiographs, including radial head and neck fractures in 5–10%, coronoid fractures in 10%, medial and/or lateral avulsion fractures in 12%, and overall periarticular fractures in up to 60% [37]. Radiographic evidence of these fractures can help direct the use of additional imaging. In addition, some radiographic signs can suggest possible elbow instability: one study assessed the ulnohumeral distance on lateral radiographs of 10 patients with dislocation versus 20 normal patients [38]. Those patients with increased ulnohumeral distance after reduction correlated with continued elbow instability.

MRI

Two review studies have shown that MRI is the best modality for evaluation of soft tissue injury,

including ligament disruption, after elbow dislocation [32, 39]. The findings at MRI give some insight into the mechanism for posterior dislocation: an MRI study in 16 patients with posterior dislocation showed complete tears of medial elbow ligaments, while lateral ligament tears were sometimes partial [40]. This suggests a pattern of ligamentous failure beginning on the medial side. MRI is more commonly utilized in the subacute or chronic setting, although urgent MRI might be needed in cases in which the extent of instability prevents early mobilization, as these cases require surgical intervention [32].

CT

CT can be used to evaluate elbow fractures, especially when there is concern for intra-articular fracture and/or fracture fragments in the joint [39]. CT often provides a better evaluation of soft tissue calcification/ossification, fracture fragments, and intra-articular bodies than MRI. While CT is widely available and readily accessible, it also has the disadvantages of radiation exposure and poor visualization of soft tissues [32, 39]. There have been no studies to date directly comparing the utility of CT versus MRI for sequela of elbow dislocation, possibly due to the clear differences in the advantages and disadvantages of each modality. Despite the high rate of surgical intervention for elbow dislocation and fracture, elbow CT is relatively uncommonly performed [41].

Vascular Imaging

Approximately 5–13% of elbow dislocations have associated vascular injury [42]. Failure to recognize the signs and symptoms of vascular injury can lead to delay in diagnosis, thus putting the patient at risk for debilitating consequences [43]. Vascular injury usually occurs with open, rather than closed, dislocations, and vascular injury in closed dislocation can be challenging to diagnose due to collateral circulation that can mask symptoms [42]. If the clinical presentation is unclear, emergent imaging should be obtained either with CTA or conventional angiography [43]. One small study evaluated nine cases of posterior elbow dislocation, in which three

patients had complete ischemia (no pulse) and six others had less severe findings [44]. Arteriogram was obtained in five of the six less severe cases, and all responded well to surgical intervention (brachial artery bypass with autologous vein in eight of nine cases). There are no studies directly comparing the use of CTA versus conventional angiography.

What Imaging Modalities Are Optimal to Evaluate for Acute Glenohumeral Dislocation?

Summary of Evidence Radiographs are the first-line imaging study in the emergency setting (strong evidence); special views might be necessary to assess for dislocation and/or associated fractures. Cross-sectional imaging might not be necessary in the ED setting, but it is frequently needed in the subacute setting to assess for the sequela of shoulder dislocation. CT is more sensitive than radiography, and sometimes superior to MRI, to evaluate for fractures that can occur with dislocation (moderate evidence). MRI provides excellent depiction of associated soft tissue injury, although MR arthrography is better than MRI for specifically assessing labral and cartilage injury (moderate evidence). CT arthrogram has been shown to be equivalent to MR arthrography in detecting labral, ligamentous, and cartilage defects by some studies (moderate evidence) and is a useful alternative, especially if the patient cannot have an MRI.

Supporting Evidence The prevalence of shoulder dislocations in the general population is as high as 2% [45]. The maximum incidence occurs between 20 and 29 years of age [46]. Recurrence is inversely related to age: more than 80% of patients with a first dislocation before the age of 20 will dislocate again, while only 16% of patients with a first dislocation after age 40 will dislocate again [47]. Repeated dislocation occurs three times more often in men than women [48].

The glenohumeral joint has the widest range of motion of any joint in the body; however, this attribute also predisposes the joint to instability

and dislocation [49]. Dislocation is most commonly anterior, and the first dislocation results from trauma over 90% of the time, often from a fall on an outstretched hand or a direct blow during sports. Common associated injuries include Hill-Sachs lesions (superolateral humeral head impaction fracture), Bankart lesions (fracture of the anteroinferior glenoid rim), and tears of the labral-ligamentous complex [50]. Imaging plays a major role in evaluation of these injuries.

Radiographs

The American College of Radiology (ACR) appropriateness criteria recommend radiographs for acute shoulder pain, including either an axillary or scapular Y view to increase sensitivity for dislocation [51]. While Y views are easier to obtain and more comfortable for the patient [52], axillary views are more sensitive for dislocation and glenoid fractures [52, 53]. Additional views can be obtained to assess for fractures typically seen in dislocation, including a Stryker notch view for Hill-Sachs deformity and a West Point view to assess for Bankart or other glenoid fracture [54]. Postreduction radiographs are warranted in the acute setting to assess for fracture [49]. However, radiographs are less sensitive than MRI for subtle fractures, such as Hill-Sachs deformities, and soft tissue injury [55], and additional imaging is often warranted after the acute dislocation (Fig. 29.3).

MRI

MRI is considered the gold standard for assessing soft tissue injury related to shoulder dislocation [56]. While suspected injuries of the rotator cuff are the most common indication for MRI, injuries of other soft tissue structures such as the labrum, ligaments, and articular cartilage can also be evaluated with great accuracy. One study evaluated MRI versus arthroscopy for evaluation of osteochondral defects in 15 patients after dislocation; the sensitivity of MRI was 87% compared to 80% with arthroscopy, with the discrepancies thought to be due to the ability of either technique to show either intra-articular or extra-articular cartilage injury [57]. Another study evaluated the ability of MRI versus MR

arthrography (MRA) to assess articular cartilage injury, Bankart lesions, and Hill-Sachs deformities, with MRI having similar sensitivity and specificity compared to MRA [58]. Some studies have even shown that non-arthrographic MRI can be quite useful for labral evaluation, with an accuracy of up to 95% [59].

MRI can be useful in the subacute setting (days to a week after injury) to help evaluate for bone marrow edema/occult fracture [49]. However, findings on MRI performed in the acute to subacute setting can sometimes resolve on follow-up studies, as shown by Liavaag et al., who found that the presence of a capsular injury within a week of injury had often resolved by 30 days [60]. Also, a joint effusion and/or hemarthrosis present after injury can act as a pseudo “contrast” agent on conventional MRI to better evaluate intra-articular structures [49].

Magnetic Resonance Arthrography

MRA has little or no role in the acute setting and is mostly used to assess intra-articular injuries before surgical planning. MRA is typically performed after the injection of a dilute gadolinium contrast solution into the joint. The use of saline only as a contrast agent has also demonstrated a high degree of accuracy for labral, ligamentous, and osseous injuries [61]. MRA is especially useful for the evaluation of labral-ligamentous injuries, for which it has a high (greater than 90%) sensitivity and specificity [62]. Overall MRA has been shown to be superior to MRI for evaluation of labral tears based on a number of direct comparison studies and reviews [63–65]. MRA has particularly good sensitivity for anterior labral tears, superior labral tear anterior posterior (SLAP) tears, and partial thickness, articular-sided supraspinatus tendon tears [63].

CT and CT Arthrography

CT can be useful in the acute setting after shoulder dislocation to evaluate for fractures [54], with glenoid fractures typically being the most important prognostic indicator for future dislocation [49]. From a surgical planning standpoint, CT is useful to show the size of Bankart lesions, the amount of glenoid bone stock, the percentage of

the humeral head involved in a Hill-Sachs deformity, and the presence of small, intra-articular fracture fragments [54]. CT arthrography has been shown by Oh et al. to be a cost-effective, useful method for preoperative evaluation of labral and ligamentous injury and full-thickness rotator cuff tears, although it is not as sensitive as MRI in evaluating partial-thickness cuff tears [66]. A study by Lecouvet et al. showed that CT arthrography is accurate in detecting cartilage substance loss [67]. Another study showed that CT arthrography is slightly more accurate than MR arthrography for detecting cartilage substance loss [68]. However, CT arthrography results in suboptimal evaluation of associated soft tissue injury [53, 69].

What Imaging Modalities Are Useful in the Evaluation of Acromioclavicular Joint Separation?

Summary of Evidence Radiographs are the first-line imaging study to evaluate ACJ separation. The evidence favors the use of bilateral radiographs with and without weights (moderate to strong evidence). MRI is useful when radiographs and/or the clinical evaluation are discrepant, as it provides excellent evaluation of soft tissue structures, including ligaments (strong evidence). CT is not typically indicated to evaluate ACJ injuries, except perhaps in cases with complex fractures. The distinction of grade 2 vs. grade 3 ACJ injury was traditionally important to determine surgical management, although the evidence does not necessarily support surgery for grade 3 injuries (strong evidence).

Supporting Evidence ACJ separation accounts for approximately 10% of shoulder injuries, and it is most common among males aged 10–20 years [70]. The mechanism of injury usually involves either a direct blow with the arm in adduction or a fall on an outstretched hand [71]. The ACJ consists of two major ligaments: the acromioclavicular ligament and the coracoclavicular ligament. The coracoclavicular ligament

has two main components, the lateral trapezoid ligament and the medial conoid ligament. One study evaluated the coracoclavicular ligament in cadavers; the conoid ligament always failed first under stress, which led to superior and posterior positioning of the clavicle on radiographs, while ligation of the trapezoid ligament led to superior displacement of the distal clavicle on radiographs [72].

The original, three-grade classification system of ACJ separation described by Tossy [73] was later expanded by Rockwood (Table 29.1). Grading depends on the degree of injury to the ligaments surrounding the ACJ, with varying imaging appearances resulting from the particular injury grade. Anatomic studies in cadavers have shown that radiographic findings correlate with the Rockwood grading system, with grade 1 and 2 injuries resulting from AC ligament ligation and grades 3–6 injuries occurring after ligation of the CC ligament [74]. The grade of injury has important treatment implications. While in the past, grade 1 and 2 injuries were typically managed conservatively with grade 3 and higher injuries treated surgically, a number of studies and at least one meta-analysis have shown that grade 3 injuries can be managed conservatively with good outcomes [75, 76].

Radiographs

Radiographs should be the first imaging study obtained in the ED setting for patients with suspected ACJ dislocation. Radiographic technique typically involves bilateral anteroposterior views for comparison of the injured and non-injured side, with Zanca views (10–15% cephalad angulation of the beam) thought to provide additional sensitivity for ACJ injury [77, 78]. Acromioclavicular distances of 6–7 mm or greater and coracoclavicular distances of 11–13 mm or greater are typically considered abnormal [71].

Weighted views, in which the patient has radiographs performed with and without a 10-pound weight affixed to the affected wrist, are commonly used to evaluate whether stress on the ACJ can “unmask” a ligamentous injury (Fig. 29.5a–c). Weights are either held or suspended from the wrist, with no apparent differ-

ence between these two methods [79]. The use of weighted views has been controversial. One recent study showed that bilateral weighted views can unmask otherwise undiagnosed grade V injuries [78]. Another study showed that only 3 cases in 84 resulted in a grade 3 injury unmasked by weights, although given that in some cases the use of weights decreased the coracoclavicular distance, the reliability of this study is somewhat questionable [80].

MRI

MRI allows excellent visualization of acromioclavicular soft tissue structures [81]. Special planes, specifically a coronal oblique plane, can be helpful for evaluating the ACJ, although even this plane can be limited when a clavicle fracture or other deformity is present [70, 81]. One study evaluated the correlation between MRI and radiographs in cadavers with ACJ injury and showed that while MRI allows excellent visualization of ligamentous structures, the ligamentous injuries seen on MRI did not necessarily correspond to the findings on radiographs [82]. Another study showed that MRI provides a better assessment than radiographs of the extent of degenerative changes of the ACJ [83]. A review article by Antonio et al. showed that ligamentous anatomy of the ACJ is best seen on T1-weighted images, although these sequences can sometimes obscure edema and hemorrhage [84]. This group concluded that MRI should be used for grade 3 injuries or higher for better assessment of soft tissue injuries.

Which Specific Considerations Should Be Taken in Children Presenting with Upper Extremity Injuries?

Summary of Evidence Conventional radiography is the first-line imaging modality in pediatric upper extremity injuries and often the only imaging required (strong evidence). Views in at least two planes are required, with adequate coverage of the injured area. Knowledge of the specific structural and functional features of the immature skeleton is essential in interpreting radiographs

correctly. Occasionally, radiography may be followed by advanced imaging modalities. Sonography plays a small role in the evaluation of those injuries (limited evidence).

Supporting Evidence The physis also known as the “growth plate” is a cartilaginous area unique to the pediatric growing bone. Physeal fractures account for about 20% of all pediatric fractures [85]. They are usually classified into five categories using the Salter-Harris classification system to indicate progressive risk of growth arrest with increasing fracture category. Salter-Harris fractures type II are the most common. Radiography is sufficient for imaging the vast majority of these injuries. However, type I (mild) and type V (severe impaction) fractures may not be radiographically apparent, except for showing nonspecific soft tissue swelling. In these cases, MRI or ultrasound may better delineate the bone marrow edema of the fracture adjacent to the physis. However, the use of ultrasound in traumatic injuries requires a level of expertise that is not typically available [11]. CT may be necessary to plan operative intervention for intra-articular displacements in physeal fractures.

As opposed to adults, elbow fractures in children are quite common and represent about 10% of all pediatric fractures [85]. Diagnosis may be challenging, as this requires distinguishing normal ossification centers from fractures in a radiograph. Applying the mnemonic CRITOE (see also Fig. 29.6), which refers to the age-related sequence of appearance of six secondary ossification centers at the elbow, is essential [2, 86]. The most frequent pediatric elbow fractures are supracondylar fractures [87].

Take Home Tables and Figures

Table 29.1 explains the Rockwood grading system of acromioclavicular joint separation, and Table 29.2 makes imaging recommendations for upper extremity injuries. Figure 29.1 presents an

Table 29.1 Rockwood grading system of acromioclavicular joint separation with radiographic findings

Grade	Soft tissue injuries	Radiographic findings
I	Sprain of AC ligament	None
II	AC ligament ruptured Sprain of CC ligament	Clavicle elevated but not above superior acromion
III	AC and CC ligaments ruptured	Clavicle elevated above superior border of acromion Coracoclavicular (CC) distance less than twice normal
IV	AC and CC ligaments ruptured Joint capsule ruptured Trapezius and deltoid muscles detached	Clavicle displaced posteriorly into trapezius
V	AC and CC ligaments ruptured Joint capsule ruptured Trapezius and deltoid muscles detached	Clavicle markedly elevated and coracoclavicular distance more than double normal Scapula droops inferiorly
VI	AC and CC ligaments ruptured Joint capsule ruptured Trapezius and deltoid muscles detached	Clavicle inferiorly displaced behind coracobrachialis and biceps tendons

Data from Mazzocca AD, Spang JT, Rodriguez RR, et al. Biomechanical and Radiographic Analysis of Partial Coracoclavicular Ligament Injuries. *Am J Sports Med.* 2008;36:1397–1402

algorithm for imaging when a scaphoid fracture is suspected. In Fig. 29.2, an imaging algorithm for acute elbow dislocation is presented. Figure 29.3 presents an imaging algorithm for acute glenohumeral dislocation. In Fig. 29.4, an imaging algorithm for acromioclavicular joint separation is presented.

Table 29.2 Summary of imaging recommendations for specific upper extremity injuries

Injury	Population mostly affected	First-line imaging tool	Second-line imaging tools ^a
Wrist: scaphoid fracture	Adolescent and young adult males	Radiography; however, these fractures are radiographically occult in at least 20% of cases	<ul style="list-style-type: none"> • vRepeat radiography in 10–14 days If still negative or equivocal: <ul style="list-style-type: none"> • MRI (96%/99%) • Scintigraphy (97%/89%) • CT (93%/99%, but evidence for these values is insufficient)
Elbow dislocation	Adolescents	Radiography	<ul style="list-style-type: none"> • MRI: when ligament injury is suspected • CT: for evaluation of possible intra-articular fracture and/or fracture fragments • CTA: if vascular injury is suspected
Elbow fracture	Children and adolescents	Radiography	<ul style="list-style-type: none"> • MRI: to clarify radiographically equivocal fractures or for further evaluation of sports-related overuse injuries
Shoulder: glenohumeral dislocation	Young adults	Radiography	<ul style="list-style-type: none"> • MRI: for the evaluation of suspected rotator cuff or other soft tissue injuries • CT or CTA: to evaluate possible fractures for surgery planning
Shoulder: ACJ separation	Adolescent and young adult males	Radiography	<ul style="list-style-type: none"> • MRI: for better visualization of ligamentous structures in ACJ Rockwood grade III–VI injuries
Salter-Harris (growth plate) fracture	Children and adolescents	Radiography; Salter-Harris fracture types I and V may not be apparent on initial radiographs, except for nonspecific soft tissue swelling	<ul style="list-style-type: none"> • CT: for surgery planning in intra-articular displacements • MRI: if radiographic findings are equivocal

^aIn case of negative or equivocal results of first-line imaging and continued clinical suspicion, percentages in brackets are sensitivity/specificity values

Imaging Case Studies

Case 1

Figure 29.5a–c presents a 22-year-old man after a fall on an outstretched hand.

Case 2

In Fig. 29.6, the six ossification centers around the elbow joint are depicted.

Case 3

In Fig. 29.7a–c, a 42-year-old man presented with humeral head dislocation after an injury.

Case 4

In Fig. 29.8a, b, a 71-year-old woman is presented with a left ACJ injury after a biking accident.

Fig. 29.1 Imaging algorithm for suspected scaphoid fracture

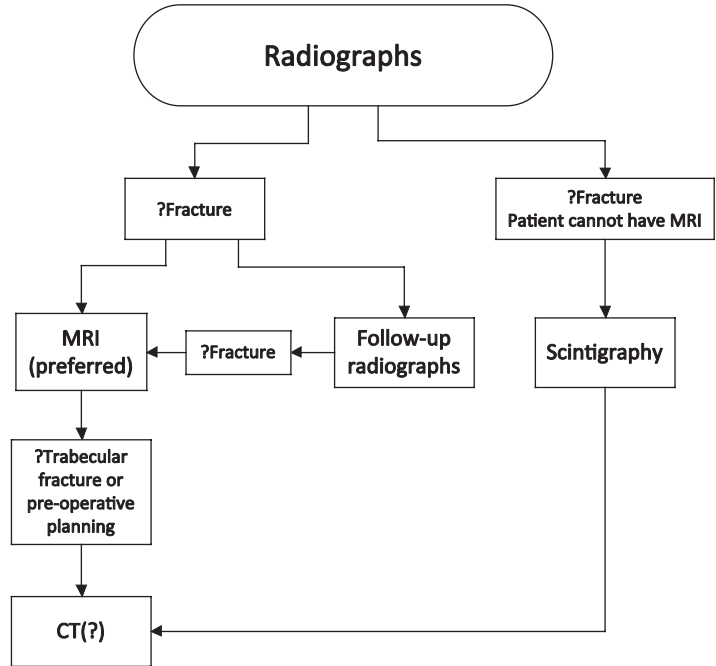
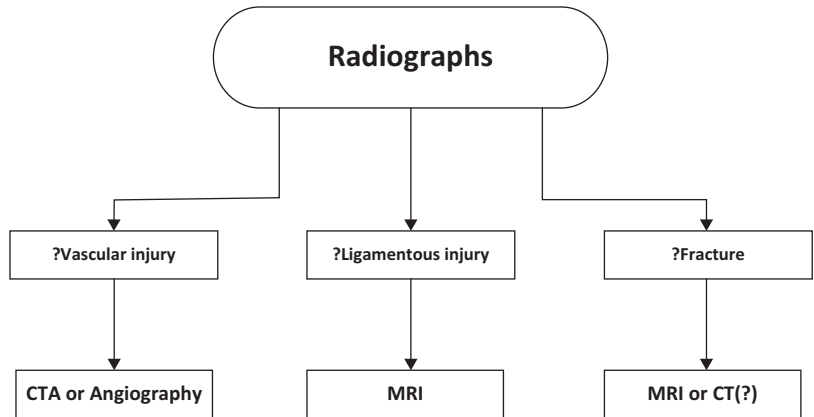


Fig. 29.2 Imaging algorithm for acute elbow dislocation



Suggested Imaging Protocols

Wrist Imaging for Scaphoid Fracture

1. Radiographs: anteroposterior, lateral, bilateral oblique views and scaphoid view (the latter usually not in children, unless requested,

because scaphoid fractures do not occur in children under 6 years and are rare in children under age 10).

2. In case of negative radiographs and persistent clinical concern, obtain MRI including at least coronal T1-weighted and coronal T2-weighted fat-suppressed sequences, usually also with T1-weighted sagittal and axial STIR.

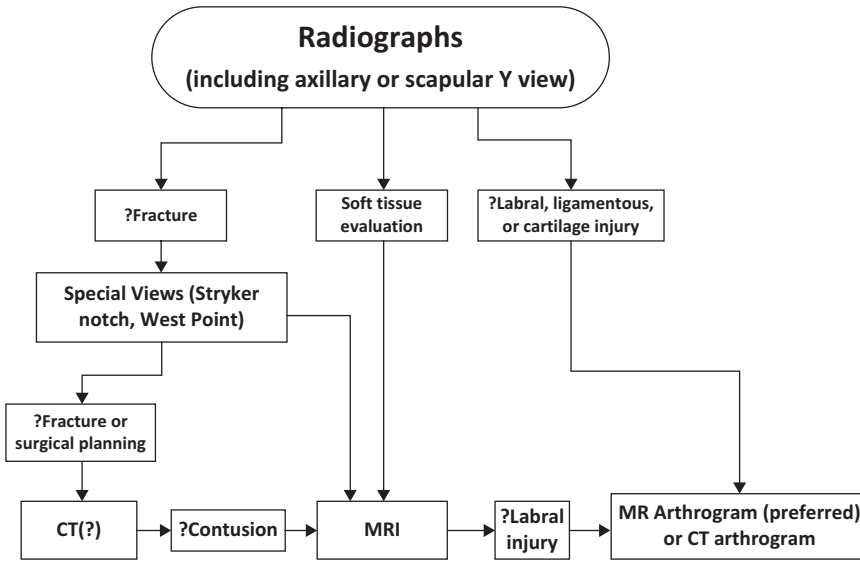
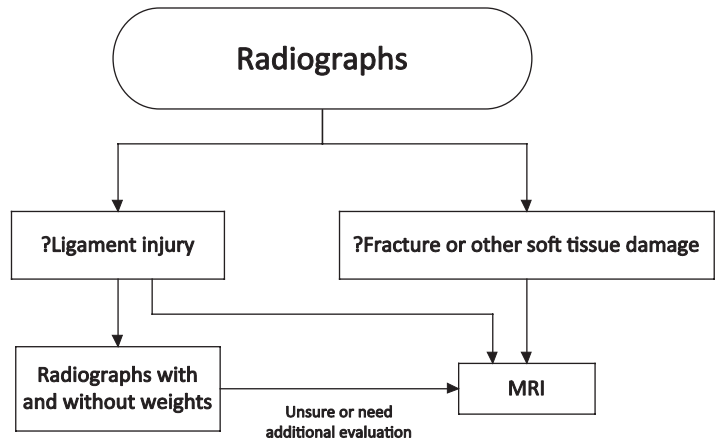


Fig. 29.3 Imaging algorithm for acute glenohumeral dislocation

Fig. 29.4 Imaging algorithm for acromioclavicular joint separation



Elbow Imaging for Dislocation (or Fracture-Dislocation)

1. Radiographs: anteroposterior, lateral.
2. If concern for vascular injury, obtain CTA: mid humerus to proximal radius/ulna including entire elbow joint, 0.625 mm axial acquisition with IV contrast administration, oblique coronal and sagittal reformats using thin (e.g., 2 mm) reformats. Depending on institution, conventional angiography might also be used.

3. If concern for ligamentous/soft tissue injury, obtain MRI including coronal T1-weighted and coronal T2-weighted fat-suppressed, sagittal and axial PD fat-suppressed.

Shoulder Imaging for Glenohumeral Dislocation

1. Radiographs: anteroposterior in internal and external rotation, axillary view (if possible) or



Fig. 29.5 (a)–(c) 22-year-old man with a radiographically occult scaphoid fracture after a fall on outstretched hand. Initial radiographs (a) were negative; the scaphoid view, shown here, does not demonstrate a fracture line. On

MRI, a T2-weighted fat-suppressed image (b) shows bone marrow edema in the scaphoid (*arrowhead*). On the corresponding coronal T1-weighted image (c), a linear, low-signal fracture line (*arrow*) is seen



Fig. 29.6 There are six ossification centers around the elbow joint. They appear and fuse to the adjacent bones at different ages. This order of appearance is specified in the mnemonic C-R-I-T-O-E (Capitulum-Radius-Internal or medial epicondyle-Trochlea-Olecranon-External or lateral epicondyle). The ages at which these ossification cen-

ters appear are highly variable and differ between individuals. (Used with kind permission from Robin Smithuis: *Elbow Fractures in Children*. 2005. [www.radiologyassistant.nl](http://www.radiologyassistant.nl/en/p420f0b3ef35c6/the-radiology-assistant.html). <http://www.radiologyassistant.nl/en/p420f0b3ef35c6/the-radiology-assistant.html>)

scapular Y view if not; consider Stryker notch and/or West Point views if further evaluation is needed for Hill-Sachs or Bankart injuries, respectively.

2. If evaluation of soft tissue injury is necessary, obtain MRI including axial PD fat-suppressed, coronal and sagittal oblique PD fat-suppressed, and sagittal oblique T1-weighted.
3. If evaluation of labrum, intra-articular ligaments, and/or cartilage is needed, get MR arthrogram including arthrogram procedure followed by axial T1-weighted fat-suppressed, coronal oblique T1- and T2-weighted fat-suppressed, and sagittal T1-weighted fat-suppressed. If CT arthrogram is used, perform arthrogram procedure followed by 0.625

oblique axial slices through shoulder (perpendicular to glenoid) with oblique coronal and oblique sagittal reconstructions.

Acromioclavicular Imaging for Joint Separation

1. Radiographs: bilateral AP radiographs with Zanca view with and without 10-pound weights.
2. If ligamentous evaluation is needed, perform MRI with axial PD fat-suppressed, coronal and sagittal oblique PD fat-suppressed, and sagittal oblique T1-weighted sequences.

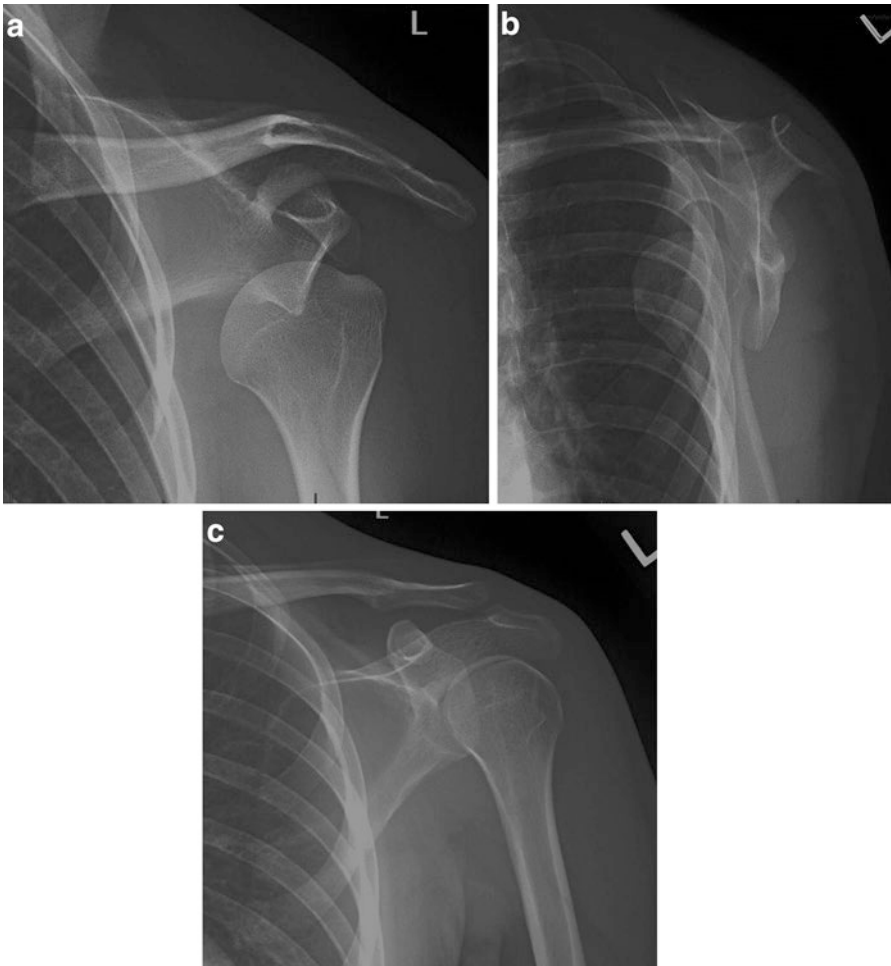


Fig. 29.7 (a)–(c) 42-year-old man with humeral head dislocation after an injury. (a) AP radiograph of the shoulder shows the humeral head located medially compared to the glenoid fossa. (b) “Y” view confirms anterior disloca-

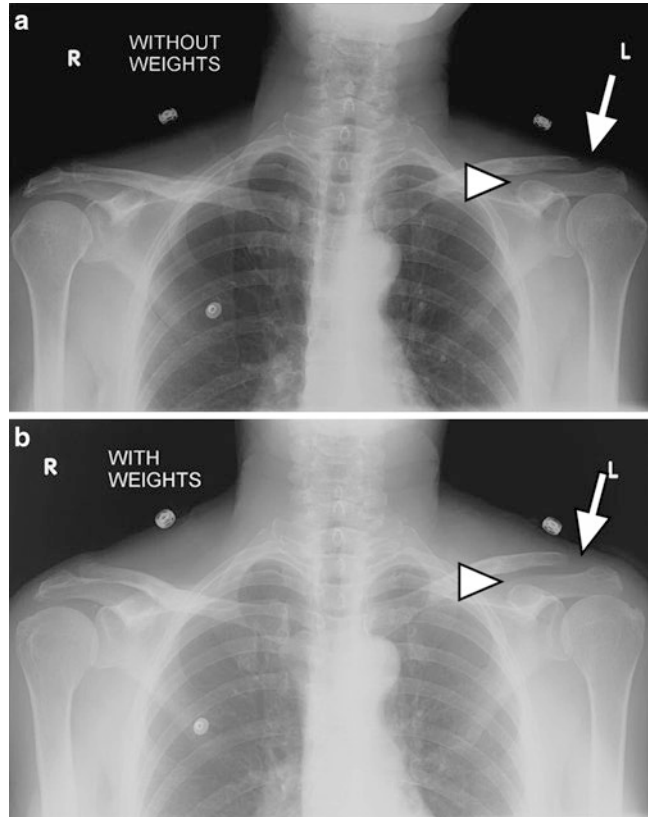
tion of the glenohumeral joint with the humeral head located anteriorly compared to the glenoid. (c) Postreduction radiograph shows the humeral head in anatomic position, aligned with the glenoid fossa

Future Research

Future studies should address the following research questions:

- Is MRI cost-effective as first-line imaging modality in suspected scaphoid fracture?
- Is there a role for CT to diagnose scaphoid fracture when radiography is negative?
- What is the optimal timing of MRI to evaluate for ligamentous injury in elbow dislocation (presently, MRI is more commonly used in the subacute or chronic setting)?
- Should all patients with shoulder dislocation undergo MRI evaluation? What is the optimal timing for MRI after reduction of shoulder dislocation?

Fig. 29.8 (a) and (b) 71-year-old woman with left ACJ injury after a biking accident. Bilateral AP radiograph (a) of the clavicles without weights shows a left acromioclavicular interval of 7 mm (arrow) and a coracoclavicular interval of 10 mm (arrowhead), both of which are at the upper limits of normal. Right acromioclavicular and coracoclavicular distances are normal. On the radiograph with weights (b), there is increased left acromioclavicular distance to 15 mm (arrow) and increased coracoclavicular distance to 15 mm (arrowhead)



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Pelvic Fractures in Adults: Evidence-Based Emergency Imaging

30

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Key Points

- In patients stable enough to undergo CT scanning, multiplanar reformations obviate the need for radiographs for identification of injury and treatment planning (moderate evidence).
- Fracture pattern, though not definitive, can predict probability of major hemorrhage and bladder or urethral injury (limited evidence).
- CT scan with intravenous contrast has high sensitivity for the identification of arterial injury related to pelvic fracture. However, the optimal CT imaging approach, including potential value of arterial and venous phases, remains unresolved (limited evidence).
- In patients at high risk, CT cystography can be used to exclude bladder injury (moderate evidence).

Definition and Pathophysiology

Pelvic fracture is a general term used to describe any fracture of the ischium, ilium, pubis, sacrum, or acetabulum. Pelvic fractures can be separated into pelvic ring disruptions, involving both the anterior and posterior pelvis in two or more places, and single-site fractures, of which acetabular fractures are the most important. Pelvic fractures commonly result from high-energy trauma and are a significant source of morbidity and mortality accounting for 0.3–9% of all skeletal fractures and with up to 25% of poly-trauma patients having an associated pelvic fracture ([1–13]). The most common mechanisms of injury include motor vehicle collisions, pedestrian vs. motor vehicle, motorcycle injuries, or falls from heights [1, 9]. Given the high-energy mechanisms involved, patients frequently have associated vascular, neurologic, thoracic, abdominal, musculoskeletal, and urologic injuries [4–7, 12, 14–25].

Pelvic ring disruptions and acetabular fractures have differing classification systems, treatments options, and implications for associated injuries, namely, hemorrhage and bladder/ure-

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thral injury, which occur in approximately 4–13% of pelvic ring disruptions but rarely in isolated acetabular fractures [1, 26–38]. The two most common classification systems for pelvic ring disruptions are the Young-Burgess and Tile/OTA (Orthopedic Trauma Association). Acetabular fractures are most commonly categorized according to the Letournel and Judet classification [7, 8, 39–41].

Epidemiology

The incidence of pelvic ring fractures is estimated to be 19–37 per 100,000 or approximately 2% of all fractures. Pelvic ring disruptions are more common in men (55–65%) than women. They are more common in young patients with mean and median age of approximately 37–42 years [4, 6–10]. The reported mortality rate for pelvic ring fractures varies widely between 4 and 33% (reportedly as high as 50% if open fracture) [1–3, 6, 12, 14–25]. Urethral injury occurs in 3–10% of pelvic fractures with men being more likely affected (20% in men vs. 0–6% in women) [12, 26–28, 30–38]. Bladder rupture occurs in approximately 3–8% of pelvic fractures [1, 27, 28, 42].

The incidence of acetabular fractures is estimated to be 3 per 100,000, with a mortality rate of approximately 3%. The mean age of injury is trending upward in the United States likely due to increasing falls in the elderly [43].

Overall Cost to Society

There is very little data regarding the total societal cost of pelvic and acetabular fractures.

Zaloshnja et al. estimate the annual cost of pelvic fractures in survivors of motor vehicle crashes in the United States to be approximately \$1.5 billion with associated bladder and urethral injuries adding an additional \$1 billion annually [44].

Goals of Imaging

The goals of imaging are to characterize the type of pelvic fracture in order to guide treatment and attempt to predict high-morbidity complications (e.g., hemorrhage, bladder rupture, urethral injury).

Methodology

A PubMed search was undertaken in June 2015, using the following terms: pelvic fracture, acetabulum fracture, hemorrhage, urethral injury, bladder injury, angiography, radiograph, CT, and epidemiology. We excluded animal experiments, case reports, review articles, editorials, and non-English language articles.

Discussion of Issues

How Should Patients with Suspected Pelvic Fracture Be Imaged?

Summary of Evidence While radiography remains a useful tool in the initial evaluation of trauma patients, it has been largely replaced by CT evaluation in those stable enough to be scanned [45]. CT has both higher sensitivity and specificity for detection of pelvic fractures, though research data on the actual accuracy of either study is limited. Staging or classification of fractures is also improved with CT scan, particularly as multiplanar, and 3D reformations can replicate the views used in conventional radiography (moderate evidence).

Supporting Evidence Victims of major trauma often receive an anteroposterior pelvic radiograph immediately after arrival in the trauma resuscitation bay (trauma series), which aids in risk stratification of patients who are too unstable to undergo CT scanning [3]. A retrospective cohort study of 12 trauma centers in North

America shows that about 80% of patients who subsequently undergo angiography receive pelvic radiography prior to embolization (Linnau unpublished data).

Classification systems have divided pelvic fractures into pelvic ring disruptions and acetabular fractures. The Young-Burgess classification system [40], which built on the earlier system of Tile [39], divides pelvic ring fractures based on primary vector force (anterior compression, lateral compression, vertical shear) with determination of stability based on direction of force and extent of injury. Identification of unstable fractures can guide treatment and have prognostic value [40, 46–49]. Instability, and therefore the need for operative intervention, increases with increasing displacement of the posterior pelvis, including diastasis of the sacroiliac joints and displaced fractures through the sacrum. The most unstable pattern includes complete disruption of the posterior arch, enabled vertical displacement of one hemipelvis with respect to the other side.

Acetabular fractures are most commonly classified based on the system of Judet [41], which is based on identification of fractures to the anterior and posterior columns, and the anterior and posterior walls of the acetabulum in various combinations. Operative repair is generally required for displaced fractures with the specific surgical approach determined by the injury pattern. The Judet classification system is based on visualizing the acetabulum in the oblique view provided by so-called Judet radiographic projections. Currently, such views can be replicated with multiplanar CT, obviating the need for radiographs [50–53] (moderate evidence). In addition to the anatomic pattern of injury, surgical approach and prognosis may be affected by the presence of intraarticular fragments, and associated fractures of the pelvic ring or femoral head, readily visible on CT [54].

What Are Predictors of Major Hemorrhage in Pelvic Fracture to Guide Further Imaging or Intervention?

Major hemorrhage either in isolation or in combination with other injuries represents an important cause of death in patients with pelvic fractures. Identifying hemorrhage and identifying those who may benefit from hemorrhage control from either surgery or angiographic embolization are potential goals of diagnostic imaging.

Does Radiographic Fracture Pattern Predict Hemorrhage or Need for Surgery/Embolization to Control Bleeding?

Summary of Evidence Pelvic fracture pattern combined with simple clinical factors can predict probability of major hemorrhage. However, the accuracy of existing clinical prediction rules is insufficient to stand alone in determining clinical management (moderate evidence).

Supporting Evidence Several studies have found a positive correlation with certain fracture patterns with hemorrhage and need for pelvic angiography or surgery [40, 43, 46–49, 55–65]. Manson et al. concluded that the Young-Burgess system is useful for predicting transfusion requirements with the system able to predict mortality and other non-orthopedic injuries if divided into stable or unstable types [62]. Osterhoff et al. concluded that one could predict the need for blood and total fluid volume with both Tile and Young-Burgess, but there was no significant relationship between fracture pattern and death [63]. Eastridge et al. classified pelvic ring fractures as stable or unstable in regard to rotational and vertical instability. They found that hemodynamically unstable patients with stable pelvic fractures were more likely to have an intra-

peritoneal source of bleeding and should undergo laparotomy, and conversely hemodynamically unstable patients with unstable pelvic fractures were more likely to have a pelvic source of bleeding and should undergo embolization as a primary method of hemorrhage control. However, they noted there were many false-positives regardless of fracture pattern [65]. Manson et al. concluded that the Young-Burgess system is useful for predicting transfusion requirements with the system able to predict mortality and other non-orthopedic injuries if divided into stable or unstable types [62]. Osterhoff et al. concluded that one could predict need for blood and total fluid volume with both Tile and Young-Burgess, but there was no significant relationship between fracture pattern and death [63].

Conversely, other studies have concluded that pelvic fracture pattern alone does not consistently correlate with the need for embolization and should not be considered in isolation to determine the need for angiography [66, 67]. Additionally, some groups have found that clinic injury scores such as the Abbreviated Injury Score (AIS) and Injury Severity Scores (ISS) may better predict major hemorrhage and the need for embolization compared to pelvic fracture pattern [66, 68, 69]. Blackmore et al. developed a prediction model based on both clinical and radiographic predictors, which included initial hematocrit, pulse rate, and pubic symphysis and obturator ring fracture diastasis of greater than 1 cm. Under this system, the probability of major hemorrhage ranged from 1.6% with no predictors to 66% with three to four predictors [55]. This clinical prediction rule has not been prospectively validated.

Does Contrast Extravasation on CT Predict Pelvic Arterial Hemorrhage?

Summary of Evidence Several studies have found that contrast extravasation on contrast-enhanced CT (CECT) is highly suggestive of active hemorrhage in patients with pelvic fractures and may warrant angiography for further evaluation and potential treatment [64, 70–75]. In contrast, however, other studies have shown that many patients with such contrast “blush” have

stable vital signs and may not benefit from embolization unless clinically indicated by signs of persistent bleeding [76, 77] (limited evidence). The lack of contrast extravasation or “blush” on CECT has a high negative predictive value (moderate evidence). The use of arterial and venous phase CT results in more radiation and may not alter management (limited evidence).

Supporting Evidence The diffusion of multidetector CT technology has led to more patients undergoing CT scans for evaluation of traumatic injuries including patients who in the past were too hemodynamically unstable to go to the radiology department. Acute pelvic hemorrhage may result from injury to aortic or pelvic iliac branches, pelvic venous plexus, and/or fractures themselves. Arterial hemorrhage may be seen as a focus of extravasated contrast (“blushing”) on CECT scans. The value of adding arterial-phase imaging has been proposed to help differentiate between venous and arterial bleeding. However, the addition of arterial-phase imaging to venous phase imaging must balance the potentially beneficial information with the cost of more radiation and may not ultimately impact subsequent treatment or outcomes [78, 79].

Several studies have reported high accuracy for CECT in identifying arterial hemorrhage, in particular, with high negative predictive value. In a large retrospective study of 660 patients diagnosed with pelvic fracture of which 290 underwent CECT, Pereira et al. found only 13 patients (4.5%) who exhibited contrast extravasation on CT. Of those 13 patients, 9 were hemodynamically unstable and demonstrated active arterial bleeding at angiography. Of the 276 patients who did not demonstrate contrast extravasation, only one hemodynamically unstable patient required later embolization. The sensitivity and specificity for arterial bleeding were thus 90% and 98.6%. While the negative predictive value was 99.6%, the positive predictive value of contrast extravasation on CT requiring embolization was only 69% [72]. Stephen et al. demonstrated similar values in a retrospective review of 111 patients diagnosed with pelvic fracture, 11 of which

required angiography due to hemodynamic instability, with a sensitivity of 80%, specificity of 98%, negative predictive value of 98%, and positive predictive value of 80% [73]. Cerva et al. found that in 30 hemodynamically stable patients with blunt trauma and pelvic fractures who underwent both CECT and angiography, the sensitivity and specificity of CECT were 84% and 85%, respectively, for the identification of arterial hemorrhage, with overall accuracy in confirming the absence of arterial bleeding to be 90% [75]. Shanmuganathan et al. [74] and Ryan et al. [71] also found that contrast extravasation on CECT is an accurate predictor of arterial hemorrhage at angiography.

In contrast, two studies have questioned the significance of contrast extravasation (or “blush”) on CECT scan in regard to predicting the need for surgical or radiographic intervention. In a retrospective study of 162 patients with high-energy pelvic ring fractures, Verbeek et al. [76] found 68 patients with contrast blush (42%), of whom only 36 (53%) required intervention for pelvic hemorrhage control. One potential difference in this study was the higher incidence of contrast blush (42%) compared to less than 20% in other studies [55, 72, 73]. This increased incidence may be due to the location of a CT scanner in the trauma bay allowing the inclusion of patients who were potentially too unstable to undergo CT in other studies. Verbeek et al. reported a high negative predictive value of a pelvic blush for the need for surgery or angiography of 93%, similar to other studies. Michailidou et al. [79] reported that 43.5% of patients with arterial blush could be managed without intervention but did not separate patients with bleeding from pelvic fractures compared to other sources. Brown et al., in a study of 37 trauma patients with pelvic fractures who underwent both admission CECT and angiography, reported a lower negative predictive value for blush (71%). Patient selection may have biased the study of Brown et al. as they only included patients with angiography [80].

Several studies have investigated adding an arterial phase in addition to portal venous phase CT scans in attempts to differentiate arterial from

venous bleeding, which could influence clinical decision making. Anderson et al. [78], in a small retrospective study of 21 patients with pelvic fractures and evidence of vascular injury by CT, reported that the addition of an arterial phase allowed them to differentiate between arterial and venous bleeds. However, the differentiation of arterial and venous hemorrhage did not significantly alter management of patients, which may be due to the limited number of patients in the subgroups. Fu et al. [70], in a retrospective study of 144 patients with pelvic fractures, reported that the sensitivities of the venous and arterial phases for detection of arterial hemorrhage were 100% (49/49) and 89.8% (44/49), respectively, and that all patients who demonstrated active arterial hemorrhage also had positive results on venous phase images. They concluded that CT multiphase angiography resulted in more radiation and ultimately did not alter management.

Does Pelvic Hematoma Size Predict the Need for Intervention?

Summary of Evidence Several studies have reported that quantifying the size of pelvic hematoma in patients with pelvic fractures can serve as a predictor of transfusions and/or need for hemorrhage control by either angiography or surgery [3, 80, 81] (limited evidence).

Supporting Evidence Blackmore et al. [3] published a retrospective cohort study of 759 consecutive patients with blunt trauma who sustained pelvic fractures and underwent CT within 48 hours of admission. The majority of the patients had volumes of hemorrhage less than 200 mL (441/592), which corresponded to a 5% risk of arterial hemorrhage, with a minority having over 500 mL (29/592), corresponding to a 45% arterial hemorrhage risk. They found that for the hematomas greater than 500 mL, the risk ratios for arterial hemorrhage by angiogram and transfusion of greater than six units in the first 72 hours were found to be 4.8 and 4.7, respectively, although the potential inaccuracy of the pelvic hemorrhage measurements is a limitation of the study. In a 2005 retrospective study of 37

patients who underwent both CECT and pelvic angiography, Brown et al. [80] attempted to determine if the size of pelvic hematoma on admission CT can be used to predict bleeding at angiography. Their findings corroborate previous reports that 73% of pelvic fracture patients with significant hematoma had arterial bleeding at angiography. However, in their study, they also found that 67% patients with hematomas categorized as minimal had arterial bleeding at angiography. The discrepancies are likely due to selection bias from only including patients sufficiently unstable as to require emergency angiography. Charbit et al. [81] noted in 185 patients with pelvic ring fractures similar findings when categorizing hemoperitoneum as none, moderate, or large using semiquantitative measurements of the volume, with a positive predictive value of 70% for the need for therapeutic intervention with large hematomas.

What Are Predictors of Bladder and Urethral Injury in Pelvic Fracture to Guide Further Imaging or Intervention?

Pelvic fractures with associated genitourinary injuries result in significant morbidity due to stricture, infection, hemorrhage, incontinence, infertility, and erectile dysfunction. A delay in diagnosis of genitourinary injuries may occur in up to one fourth of patients with pelvic fractures [82]. Radiologic studies in concert with clinical factors (inability to void, blood at urethral meatus, boggy or high riding prostate, and/or gross hematuria) can help predict and identify bladder and urethral injuries aiding traumatologists, orthopedists, and urologists in making appropriate and timely management decisions.

Does Fracture Pattern Predict Urethral and/or Bladder Injury?

Summary of Evidence Pelvic fractures that involve the anterior arch are associated with urethral and bladder injuries. Medial pubic ramus fractures, sacroiliac joint diastasis, and public

symphysis diastasis are independent risk factors for urethral and bladder injury, although the positive predictive value is low given the low incidence of urethral injuries with pelvic fractures. The risk of urethral and bladder injuries increases with the degree of pubic symphysis diastasis as well as the overall severity of the fracture pattern. Isolated iliac and acetabular fractures are not associated with urogenital injuries [26–28, 30, 31, 36, 37, 42, 83–93] (limited evidence).

Supporting Evidence Aihara et al. [93] conducted a retrospective review of 362 patients in which they classified pelvic fractures according to anatomic location. The fracture locations included superior pubic ramus, inferior pubic ramus, pubic symphysis, sacrum, sacroiliac joint (SI), ilium, ischium, and acetabulum. Associations between these fractures and/or disruptions and bladder and urethral injury were investigated using Fisher exact test and multiple logistic regression analysis. They found that inferior ramus fractures, pubic symphysis diastasis, and sacroiliac joint disruption carried relative risks of 4.6 ($p = 0.008$), 2.9 ($p = 0.003$), and 1.8 ($p = 0.04$), respectively. The relative risk for bladder injury with pubic symphysis diastasis was 2.1 and with sacroiliac joint disruption was 2.0.

Basta et al. [31] performed a retrospective, nested case-control study of 119 male patients with pelvic fracture to identify predictors of urethral injury. They identified 25 eligible patients who sustained a urethral injury and randomly selected controls (four controls per injury case) who sustained a pelvic fracture with no urethral injury identified. The injury cases were similar to the controls in demographics but had more severe injuries (mean injury severity score was 23.9 vs. 17.4). Using multiple logistic regression, they found displaced fractures (1 cm or greater) of the inferomedial pubic bone (odds ratio 6.4, 95% CI 1.6–24.9) and symphysis pubis diastasis (odds ratio 11.8, 95% CI 4.0–34.5) to be independent predictors of urethral injury. They did not find any other pelvic fracture patterns that were predictive of urethral injury.

Pokorny et al. [92] found similar results with increased risk of urethral injury with pubic symphysis diastasis, unstable pelvis fractures involving both the anterior and posterior arches, and bilateral pubic rami fractures. Their group also reported an associated risk of urethral injury if there were midline fracture fragments. Lowe et al. [36] found that fractures of the pelvic fractures involving the anterior arch, multiple pubic rami fractures, or sacroiliac fractures had high sensitivity and specificity for predicating urethral injury. Devine et al. [91] found an increased risk with sacroiliac joint disruption, pubic symphysis diastasis, and crush injury involving the ischiopubic rami. Koraitim et al. [89, 90] reported that risk of urethral injury as well as erectile dysfunction increases with the number of public rami fractured, pubic symphysis diastasis, and sacroiliac joint disruption.

Diagnosis of Bladder Injury

Summary of Evidence Retrograde cystography is the gold standard for diagnosing bladder injuries. It can be performed as a conventional cystogram with radiographs or fluoroscopy or as a CT cystogram. CT cystograms and conventional cystograms have similar sensitivity and specificity [88]. The sensitivity and specificity for CT cystography for diagnosing bladder rupture are

greater than 95% [94, 95] (limited evidence). Standard CT scan of the abdomen and pelvis is neither sensitive nor specific for the diagnosis of bladder injury [96, 97]. If concern for pelvic hemorrhage exists, cystography should be performed following CT scan of the pelvis as the contrast extravasation from bladder disruption can lead to false negatives or indeterminate scans for pelvic hemorrhage [98] (limited evidence).

Diagnosis of Urethral Injury

Summary of Evidence Retrograde urethrogram (RUG) is considered the standard imaging study for diagnosing a suspected urethral injury in male patients and can also be used along with urethroscopy in female patients. Urethrography can be useful in both identifying the location and extent (stretch injury, partial or complete disruption) of the injury [99–102], though information on diagnostic accuracy is lacking (insufficient evidence).

Take-Home Table and Figure

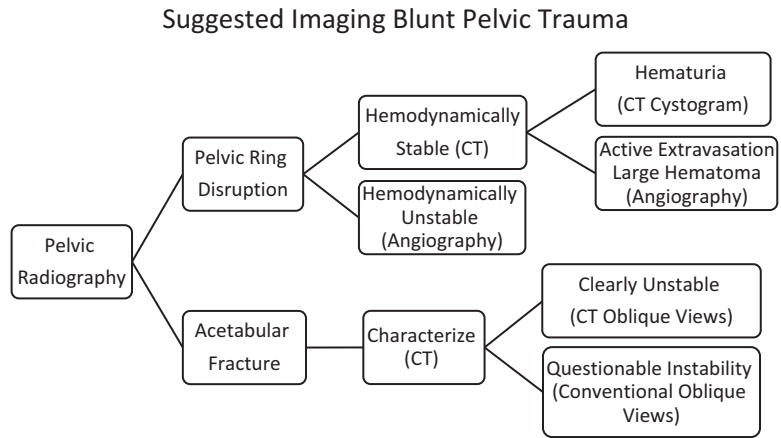
Table 30.1 highlights and summarizes prediction of arterial hemorrhage from pelvic fracture. Figure 30.1 presents an algorithm for suggested imaging for a pelvic fracture.

Table 30.1 Prediction of arterial hemorrhage from pelvic fracture

	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	References
<i>Radiography</i>					
Young-Burgess unstable pattern			59		[65]
Clinical predictors ^a					[55]
0			0.2		
1			1.4		
2			46		
3 or 4			66		
<i>CT</i>					
Contrast extravasation	80–90	85–99	44–69	93–99	[72, 73, 76, 77]
Hematoma size					[3]
<200 mL			5		
>500 mL			45		

^aDisplaced obturator ring fracture, displaced pubic symphysis, hematocrit < 30%, pulse > 130 beats/min

Fig. 30.1 Flow chart for suggested imaging in pelvic fracture



Imaging Case Studies

Case 1

Figure 30.2a–d presents the case of a hemodynamically unstable 49-year-old man after a motorcycle crash.

Case 2

Figure 30.3a–e presents the case of a 44-year-old man who fell 15 feet.

Case 3

The case of a 26-year-old man who sustained a pelvic ring disruption in a motor vehicle crash is presented in Fig. 30.4a, b.

Case 4

The case of a 7-year-old girl involved in a motor vehicle crash is presented in Fig. 30.5a–c.

Suggested Imaging Protocols

CT Technique

At our trauma center, victims of major blunt trauma usually undergo whole body CT which includes a non-contrast CT of the head, followed by a 20-second-delayed arterial-phase CTA of the neck and chest and a 70-second-delayed portal venous CT of the abdomen and pelvis. From this CT data, reconstructions of the entire spine are routinely obtained in bone algorithm. If the resuscitation AP pelvic radiograph shows findings concerning for major pelvic hemorrhage, the arterial phase of the CT scan is extended through the pelvis in order to show arterial vascular contrast extravasation, if present. Each portal venous CT scan is reviewed by a radiologist at the CT console while the patient is still on the table to determine the need for delayed imaging (renal injury). During this brief image review, the decision is also made if CT cystogram is indicated and necessary. Delayed images 10 min after the start of contrast injection are obtained in the same pass as the CT cystogram (if indicated).

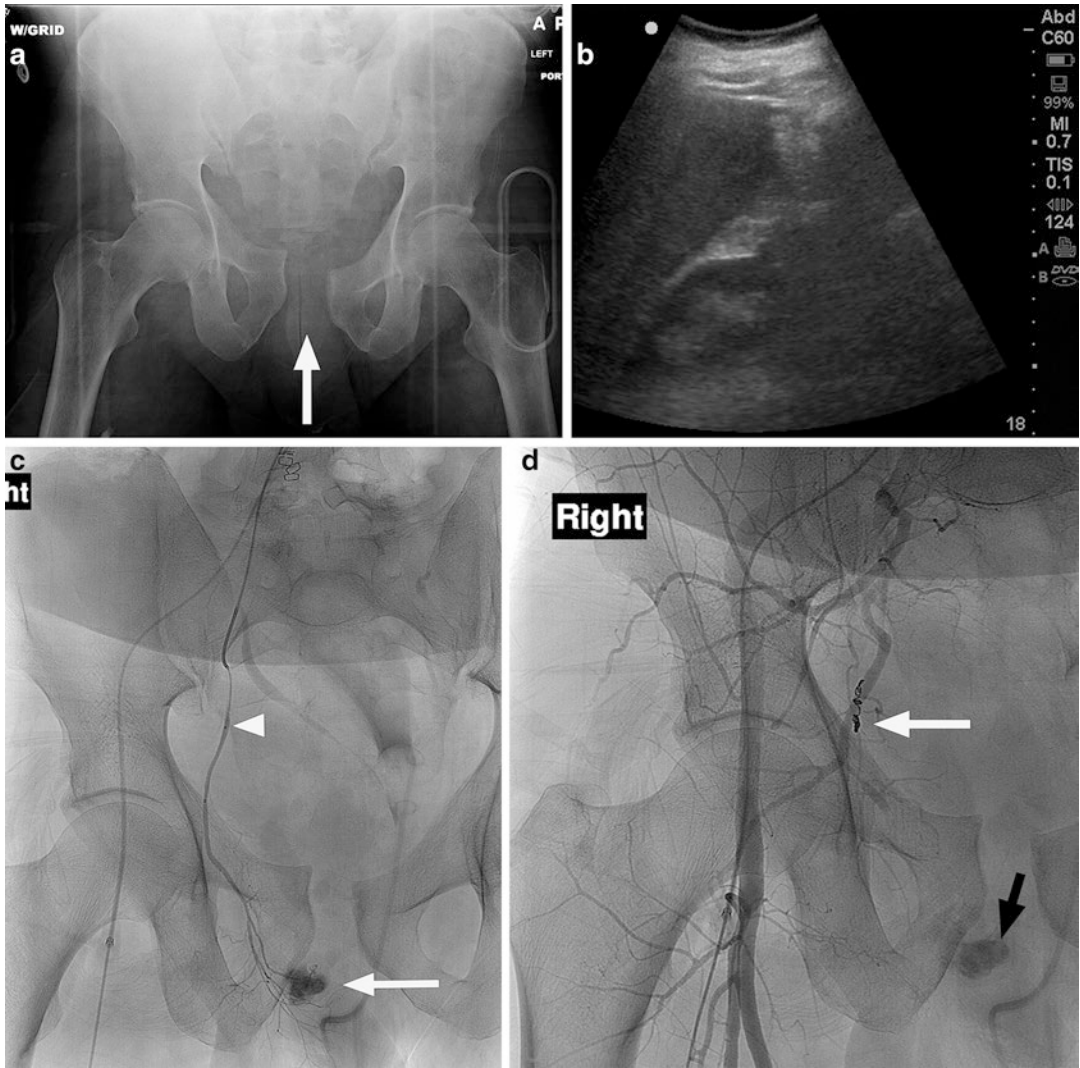


Fig. 30.2 (a) Initial anteroposterior (AP) pelvic radiograph of a hemodynamically unstable 49-year-old man after motorcycle crash shows widening of the symphysis pubis (*white arrow*), which represents a risk factor for major pelvic hemorrhage. Bilateral sacroiliac joint widening is also present. (b) A representative right upper quadrant image of the concomitantly obtained bedside sonography (FAST) shows normal appearance of Morrison’s pouch and the right free edge of the liver. This negative FAST exam makes hemoperitoneum as the cause for the patient’s hemodynamic instability unlikely. (c) Based on radiographic and clinical risk factors and the

absence of alternative explanations for the patient’s hemodynamic instability, a conventional angiogram was performed. Super-selective microcatheter angiogram (*white arrowhead*) shows brisk contrast extravasation and pooling from the disrupted right internal pudendal artery (*white arrow*). (d) Embolization of the anterior division of the right internal iliac artery was performed using coils (*white arrow*) and gel-foam slurry until hemostasis was obtained. Due to the large amount of arterial extravasation, residual contrast pooling from the preceding diagnostic angiogram is still visualized on the post-embolization image (*black arrow*)

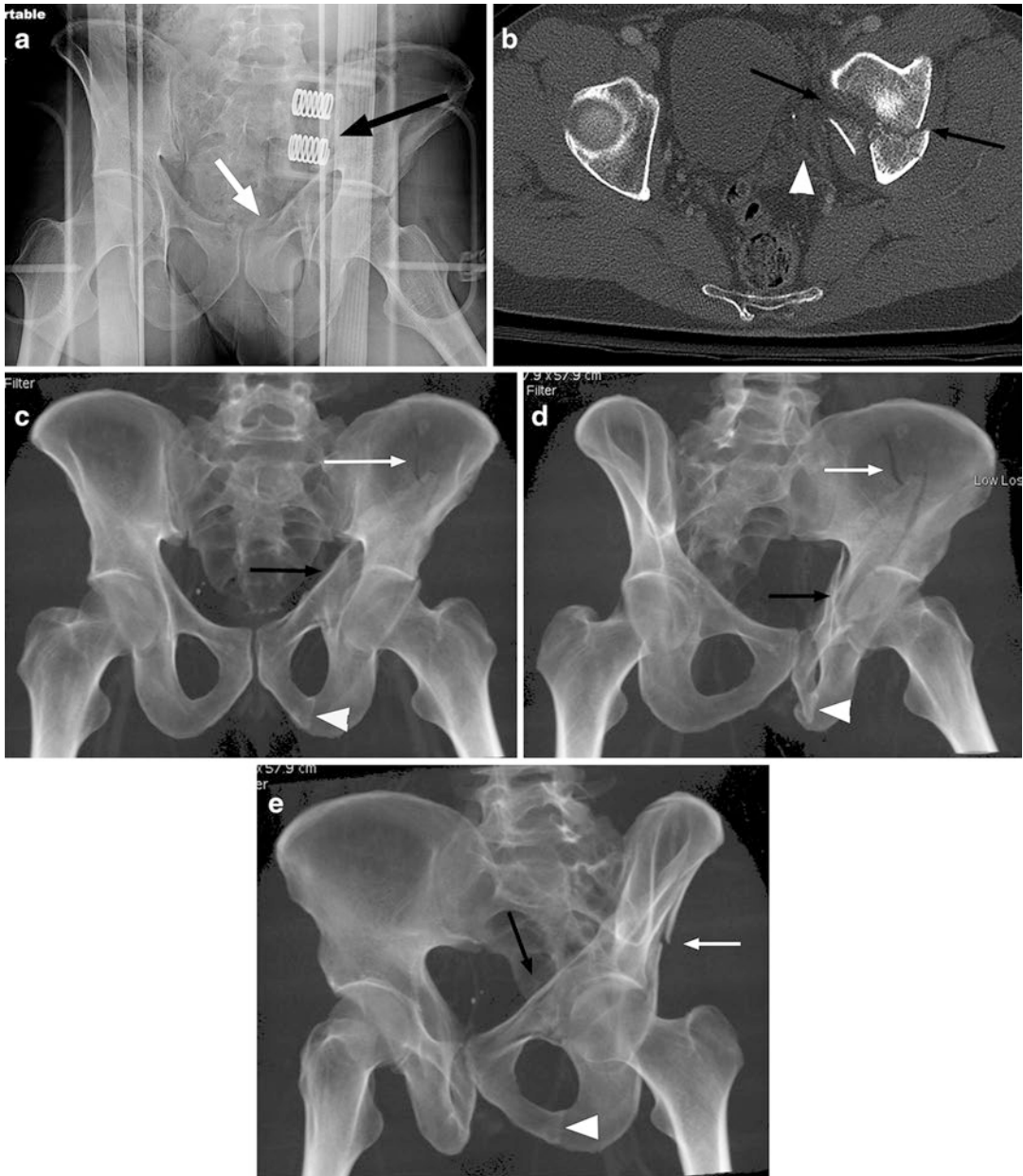


Fig. 30.3 (a) On the initial resuscitation anteroposterior pelvic radiograph of a 44-year-old man who fell 15 feet (5 m), the left acetabulum is partially obscured by a pelvic binder and radiodense parts of the trauma backboard (*black arrow*). A cortical irregularity suspicious for injury in the anterior portion of the acetabulum is seen (*white arrow*). (b) Axial image of the subsequently obtained bony pelvis CT shows a primarily coronal fracture through the roof of the left acetabulum (*white arrows*), typical for both column acetabular fracture patterns. There is a small associated pelvic wall hematoma (*small arrows*). (c) On the semitransparent 3D volume

rendered anteroposterior virtual radiograph generated from the CT data set, the artifacts present on trauma radiography (a) have been electronically removed. The associated (complex) column fracture of the left acetabulum is characterized by disruption of the iliopectineal and ilioischial lines (*small arrows*) with fracture extension into the iliac wing (*white arrow*, anterior column) and through the inferior obturator foramen (*white arrowhead*). (d) Semitransparent 3D volume rendered virtual oblique Judet radiograph: The iliac oblique view of the left acetabulum lays out the iliac wing and allows visualization of the posterior column of the acetabulum. Fracture

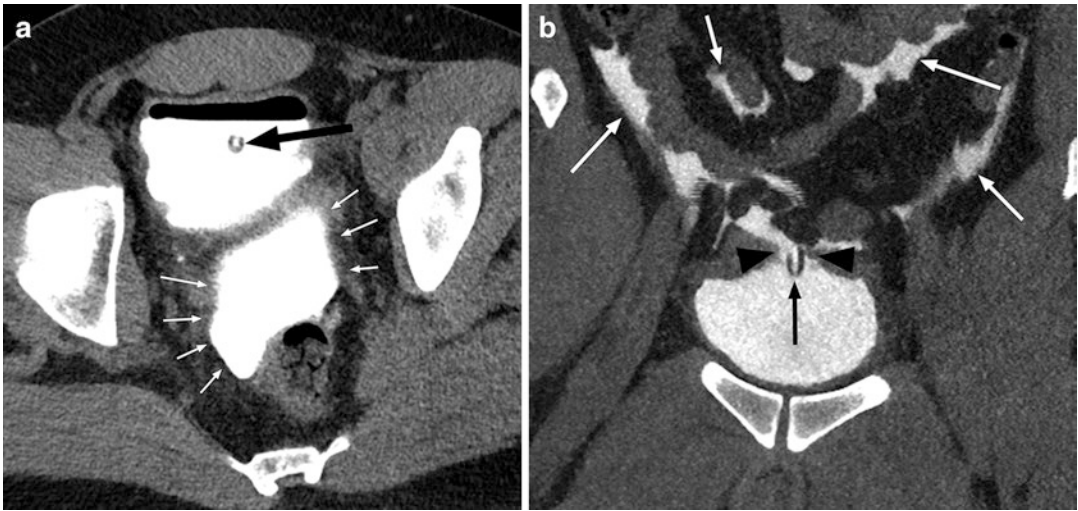


Fig. 30.4 (a) The axial CT cystogram image of a 26-year-old man who sustained a pelvic ring disruption in a motor vehicle crash shows a Foley catheter used for retrograde instillation of contrast into the urinary bladder (black arrow). There is an abnormal accumulation of contrast in the retrovesical space (white arrows) outside the urinary bladder, suggestive of intraperitoneal bladder rupture. (b) Low-dose coronal CT cystogram image confirms

intraperitoneal bladder rupture with multiple contrast collections between bowel loops (white arrows), which assume a polygonal shape, characteristic of intraperitoneal bladder rupture. There is direct visualization of the bladder wall defect near the dome of the injured urinary bladder (white arrowhead) adjacent to the tip of the Foley catheter (black arrow)

Dedicated bony pelvic CT images are retrospectively reconstructed from the portal venous CT data of the whole body CT scan for all pelvic ring disruptions and acetabular fractures. Using a bone algorithm, axial, sagittal, and coronal images are generated. Additionally, semi-transparent 3D volume rendered virtual radiographs of the pelvis are created from the CT data set to correspond with anteroposterior, inlet, outlet, iliac oblique and obturator oblique radiographic views. Conventional inlet, outlet, and Judet radiographs are only obtained if specifically requested by the pelvic surgeon. To aid in operative planning of acetabular fractures, surface-rendered 3D image series (loops) are created after the proximal femur image data is removed.

CT Cystography Technique

Patients who sustain a pelvic ring disruption and have hematuria require CT cystographic evaluation for bladder injury. To insure adequate distension of the urinary bladder, retrograde instillation of sterile dilute contrast (30 cc of IV contrast dissolved in one 500 cc bag of sterile saline) is performed in these patients through a Foley catheter. Thereby, the bladder contrast bag is mounted 40 cm above the patient’s abdomen in order to obtain a defined pressure equivalent to 40 cm water column. The pressurized instillation of contrast into the bladder results in sufficient stretching of the bladder wall to reveal bladder wall injury, which may be temporarily tamponaded. CT cystogram images are obtained in the same pass as the 10 min delayed images at low-dose technique (reduced mAs).

Fig. 30.3 (continued) extension into the sciatic notch (black arrow) and inferior obturator ring (white arrowhead) indicates posterior column disruption. Fracture extension into the iliac wing (white arrow) indicates disruption of the anterior column, confirming the both column fracture pattern. (e) Semitransparent 3D volume

rendered virtual oblique Judet radiograph: The obturator oblique view lays out the obturator ring and confirms anterior column disruption (black arrow) as suspected on the initial radiograph (a), inferior obturator ramus fracture (white arrowhead), and iliac wing fracture (white arrow)



Fig. 30.5 (a) The axial CT cystogram image of a 7-year-old girl involved in a motor vehicle crash shows a transverse left acetabular fracture (*black arrows*). On axial CT images, transverse acetabular fractures are sagittally oriented at the level of the acetabular roof. The body of the urinary bladder (*asterisk*) shows smooth normal contours without evidence of bladder injury. (b) An axial CT cystogram image of the inferior pelvis shows injury to the anterior pelvis with symphyseal asymmetry (*black arrow*). A

Foley catheter is shown in cross section (*black arrowhead*). Posterior to the Foley, there is a small H-shaped contrast collection (*white arrowhead*), which could be mistaken for a bladder neck injury. (c) Sagittal CT cystogram image confirms the absence of bladder injury in the body of the urinary bladder (*asterisk*) and at the bladder neck. There is pericatheter contrast reflux (*black arrowheads*) with retrograde contrast flow into the vagina (*white arrowheads*), which should not be confused with injury

Future Research

- Most evidence on injuries to the pelvic vessels focuses on the accuracy of imaging, with only limited research on the clinical implications of such injury identification and the optimal treatment.
- Clinical prediction rules for pelvic arterial, urethral, and bladder injury have not been validated.

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Lower Extremity Injuries in Adults and Children: Evidence-Based Emergency Imaging

31

Sarah D. Bixby and Stefan Puig

Key Points

- Radiography is the initial imaging strategy in a child or adult with lower extremity injury in the emergency department (ED) setting (strong evidence).
- However, many emergent radiographs can be omitted without missing a clinically significant fracture when well-validated clinical decision rules, such as the Ottawa knee and ankle rules in children and adults, are followed (strong evidence).
- Noncontrast computed tomography (CT) is infrequently indicated for further characterization of fracture patterns that may require surgical fixation or in severely injured patients in need of a rapid diagnostic work-up (moderate evidence).

- Magnetic resonance imaging (MRI) is much more sensitive for diagnosis and characterization of soft tissue injury and radiographically occult fractures, though the decision to proceed to MRI depends upon location of injury and findings on initial radiographs (strong evidence).

Definitions and Pathophysiology

This chapter focuses on imaging the child, adolescent, and adult presenting with lower extremity trauma from the hip to the toe, with specific attention on conditions that require imaging, as well as the most accepted imaging approach. Lower extremity injuries are common in patients of all ages, particularly in children who are active and involved in activities that place stress on their growing bones. Overuse injuries are far more common in the older child, adolescent, and young adult involved in organized athletic activities, particularly high-impact activities. Pediatric patients are at greater risk of overuse injuries compared to their adult counterparts because growing bones are relatively weak, particularly when the growth plates are unfused [1]. There are a number of lower extremity injuries that are unique to children, which vary depending on the age of the patient and the mecha-

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nism of injury. Since there are not (yet) enough studies to support specific imaging recommendations of lower extremity injuries in pediatric patients, this chapter will describe pediatric injuries in more detail while it will discuss injuries affecting adults and older children, for which evidence-based imaging guidelines are available, only briefly.

Epidemiology

Lower extremity injuries have a high incidence and place a major burden on health care. A data analysis of the US National Electronic Injury Surveillance System gave insight into the distribution of lower extremity injuries in patients presenting to US EDs [2]: The most common area of injury is the lower trunk (28%), followed by the ankle (20%), knee (16%), foot (15%), lower leg (11%), toe (7%), and upper leg (4%). Strains and sprains account for 36% of all lower extremity injuries followed by contusions/abrasions (19%), fractures (18%), and lacerations (8%). Fractures are the most common injuries to the toe, lower leg, and upper leg. Strains or sprains are the most common injuries in the ankle, the knee, and the lower trunk. Younger patients are more likely to have ankle sprains, foot contusions/abrasions, and foot strains/sprains. Older patients are more likely to have lower trunk fractures and lower trunk contusions/abrasions.

Overall Cost to Society

Injuries are a major cause of total health-care costs in the industrialized world. An analysis of hospital discharge registers of ten European countries was used to estimate injury incidence and costs per capita by sex, age, and type of injury [3]. The patterns of costs by these criteria were quite similar between countries. Costs per capita increase exponentially in older age groups, due to the combined effect of high incidence and high costs per patient. Elderly women, young children, and male adolescents are high-cost groups. In lower extremity injuries, the highest costs arise for fractures of the hip, pelvis, and

femur shaft (mean, 5530 € or \$6083), followed by complex soft tissue injury (mean, 3535 € or \$3889), fracture of the knee or lower leg (mean, 3504 € or \$3854), and ankle fractures (2636 € or \$2900). This cost distribution may be similar for the USA with higher mean costs per injury because of the more expensive health-care system as compared to Europe. Fractures of the hip, pelvis, or femur shaft also raise the highest cost per capita of all types of injuries and other locations than the lower extremities.

Goals of Imaging

The primary goal of imaging in patients presenting after lower extremity trauma is to identify fractures that require immediate immobilization and/or identify other explanations for pain and disability. The ultimate goal of imaging is to assist clinicians with appropriate treatment strategies to allow the patient to ultimately return to normal activities and avoid untoward complications.

Methodology

A Medline search (US National Library of Medicine database) for original articles published between 1966 and 2015 using Ovid and PubMed search engines was performed using different key search terms including (*pediatric lower extremity trauma, imaging (pediatric) knee injury, imaging (pediatric) hip injury, imaging (pediatric) ankle injury, imaging (pediatric) foot injury, imaging (pediatric) fractures, (pediatric) lower extremity imaging, (pediatric) osteochondral lesions, traumatic hip dislocation, imaging slipped capital femoral epiphysis, pelvic avulsion fracture, femoral neck fracture imaging, physeal fractures, traumatic patellar dislocation, Ottawa ankle rules (children), and Ottawa knee rules (children)*). The search was limited to human studies written in English. Abstracts were reviewed and selected based on applicability of the subject matter and the overall methodology. Additional articles were reviewed and selected based on the references of the reviewed articles.

Discussion of Issues

Which Imaging Modalities Are Used in the Initial Evaluation of Lower Extremity Injury?

Summary of Evidence There is strong evidence to support the use of radiographs in the evaluation of lower extremity trauma. While CT is not routinely used to evaluate fractures, it may be helpful to surgeons for presurgical planning and management (moderate evidence). MRI is considered on a case-by-case basis depending on the area of concern (strong evidence). While there are settings in which ultrasound may be useful, ultrasound is operator dependent, and there is little data supporting its routine use in the imaging evaluation of injured patients (limited evidence).

Supporting Evidence

Radiography

With few exceptions, the initial imaging strategy for a patient with concern for lower extremity trauma is radiography [4–7]. Despite widespread availability of more advanced imaging such as computed tomography (CT) and magnetic resonance imaging (MRI), radiographs remain the first-line imaging tool for detection of fractures. Standard radiographic views are acquired in two orthogonal planes. Additional views may be indicated depending on the anatomic area and the clinical concern (Table 31.1). In pediatric patients, comparison views of the unaffected limb are not routinely helpful if the initial interpretation is from a pediatric radiologist [8]. In some specific fractures, additional cross-sectional imaging may be necessary to determine an appropriate management plan. In the setting of normal radiographs, cross-sectional imaging may be warranted to evaluate for subtle fractures or soft tissue injuries that are not visible on radiographs. Radiographic approaches to specific injuries will be described in the various subsections.

Table 31.1 Suggested radiographic views for both children and adults of lower extremities after trauma

Body part	Standard views
Hip	Anteroposterior and cross-table or frog-leg lateral of affected hip
Femur	Anteroposterior and lateral
Knee	Anteroposterior and lateral ^a
Tibia and fibula	Anteroposterior and lateral
Ankle	Anteroposterior, oblique (ankle mortise), and lateral
Foot	Anteroposterior, oblique, and lateral
Calcaneus	Harris-Beath (axial) and lateral

Used with permission from Ha AS, Porrino JA, Chew FS. Radiographic Pitfalls in Lower Extremity Trauma. AJR 2014;203:492–500

^aBoth oblique view and sunrise (skyline) view may be added when a tibial plateau fracture or a patellar fracture, respectively, is suspected

Computed Tomography

Computed tomography may be useful in patients with displaced or complex fractures for a more thorough evaluation of the fracture pattern and degree of displacement of fracture fragments [4–7]. Computed tomography may also be useful when a fracture through a pathologic lesion is suspected, to better characterize the lesion. CT is most often reserved for patients for whom surgical management is deemed likely. The multiplanar and 3D imaging capabilities of CT allow surgeons to better understand the fracture pattern before deciding upon the most appropriate treatment strategy [9–12]. Computed tomography is otherwise not indicated in routine characterization of fracture patterns.

Magnetic Resonance Imaging

Magnetic resonance imaging is useful for identifying fractures that have no radiographic abnormality as well as ruling out other pathologies [4–7, 13]. The knee and the ankle are two of the most commonly injured joints [14]. While MRI findings in the knee often result in a change in diagnosis that carries treatment implications for the patient, MRI findings in the ankle rarely lead

to a substantive change in therapeutic management [14]. Magnetic resonance imaging is therefore most useful for evaluation of knee injuries that are concerning for ligamentous injury or internal derangement or as a problem-solving tool when radiographs fail to identify a source of pain in a patient with persistent pain after trauma, such as stress fractures or muscle injury.

Ultrasound

Though there are reports that ultrasound (US) has the ability to detect occult fractures in pediatric patients [15, 16], the use of US is not routine in the immediate work-up of a child with concern for lower extremity fracture. There are some indications for which US may be useful in conjunction with other imaging. Ultrasound is an excellent means of assessing for joint effusion, particularly within the hip where radiographs are insensitive [17]. Ultrasound is also useful for evaluating peripheral vascular injuries in the lower extremity [18]. It also plays a unique role in the imaging of neonates with concern for fracture, given that the epiphyses of the long bones are unossified [19]. It is also helpful in the detection of soft tissue injuries such as muscle hernias [20] and intramuscular hematomas [21]. Dynamic US is also useful in evaluating tendon dysfunction and tendon tear [22, 23]. Given that this chapter primarily focuses on evaluating for osseous injury after trauma, US will not figure prominently into the subsequent discussions despite the excellent capability of ultrasound to evaluate for soft tissue injury.

What Is the Imaging Approach to Hip Injury?

Summary of Evidence There are no strict or specific imaging recommendations for the pediatric hip in the setting of an acute injury (limited evidence). The decision to image, and which imaging modalities are most effective, will depend on clinical history and symptoms. In middle-aged and elderly patients presenting with acute hip pain, radiography is the established initial imaging tool, although its diagnostic accuracy is not very high (strong evidence). MRI is the most

appropriate modality to use in patients with radiographically indeterminate findings (strong evidence). Head-to-head comparisons of CT and MRI showed the superiority of MRI in the evaluation of hip injury (moderate evidence). Bone scintigraphy and US play a minor or no role, respectively, in hip injury of adults (limited evidence).

Supporting Evidence

Pediatric Hip Injuries

Pelvic avulsion fractures occur in the active adolescent population, particularly those engaged in high-intensity sporting activities. In skeletally immature patients, the pelvic apophyses serve as attachment site of major tendons. Apophyses are secondary growth centers with a physal equivalent, which renders them inherently weaker than the adjacent bone. Pelvic avulsion injuries may occur at different sites [24]. Apophyseal avulsions occur prior to physal closure and are caused by forceful contraction of the attaching muscles. An anteroposterior (AP) radiograph of the pelvis is sufficient in the initial evaluation of most avulsion fractures, with an additional oblique view when an anterior inferior iliac spine (AIIS) (straight head of the rectus femoris) fracture is suspected [25]. The fractures may be recognized on radiographs by the displacement of an ossified apophyseal fragment [26, 27]. Magnetic resonance imaging is more sensitive for unossified apophyseal fractures and has the added advantage of detecting other causes of hip pain [28]. Magnetic resonance imaging should be considered if the clinical suspicion for an avulsion fracture is high in the setting of normal radiographs. The degree of displacement of the avulsed apophysis is important, particularly at the ischial apophysis where displacement of greater than 2 cm may result in an unstable fibrous union [29]. As avulsion fractures heal, they become more visible on radiographs as heterotopic new bone forms around the avulsed fragment, oftentimes forming a bridge between the fragment and the pelvis. When repetitive forces are placed on a tendon insertion, a chronic traction apophysitis may result [30]. These inju-

ries are analogous to a nondisplaced Salter I fracture and may be undetectable with radiographs in the acute stages. Over time, the osteoblastic healing response leads to increased sclerosis on plain radiographs such that the diagnosis can be made without the need for advanced imaging.

Slipped capital femoral epiphysis (SCFE) is a hip disorder often related to trauma but may also be seen in children with other predisposing factors (e.g., obesity, hypothyroidism). SCFE is the most common physeal injury of the proximal femur. The femoral head is most often displaced posteriorly and medially. Radiographs are the preferred imaging modality [31–34], though early or mild SCFE may have subtle radiographic findings that may be overlooked [34]. Anteroposterior (AP) and frog-leg lateral radiographs are the most recommended views. On the frontal projection, the height of the femoral head is diminished and the physis is widened. The Klein line along the superior margin of the femoral neck may remain normal on the AP view, and therefore a frog-leg view is also recommended [35] where the degree of posterior displacement is best appreciated. When SCFE is suspected clinically but radiographs are not definitive, MRI may be performed for confirmation [36]. Magnetic resonance imaging findings of SCFE include abnormal marrow edema around the physis in addition to physeal widening and/or fluid in the physis [37].

Traumatic posterior dislocation of the hip is an uncommon but serious injury in children resulting from high-impact trauma. Often the femoral head relocates spontaneously shortly after the dislocation event. Imaging of the hips and pelvis is critical in any patient who has sustained high-impact trauma with complaints of hip pain. Initial radiographs should consist of an AP radiograph of the pelvis. If the femoral head remains dislocated on this initial view, reduction of the dislocation should take place before any additional imaging. Imaging clues that suggest that a transient traumatic dislocation event has occurred include nonconcentric position of the femoral head within the acetabulum on radiography or cross-sectional imaging or a posterior wall “fleck” sign (small fragment of bone adja-

cent to the posterior acetabular rim) on cross-sectional imaging [38]. Radiographs and CT both underestimate the presence of posterior acetabular injury after hip dislocation [39]. Magnetic resonance imaging is more sensitive for detecting bony, cartilaginous, and soft tissue injuries following posterior hip dislocation in children compared to CT [40, 41]. Patients who experience reduction of the femoral head after a traumatic dislocation often have posterior labral avulsion and also suffer posterior wall acetabular fractures and damage to the chondral surface of the femoral head [42].

Fractures of the hip are rare in children and comprise less than 1% of all pediatric fractures [43]. Femoral neck fractures in children are most often the result of high-energy rather than low-energy traumatic events. Although they are rare injuries, they are associated with a high rate of complications, including a 20% risk of osteonecrosis [44]. Radiographs of the child with a suspected femoral neck fracture should include an AP and cross-table lateral radiograph of the hip. An AP view of the entire pelvis may be helpful to evaluate for asymmetry in the proximal femoral physes or to detect subtle fracture lines. When radiographs are normal but a minimally displaced fracture is suspected, cross-sectional imaging is recommended over bone scintigraphy. Magnetic resonance imaging is the most useful imaging test for femoral neck stress fracture with a sensitivity of 100%, versus 68% sensitivity of radio-nuclide bone scans [45].

Adult Hip Fracture

The initial imaging study for suspected hip fracture in low-energy trauma is radiography. However, Ward et al. list a number of studies showing that radiographs alone cannot reliably exclude fracture in older patients while relevant studies in younger patients are missing [7]. Therefore, in many cases, MRI is needed as follow-up study, also because it reveals the extent and morphology of proximal femoral fractures more accurately [46–48]. Some studies have also shown that MRI is useful in detecting other etiologies for hip pain in patients in which a proximal femur fracture was suspected [49–51].

Although MRI is a costly procedure, it may help to shorten the time to surgery resulting in cost savings, with a systematic review of 52 studies showing that delaying surgery was likely to increase the rate of complications and the length of hospital stay [52].

CT would be able to provide a diagnosis in a more timely manner and has therefore been suggested for the evaluation of radiographically occult hip fractures in patients presenting to the ED after high-energy trauma. The evidence, however, is not (yet) very convincing because the majority of studies comparing CT to MRI results have shown the superiority of MRI in terms of diagnostic accuracy [7].

As far as bone scintigraphy is concerned, Ward et al. list several limitations, such as a higher number of false-positive studies relative to MRI, compromised cardiac and renal function in elderly patients, increased bone turnover related to osteoporosis, and time-consuming procedure [7]. There is a lack of studies and currently, US plays no role for an evidence-based imaging of hip injuries in adults.

What Is the Imaging Approach to Knee Injury?

Summary of Evidence There is strong evidence that the Ottawa knee rules can be applied to children >5 years of age and adults with high sensitivity for detection of significant fractures. Magnetic resonance imaging is more sensitive in the evaluation of certain pediatric knee injuries such as physeal fracture, juvenile osteochondritis dissecans, and lateral patellar dislocation and should be considered on a case-by-case basis on the basis of clinical symptoms and history (moderate evidence). Magnetic resonance imaging is also a valuable and accurate diagnostic tool for the diagnosis of meniscal, cruciate ligamentous, and chondral knee injuries (strong evidence).

Supporting Evidence The Ottawa knee rules (OKR) are a guideline aimed to aid clinicians in determining when radiographs are indicated in the case of knee pain/injury [53]. There are some

alternative guidelines available, but the OKR are to date the ones that have undergone the most extensive validation. According to the OKR, radiographs are indicated if a patient is >55 years old, and/or is unable to bear weight immediately and in the ED, and/or has isolated tenderness of the patella, and/or has tenderness at the head of fibula, and/or has inability to flex the knee to 90° [54] (Table 31.2). The reason for the necessity to apply the OKR refers to the fact that only about 5% of patients with acute knee trauma have a fracture on radiographs, while radiographs have been routinely requested in up to 70% [53]. But clinicians should exercise caution in relying solely on a nonsystematic clinical examination, because this may raise the likelihood of missing certain knee injuries, such as fractures of the patella, tibial spine, or fibular head [6].

The OKR can be applied with high sensitivity (92–100%) for children over the age of 5 years and adults, with a 30–40% predicted reduction in radiography rates [6, 55, 56]. One study in particular found that the inability to bear weight was the most sensitive predictor of fracture and would not have missed any fractures in a population of 146 pediatric patients [57]. The proximal tibia was the most common site for fracture in pediatric patients after knee injury, representing 47% of fractures [57]. Below is a discussion of several unique injury patterns in the pediatric knee and their imaging findings.

Specific Pediatric Knee Injuries

Transverse supracondylar fractures are the most common type of distal femur fracture in young children [58]. A supracondylar fracture is a fracture whose center is closer to the knee joint than the width of the femoral condyles and can be diagnosed on the basis of radiographs. These injuries are the result of forced hyperextension after a fall from a height or the result of a direct blow to the leg. Children between 5 and 13 years are most commonly affected [59].

Distal femoral physeal fractures are more common in older children and adolescents. Salter I fractures may occur with a sports-related injury in adolescent patients. Magnetic resonance imaging may be helpful for the diagnosis of distal femoral

Table 31.2 Clinical decision rules for radiography of acute knee, ankle, or foot injury

Ottawa knee rule	Ottawa ankle rule	
	Trauma to the ankle	Trauma to the foot
Knee imaging maybe required if ^a	An ankle radiograph series is only required if	A foot radiograph series is only required if
<i>Adult</i>		
Age 55 or older	There is any pain in the malleolar zone	There is any pain in the midfoot zone
Palpable tenderness of head of fibula	And any of the findings below	And any of the findings below
Isolated tenderness of patella (no other bone tenderness)	1. Bone tenderness at the posterior edge or tip of lateral malleolus	1. Bone tenderness over the base of the fifth metatarsal
Inability to flex the knee 90°	2. Bone tenderness at the posterior edge or tip of medial malleolus	2. Bone tenderness over the base of the navicular
Inability to bear weight both immediately and in the ED (four steps, limping is OK)	3. Inability to bear weight both immediately after the injury and in the ED for four steps	3. Inability to bear weight both immediately after the injury and in the ED for four steps
<i>Child</i>		
	There is any pain in the malleolar zone	There is any pain in the midfoot zone
Palpable tenderness of head of fibula	And any of the findings below	And any of the findings below
Isolated tenderness of patella (no other bone tenderness)	1. Bone tenderness at the posterior edge or tip of lateral malleolus	1. Bone tenderness over the base of the fifth metatarsal
Inability to flex the knee 90°	2. Bone tenderness at the posterior edge or tip of medial malleolus	2. Bone tenderness over the base of the navicular

(continued)

Table 31.2 (continued)

Ottawa knee rule	Ottawa ankle rule	
	Trauma to the ankle	Trauma to the foot
Knee imaging maybe required if ^a	An ankle radiograph series is only required if	A foot radiograph series is only required if
Inability to bear weight both immediately and in the ED (four steps, limping is OK)	3. Inability to bear weight both immediately after the injury and in the ED for four steps	3. Inability to bear weight both immediately after the injury and in the ED for four steps

Radiography is indicated if at least one of these characteristics is present [4–6]. These rules apply to both adults and children

^aIf any of the above criteria are met, this patient may need knee imaging: The rule is sensitive to rule out fractures, but not specific to suggest who may have a fracture

physeal fracture when radiographs are equivocal [60, 61]. Salter 2 fractures are more common than Salter 1 fractures of the distal femur, and may be subtle and difficult to detect if there is no fracture displacement, or the metaphyseal fracture line is mistaken for an overlying fat plane. Salter 3, 4, and 5 fractures of the distal femur are much less common and are usually the result of significant force such as motor vehicle collision.

Tibial tubercle fractures usually are sustained as a result of jumping activities with forceful extension or passive flexion against a contracted quadriceps muscle [24]. These injuries may occur prior to the point of fusion of the physis of the tibial tubercle. A defect in the anterior cortex of the tibial tubercle is present, distinguishing this entity from a similar condition, Osgood-Schlatter disease. In the setting of a tibial tubercle fracture, the tubercle may be frankly displaced, or the patellar tendon may be disrupted at its attachment. There are three types of tibial tubercle fracture: Type 1 fractures occur in young adolescents and involve an avulsion of the apophysis without injury to the epiphysis. Type 2 fractures occur in the same age range, but the fracture extends slightly into the epiphysis, which is slightly lifted. Type 3 fractures occur in older adolescents and include a fracture through the epiphysis into the joint [24].

While adults and older adolescents are prone to mid-substance tears of the anterior cruciate ligament (ACL), younger children who are still actively growing are more likely to avulse the tibial eminence at the attachment site of the ACL than to rupture the ACL itself. There are three types of *tibial eminence fractures* based on the degree of displacement of the fracture fragment into the joint space: Type 1 fractures are nondisplaced, type 2 fractures demonstrate elevation of the anterior fragment and no displacement posteriorly (a hinged fragment), and type 3 fractures are displaced in their entirety [62].

Also termed “osteochondral defect,” *juvenile osteochondritis dissecans* (OCD) is characterized by abnormalities within the subchondral bone and overlying articular cartilage at focal areas within the knee. OCDs are a common cause for knee pain in young patients who may present at the ED. These lesions are characterized by alterations in the subchondral bone and articular cartilage along the femoral condyles, patella, or trochlear groove of the distal femur and may be considered either stable or unstable by virtue of the status of the overlying cartilage and the presence of fluid undermining the lesion at MRI [63]. The medial femoral condyle is the most common site of involvement followed by lateral femoral condyle, patella, and trochlea [64]. The cartilage overlying the lesion may be intact, deficient, or abnormally thickened. Even when the cartilage is intact, however, the cartilage may still be abnormal. These lesions are associated with abnormal fibrovascular tissue at the cartilage/bone interface which manifests as T2-bright cystic appearing lesions at MRI [65].

Normal ossification variants of the femoral condyles may mimic OCD on radiography and MRI. The confusion between the two (normal variation in ossification versus OCD) may also explain why the prognosis is better for juvenile OCD compared to adult forms. Ossification variants are also more common in patients with OCD, but they regress spontaneously and do not evolve into an OCD [66]. They are located within the posterior third of the femoral condyle, lack surrounding marrow edema, and generally have a wedge-shaped configuration [66]. These ossification variants regress spontaneously.

Knee Injuries in Older Children, Adolescents, and Adults

Ligamentous sprains, soft tissue contusions, and muscle strains far outnumber osseous lesions in the lower extremity after trauma in general [6, 67], though in pediatric patients, ligamentous injuries are less common than physeal injuries [1]. The knee is a commonly injured joint, and numerous studies have shown that MRI is the imaging modality of choice to identify *meniscal, ligament, chondral, and nondisplaced bone injuries* around the knee [68]. A *Segond fracture* which is seen on a radiograph is, while small, clinically relevant because of its high association with ACL tears and meniscal tears in most cases [69].

Patellar fractures may be sustained by direct trauma or an avulsion fracture at the site of tendon attachments. These fractures are caused by a rapid contraction of the quadriceps muscle. The patella has several central ossification centers, and ossification progresses peripherally during growth. The injury may not be visible on radiographs if bone is not avulsed with the cartilage, but the stripped cartilage may go on to ossify on follow-up radiographs. *Patella alta* may be the sole radiographic evidence of the injury. For imaging findings of *transient patellar dislocation*, MRI is more sensitive than radiographs, including injury to the medial patellofemoral ligament, bone contusions, and osteochondral injuries [1, 6, 70].

In severely injured patients in which knee dislocation, a tibial plateau fracture or another *complex knee injury* is suspected, multidetector CT may be a useful alternative to radiography and MRI because it is fast and has demonstrated satisfying diagnostic accuracy [6].

What Is the Imaging Approach to Long Bone Fractures in Adults and Children?

Summary of Evidence There are scarcely any evidence-based guidelines or algorithms for the imaging of long bone injury available. Therefore, clinicians have to rely on professional judgment when requesting imaging studies based on pre-

senting signs and symptoms of the patient. Radiography is the only imaging tool that is necessary in most cases; however, this knowledge is based rather on a large number of clinical observations and pictorial essays than on results of diagnostic accuracy studies (moderate evidence). Magnetic resonance imaging has replaced scintigraphy and is superior to CT as confirmation test used in the evaluation of stress fractures (strong evidence).

Supporting Evidence The *femur* is the longest and strongest bone within the body and therefore requires a significant amount of force to cause a fracture. Although these injuries are often associated with additional injuries including additional fractures, dislocations, and ligamentous or meniscal injuries of the knee [71, 72], isolated femur fractures are more common in children than in adults. Femoral diaphyseal fractures are categorized based on the *Arbeitsgemeinschaft für Osteosynthesefragen* or Society for Bone Healing (AO) Foundation or Müller classification [73]. The femur is a common location for pathologic fractures, and it is important to scrutinize imaging studies of the fractured bone for signs of a focal lesion or a more diffuse, bone-weakening process. Anteroposterior and lateral radiographs are indicated in the evaluation of any potential femur fracture. Cross-table lateral radiographs of the femur can be performed without moving the femur and are often the preferred lateral view in a patient with significant pain or disability after trauma. If the patient is able to move without significant pain, and the injury is more distal in the thigh, a frog-leg lateral view may be preferred.

If a femoral stress fracture is suspected, radiography should be the initial imaging evaluation. If radiographs are negative and symptoms persist, the study should be repeated in 10–14 days [74]. For further evaluation, MRI may be considered because it is very sensitive and specific and outperforms other imaging modalities in this regard [74].

Tibia fractures are the third most common long bone fracture in children [75]. In younger children, twisting injuries and low-energy falls account for the majority of injuries, including the

classic toddler's fracture. In older children, adolescents, and adults, sports-related injuries and motor vehicle accidents are the most common mechanisms of injury. In 30% of cases, there is an associated fibular fracture [76]. The internal oblique radiograph increases the conspicuity of a tibial toddler's fracture and should be obtained if the initial AP and lateral radiographs are normal, and there is high clinical concern [77]. In a young child who is non-weight-bearing, radiographs of the tibia only are as effective as total lower extremity radiographs when there are no localizing signs [78]. Radiation and cost can be spared by reserving additional imaging to the non-weight-bearing child for patients with localizing signs and/or negative tibia radiographs [78].

Magnetic resonance imaging should be considered if there is a concern for a stress fracture when no fracture line is noted on radiographs [13, 74]. They most commonly occur at the posteromedial tibial border.

Fractures of the tibial shaft vary in appearance depending on the mechanism of injury. Spiral fractures tend to be the result of a twisting injury, such as rotating the body around a fixed foot. In toddlers, the force required to cause a spiral fracture may be insubstantial [77], whereas in older children, adolescents, and adults, these injuries are often the result of high-force injuries sustained in sporting activities. Direct trauma to the lower leg results in a transverse fracture through the diaphysis. Buckle fractures (or torus fractures) may be caused by axial-loading injuries or compressive forces along the long axis of the cortex, leading to buckling of the cortex. These may occur in the proximal tibia or the distal fibula. Lastly, bowing fractures are uncommon in the lower leg and usually affect the fibula secondary to an axial-loading injury that causes cortical microfractures [78].

A fracture of the proximal *fibula* with an associated ankle joint injury is termed a *Maisonneuve* fracture after the French surgeon who first described it in 1840 [79]. This type of fracture is seen in 7% of ankle injuries [80]. This is a rare but important fracture because it may be missed in the setting of ankle injury if the pattern of injury is not well understood. The presence of a *Maisonneuve*

fracture indicates underlying ligamentous ankle injury such as deltoid ligament tear, tibiofibular ligament tear, or interosseous membrane rupture/avulsion. Static images of the ankle may appear normal, while stress images reveal widening of the tibiofibular syndesmosis and lateral talar shift, which is an unstable injury that may require operative fixation [81]. When these findings are noted, dedicated imaging of the proximal fibula is useful for detecting Maisonneuve fracture [81].

What Is the Imaging Approach to Ankle and Foot Injuries?

Summary of Evidence Based on strong evidence, clinical decision rules such as the Ottawa ankle rules (OAR) and the low-risk ankle rule (LRAR) are highly sensitive for predicting which patients have sustained a significant foot or ankle fracture that requires treatment. These rules may miss a small number of insignificant fractures in very young children who are either non-ambulatory or nonverbal and unable to localize symptoms, and therefore some variation in practice exists among pediatric clinicians in deciding how and when to image these youngest patients. For patients, both adults and children of >5 years, meeting the criteria of those rules, radiography is the primary imaging modality and in many instances, the only one required (strong evidence). Cross-sectional imaging has a limited role in ankle and foot injuries and may be considered on a case-by-case basis when radiographs are normal or in specific injuries, e.g., in talus fracture or osteochondral injury (moderate evidence).

Supporting Evidence The Ottawa ankle rules (OAR) are guidelines meant to help physicians determine the need for imaging after ankle and foot injury [82] (Table 31.2). These rules have been validated as an effective screening tool in adults [5, 83–85] and state that tenderness over the lateral malleolus, inability to bear weight, and tenderness over the posterior tibia and fibula are all indications for radiographs. Ottawa ankle rules apply to patients who are ambulating and who can verbalize pain symptoms [86, 87].

Application of clinical decision rules does have the ability to decrease radiographs by up to 62% [88–90]. Studies have shown that the OAR can be applied also to children with excellent validity. Sensitivity for detecting fracture in children using OAR is 95–100% [86, 90–93] with an estimate for overall reduction in radiograph by ~24% [92, 93]. These results are similar to those achieved for the evaluation of the OARs in adult patients, shown, e.g., by a systematic review of 32 studies [94]. The low-risk ankle rule (LRAR) is another clinical decision-based rule indicating that radiographs are necessary in any child with tenderness and/or swelling isolated to the distal fibula and/or the adjacent lateral ligaments distal to the tibial anterior joint line. The LRAR has been shown to detect 100% of high-risk fractures in children and reduce radiographs in 62.8% of children with low-risk examinations [89]. The LRAR is not widely known or applied by emergency physicians in the USA [88].

Physeal Fractures in Pediatric Patients

Radiographs are the mainstay of imaging ankle and foot injuries in the pediatric population [9]. The *distal tibia* is one of the most common locations for an *epiphyseal injury* in a child, second only to the distal radius [95] and finger. As is true of all physeal injuries, it may be difficult to distinguish a subtle physeal fracture from the normal irregularity and undulation of the physis. There is a normal undulation within the medial aspect of the distal tibial physis where physeal fusion begins, which is termed “Kump’s bump” [96]. Physeal closure of the distal tibia takes approximately 18 months to complete once it has begun and follows a typical pattern of closure. The distal fibula usually fuses 1–2 years after the distal tibial physis. There are various accessory ossification centers of the distal fibula and tibia that contribute to growth and may be mistaken for fractures. The os subfibulare is present in 2.1% of the population [97]. These accessory ossification centers may be mistaken for fractures after an ankle injury, but the round shape and well-corticated margins, as well as the location, usually point toward the correct diagnosis. In some cases, the clinical history may be

confounding, as patients may sustain stress injuries at the accessory ossicles related to motion at insertion sites of the talofibular ligaments directly onto the ossicle [98]. A standard Salter 2 fracture of the distal tibia is the most common ankle fracture with premature physal fusion occurring in 25% [99].

The *triplane fracture* is a distinct type of fracture that occurs in the distal tibia of skeletally immature patients near the end of growth. Aptly named, the triplane fracture consists of three distinct components: a vertical epiphyseal fracture, a horizontal physal fracture, and an oblique metaphyseal fracture. Minimally displaced, extra-articular triplane fractures may be treated conservatively, while surgery may be indicated for fractures with >2 mm articular surface step-off. While radiographs are usually diagnostic of the fracture, computed tomography may be helpful in making this determination if there is concern for displacement of fragments. Computed tomography of complex tibial fractures does not improve fracture classification or treatment decision, though it has been reported to help surgeons plan surgery [100].

The *juvenile Tillaux fracture* is a Salter 3 fracture with a vertical component through the epiphysis and a horizontal fracture through the physis. The insertion of the anterior inferior tibiofibular ligament on the lateral aspect of the distal tibial epiphysis results in various degrees of avulsion and displacement of the lateral epiphyseal fracture fragment when such an injury is sustained. The pattern of these fractures, particularly the propagation of the fracture plane through the lateral aspect of the physis, is very much related to the ossification pattern of the distal tibia, given that physal fusion begins anteromedially and progresses posteriorly and laterally, such that the lateral portion of the physis may be the only portion that remains unfused at the time of injury [101].

Radiographs remain the mainstay for diagnosis and characterization of distal tibia and fibular fractures. Findings to note on radiographs include the degree of epiphyseal displacement, widening of the physis, and alignment of articular surfaces [95]. Computed tomography is reserved for fur-

ther evaluation of injuries when surgery is being considered [100]. Computed tomography or MRI may be used to characterize and quantify the amount of growth arrest and physal bar formation after fracture healing.

Although the fibula is not the primary weight-bearing bone in the ankle, *distal fibular fractures* also occur though with less frequency than fractures of the tibia. The physis of the fibula fuses after the distal tibial physis [101], and therefore it should not be concerning to see an open fibular physis even if the tibial physis is fused. Salter fractures of the fibula may be detected on radiographs with soft tissue swelling centered at the physis and widening or asymmetry of the physis as clues to the presence of an underlying fracture. About 7% of children with lateral malleolar tenderness after ankle sprain and normal radiographs will have an occult distal fibular fracture, as evidenced by healing on follow-up radiographs [102]. Radiographs often “overcall” the presence of a Salter I fracture of the distal fibula when compared to MRI [103]. Despite this, there is no convincing evidence to support the routine use of MRI for evaluation of distal fibular fractures after ankle sprain [102, 103].

Sever's lesion, otherwise known as calcaneal apophysitis, is the most common overuse injury seen in school-age children [67]. It is also the most common cause of heel pain in skeletally immature athletes. It is considered a self-limiting condition characterized by heel pain with running or jumping activities. The diagnosis is most often made clinically by eliciting pain during medial and lateral compression of the heel at the attachment site of the calcaneal apophysis. While radiographs are often requested to evaluate for Sever's disease, there are no radiographic imaging signs that are considered to be sensitive for the diagnosis. When radiographs are performed, the goal is to evaluate for other pathology that could explain the pain (such as calcaneal fracture) rather than to confirm a diagnosis of Sever's [102].

The open epiphyseal plate is a potential site of weakness in the developing pediatric skeleton. Salter 1 *fractures of the phalanges* of the toes may be subtle on AP radiographs of the foot, par-

ticularly when nondisplaced. These injuries best detected on oblique radiographs manifested as widening and irregularity of the physes [26].

Intra-articular fractures of the great toe are a unique fracture in the pediatric population. These fractures often involve the proximal phalanx of the great toe and are the result of hyperflexion from a direct impact. The physis of the proximal phalanx is located at the base of the phalanx and is highly susceptible to injury. These fractures are most common in children who are near skeletal maturity. Radiographs are usually all that is required for diagnosis and management planning for these patients. In general, unless there is >2 mm of displacement of the fracture fragment, they are usually managed conservatively and nonoperatively [103].

Specific Ankle and Foot Injuries in Children, Adolescents, and Adults

Ankle sprains are common injuries in both children and adults. Ligament injuries in the ankle are the most frequent sports injury [104]. Most of these injuries are inversion injuries with damage to the lateral ligamentous structures in the ankle, though uncommonly an eversion-type injury may occur. The lateral collateral ligament complex is the most commonly injured and consists of the anterior talofibular (ATFL), calcaneofibular (CFL), and posterior talofibular ligaments (PTFL). Of these, the ATFL is the most commonly injured, followed by CFL and then PTFL [104, 105]. “High” ankle sprains refer to an injury of the syndesmototic ligaments. On radiographs, the presence of abnormal widening of the joint space may point toward an underlying ligamentous rupture. While MRI is more sensitive for detection of ligamentous injuries in the ankle of patients after a sprain injury, MRI findings sometimes do not correlate with clinical findings and do not bring additional therapeutic value to the work-up of the patient in the acute setting [14, 106]. Therefore, although MRI may detect ligamentous injury, there is little evidence to support routine use of MRI in the evaluation of ankle sprains.

Osteochondral lesions in the ankle are injuries to the talus that involve both the bone and the

overlying cartilage. They can occur after a single traumatic injury or as a result of repeated trauma. Radiography cannot demonstrate cartilage or bone contusions related to those lesions. Therefore, MRI is the diagnostic modality of choice to evaluate for these injuries [5].

A significant minority of patients with ankle trauma are diagnosed with *syndesmototic injury*. Due to limitations of the physical examination and radiography in establishing the diagnosis, MRI should be performed in cases which need further evaluation and/or to avoid misdiagnosis [5].

Talar fractures are relatively uncommon and usually sustained after high-impact trauma. There are multiple varieties of talar fractures, defined by the anatomic areas involved with the fracture (talar head, neck, body, etc.) [107]. The lateral process talar fracture has an unusually high prevalence in snowboarders, victims of motor vehicle collisions, and falls secondary to an external rotation force placed on a dorsiflexed foot during axial loading [107]. These fractures are frequently missed on radiographs [5, 108], and CT imaging may be considered in patients with negative ankle radiographs but a high suspicion of injury. There are no strict imaging recommendations in this regard.

Fractures of the foot are common in both adults and children, and the *metatarsals* are among the bones most commonly *fractured*. Acute foot fractures of normal bones are usually caused by the dropping of heavy objects on the foot or by stress associated with abnormal repetitive trauma. In deficient bones, insufficiency fractures may result from normal stress. The mechanism for metatarsal fractures differs between older and younger patients. Patients greater than age 5 years are more likely to fracture a metatarsal while falling on a level surface or twisting their foot, while younger patients under the age of 5 years are more likely to fracture a metatarsal after falling from a height.

Patients with concern for midfoot injury and possible *Lisfranc joint disruption* should undergo three-view radiographic evaluation of the foot, with weight-bearing on at least the AP view [4].

If radiographs are normal, MRI may then be considered on a case-by-case basis [4].

In suspected *acute tendinous rupture or dislocation in the foot*, radiography may be indicated, but findings often are negative. As second-line imaging studies and if the patient's condition fails to improve, MRI or US has been suggested, and both show similar sensitivities for tendon injuries about the foot and ankle, specifically the tibialis posterior tendon [5].

Take-Home Tables

See Tables 31.1 [109] and 31.2; highlight and summarize suggested radiographic views for lower extremity trauma and clinical decision rules for radiography of acute knee, ankle, or foot injury, respectively.

Take-Home Points

The Ottawa Knee Rule

The Ottawa knee rule was derived to aid in the efficient use of radiography in acute knee injuries:

- The rule has been prospectively validated on multiple occasions in different populations and in both children and adults.
- Numerous studies found sensitivities for the Ottawa knee rules of 98–100% for clinically significant knee fractures. One study did find a sensitivity of just 86%.
- Specificities for the Ottawa knee rules typically range from 19% to 50%, though the rule is not designed/intended for specific diagnosis.
- When used appropriately, the amount of knee X-rays obtained can be reduced by around 20–30%.
- The Ottawa knee rules are useful in ruling out fracture (high sensitivity) when negative, but poor for ruling in fractures (many false positives).

Tips for Use of the Ottawa Knee Rule

- Tenderness of patella is significant only in an isolated finding.
- Use only for injuries <7 days.
- “Bearing weight” counts even if the patient limps.

Precautions for Use of the Ottawa Knee Rule

- Clinical judgment should prevail if examination is unreliable:
 - Intoxication
 - Uncooperative patient
 - Distracting painful injuries
 - Diminished sensation in legs
- Always provide written instructions.
- Encourage follow-up in 5–7 days if pain and ability to walk is not better.
- The Ottawa knee rules should be applied to all patients aged 2 and older with knee pain/tenderness in the setting of trauma.
- Patients without criteria for imaging by the Ottawa knee rules are highly unlikely to have a clinically significant fracture and do not need plain radiographs.
- Application of the Ottawa knee rules can cut down on the number of unnecessary radiographs by 20–30%, which has proven to be cost effective for patients without reducing quality of care.

The Ottawa Ankle Rule

The Ottawa ankle rule was derived to aid in the efficient use of radiography in acute ankle and midfoot injuries:

- The rule has been prospectively validated on multiple occasions in different populations and in both children and adults.
- Sensitivities for the Ottawa ankle rule range from the high 90% to 100% range for “clini-

cally significant” ankle and midfoot fractures. This is defined as a fracture or an avulsion greater than 3 mm.

- Specificities for the Ottawa ankle rule are approximately 41% for the ankle and 79% for the foot, though the rule is not designed/intended for specific diagnosis.
- The Ottawa ankle rule is useful in ruling out fracture (high sensitivity), but poor for ruling in fractures (many false positives).

Tips for Use of the Ottawa Ankle Rule

- Palpate the entire distal 6 cm of the fibula and tibia.
- Do not neglect the importance of medial malleolar tenderness.
- “Bearing weight” counts even if the patient limps.
- Be caution in patients under age 18.

Precautions for Use of the Ottawa Ankle Rule

- Clinical judgment should prevail if examination is unreliable:
 - Intoxication
 - Uncooperative patient
 - Distracting painful injuries
 - Diminished sensation in legs
 - Gross swelling which prevents palpation of malleolar tenderness
- Always provide written instructions.
- Encourage follow-up in 5–7 days if pain and ability to walk is not better.
- The Ottawa ankle rule should be applied to all patients aged 2 and older with ankle or mid-foot pain/tenderness in the setting of trauma.
- Patients without criteria for imaging by the Ottawa ankle rule are highly unlikely to have a clinically significant fracture and do not need plain radiographs.

- Application of the Ottawa ankle rules can reduce the number of unnecessary radiographs by as much as 25–30%, improving patient flow in the ED.

Imaging Case Studies

Case 1

Figure 31.1a, b presents a 75-year-old woman who has fallen and has left buttock pain.

Case 2

In Fig. 31.2a, b, a 46-year-old man presents with a sports injury.

Case 3

In Fig. 31.3a, b, a 36-year-old man presents with a sports-related injury.

Case 4

Figure 31.4a, b shows a 14-year-old male with right AIIS (anterior inferior iliac spine) avulsion.

Case 5

A Salter 1 fracture of the distal femur in a 13-year-old female is presented in Fig. 31.5a, b.

Case 6

Figure 31.6a, b presents a triplane fracture of the tibia in a 12-year-old female.

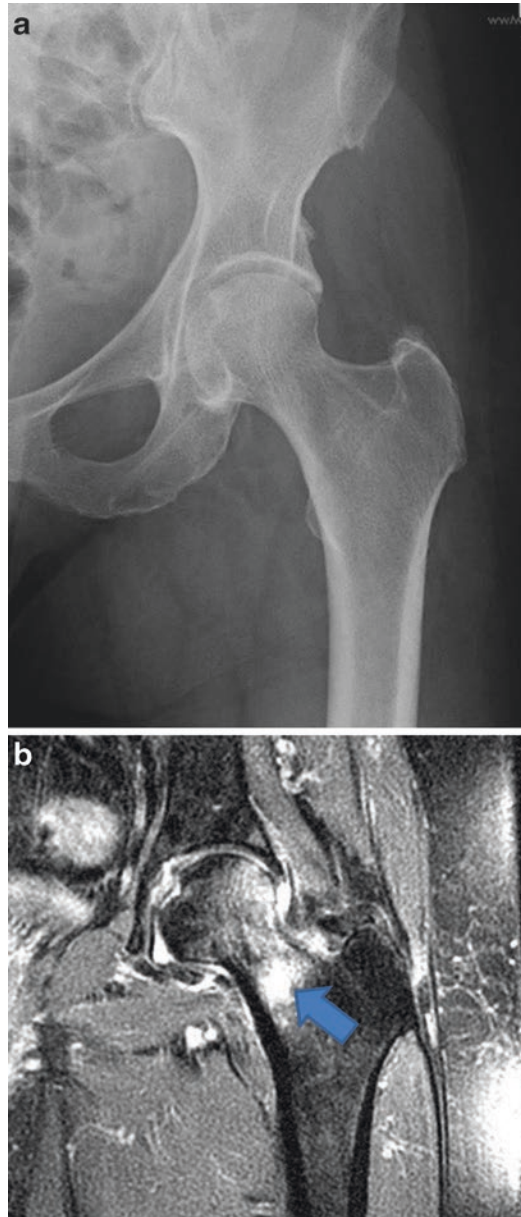


Fig. 31.1 A 75-year-old woman with fall and left buttock pain. (a) Frontal radiograph of the left hip does not reveal a fracture. (b) Coronal proton density fat-suppressed (PDFS) MR image shows a band of high signal (*blue arrow*) through the femoral neck, which had correspond-

ing linear low signal on T1-weighted images, consistent with a radiographically occult, nondisplaced fracture (Images kindly provided by Dr. Kara Gaetke-Udager, University of Michigan Health System, Ann Arbor, MI, USA)

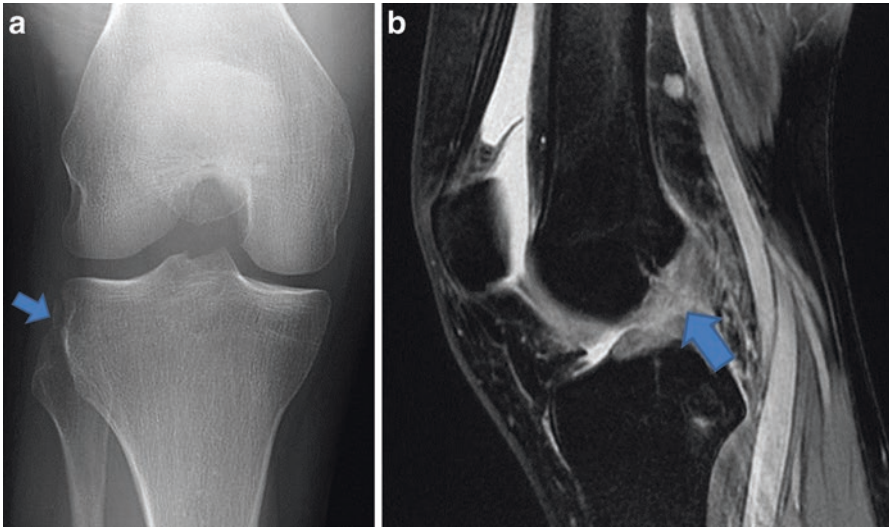


Fig. 31.2 A 46-year-old man with a sports injury. (a) Frontal radiograph of the knee shows that there is a mildly displaced, small fracture fragment seen along the lateral tibial plateau, consistent with a Segond fracture (*blue arrow*). (b) Sagittal PDFS MR image shows a complete

tear of the anterior cruciate ligament (ACL) (*block blue arrow*), which is associated with Segond fractures (Images kindly provided by Dr. Kara Gaetke-Udager, University of Michigan Health System, Ann Arbor, MI, USA)

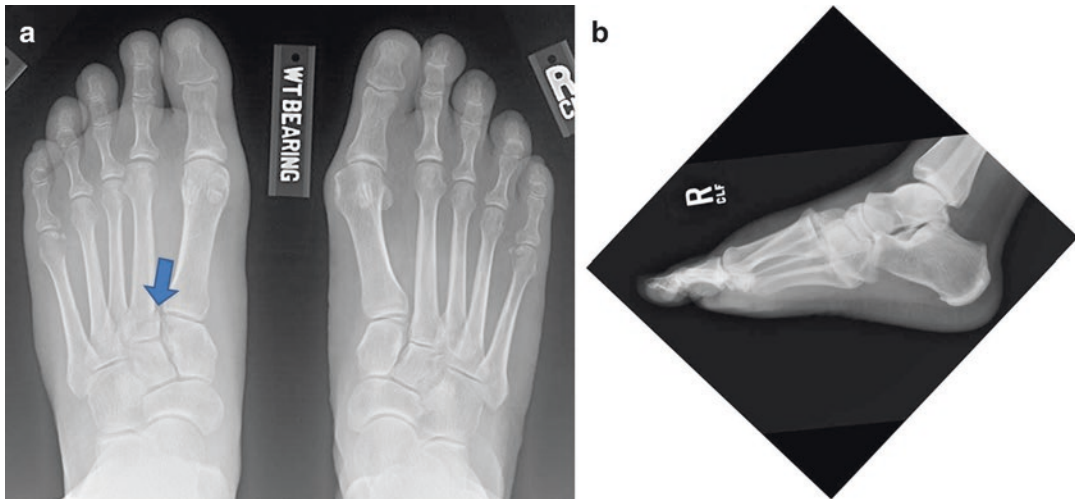


Fig. 31.3 A 36-year-old man with a sports-related injury. (a) Bilateral standing AP radiograph of the feet shows asymmetric widening of the left Lisfranc joint with a minimally displaced fracture of the base of the second metatarsal (*blue arrow*), consistent with a Lisfranc fracture/dislocation. (b) Lateral radiograph of the left foot shows

dislocation of the first tarsometatarsal (TMT) joint with the base of the first metatarsal mal-aligned with the cuneiform (Images kindly provided by Dr. Kara Gaetke-Udager, University of Michigan Health System, Ann Arbor, MI, USA)

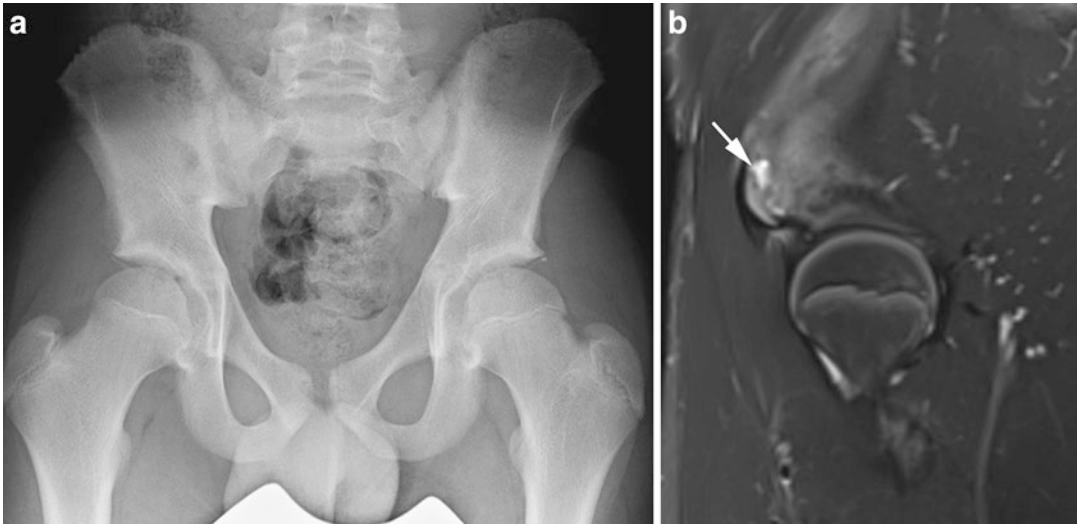


Fig. 31.4 A 14-year-old male with right AIIS (anterior inferior iliac spine) avulsion. (a) Radiograph of the pelvis is normal. (b) Sagittal FSEIR images from an MRI of the pelvis demonstrates abnormal marrow signal within the right AIIS and the surrounding iliac bone with fluid separating the apophysis from the bone (*arrow*)



Fig. 31.5 Salter I fracture of the distal femur in a 13-year-old female. (a) The AP radiograph of the knee demonstrates abnormal widening of the distal femoral physis (*black arrows*). (b) Coronal proton density-weighted magnetic resonance image with fat suppression of the knee demonstrates abnormal fluid signal within the physis (*black arrow*) and abnormal marrow edema within the metaphysis

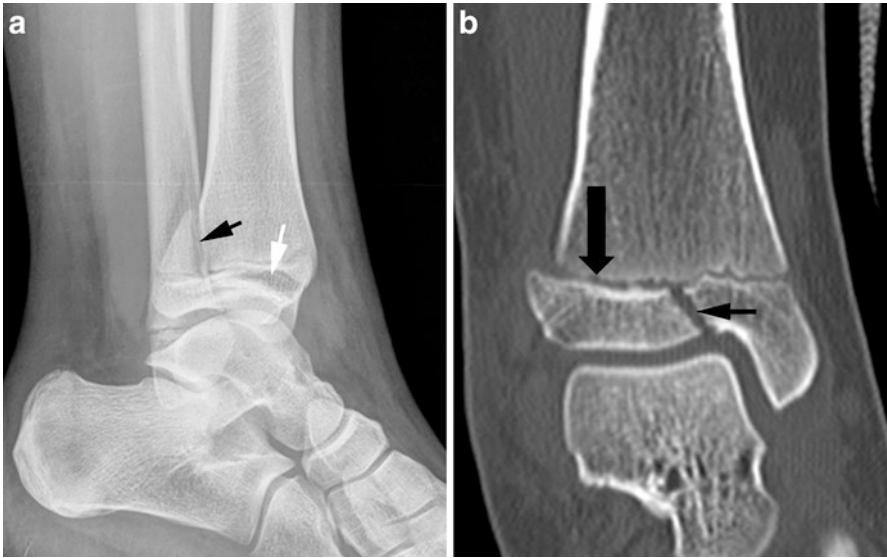


Fig. 31.6 Triplane fracture of the tibia in a 12-year-old female. (a) Lateral radiograph of the ankle demonstrates widening of the distal tibial physis (*white arrow*) and fracture line within the tibial metaphysis (*black arrow*). (b) Coronal reformatted image from a CT study demonstrates

the vertical fracture line extending into the epiphysis (*small black arrow*). There is widening of the lateral aspect of the physis (*large black arrow*). The involvement of both the metaphysis and epiphysis makes this fracture a Salter-Harris type IV fracture

Future Research

- Recommendation for specific radiographic views in the setting of pediatric hip injury: algorithms for the specific views that are most indicated in different clinical settings
- Indications for MRI in the acutely injured child
- Indications for CT in the setting of lower extremity injury in both children and adults

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Evidence-Based Emergency Imaging for Acute Musculoskeletal Infections in Adults and Children: Osteomyelitis, Septic Arthritis, and Soft Tissue Infection

Boaz Karmazyn and Trenton D. Roth

Key Points

- If signs and symptoms of osteomyelitis cannot be localized, bone scintigraphy is the preferred imaging modality (limited evidence).
- MRI is the imaging modality of choice in the diagnosis of AHOM and to evaluate for complications when symptoms are localized (limited evidence).
- Ultrasound is the imaging modality of choice for the evaluation of septic hip in children (moderate evidence).
- Imaging is usually not necessary in the diagnosis and management of soft tissue infections. However, ultrasound improves diagnostic accuracy of abscess detection (moderate evidence).

- The diagnosis of necrotizing fasciitis should be based on clinical evaluation and surgical exploration. In selected patients MRI or CT can help to evaluate the extent of deep soft tissue infection and necrosis (insufficient evidence).

Abbreviations

FSE	Fast spin echo
MDP	Methylene diphosphonate
SE	Spin echo
SPECT	Single photon emission computed tomography
STIR	Short tau inversion recovery

Definition and Pathophysiology

This chapter focuses on acute musculoskeletal infections that may present and pose diagnostic challenges in the emergency department. We will discuss acute hematogenous osteomyelitis (AHOM) of the appendicular skeleton, septic hip arthritis, and soft tissue infection. Acute hematogenous osteomyelitis is the rapid onset of a blood-borne pyogenic infection of the bone and is most common in young children.

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Diagnosis of AHOM in children can be a diagnostic challenge as presentation varies and depends on the child's age, location of infection, microorganism, and complications [1–6]. Hematogenous spread usually seeding the metaphyses of long bones due to sluggish blood flow of the capillary loops and venous sinusoids. These vessels have a poorly developed reticulo-endothelial system. Therefore, there is increased risk of bacteria seeding the metaphysis. In children younger than 18 months, there are vessels crossing the growth plates allowing the metaphyseal infection to spread contiguously to the epiphysis and the adjacent joint [1, 5, 6]. When the transphyseal vessels involute later in childhood, the growth plate functions as a natural barrier to spread of metaphyseal infection, and secondary involvement of osteomyelitis at the epiphysis becomes uncommon. As infection spreads from the metaphysis within the intramedullary cavity, increased pressure can lead to extension to the cortex by the Haversian and Volkmann's canal. Once in the cortex, the infection may subsequently spread to the subperiosteal space and through the periosteum into the adjacent soft tissues. Elevation of the periosteum and subsequent formation of subperiosteal abscess are common in infants and children, whereas in adults the periosteum is more firmly attached to the bone, and subperiosteal abscess is an uncommon occurrence [1, 5]. *Staphylococcus aureus* is the most common pathogen in hematogenous osteomyelitis with increased incidence of community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) osteomyelitis in children. Pantone-Valentine leukocidin (PVL) is a necrotizing toxin that is secreted by some forms of methicillin-susceptible *Staphylococcus aureus* and MRSA and is associated with increased complications [3]. MRSA AHOM is associated with multifocal infection and more aggressive course of disease with increased complications. MRSA AHOM is more commonly associated with lung infection and deep venous thrombosis [2, 5–8]. The incidence of *Haemophilus influenzae* type b and *Streptococcus pneumoniae* has been reduced following implementation of universal child-

hood immunization against these pathogens [6]. Tuberculous osteomyelitis remains a major cause of skeletal infection in less-developed countries. *Mycobacterium tuberculosis* most commonly affects the spine (50%) but also the appendicular skeleton. Less common causes of acute hematogenous osteomyelitis include *S. pyogenes* and *Kingella kingae*. For children born with hemoglobin SS or SC disease, *Salmonella* is the most common cause of osteomyelitis [2]. In these children, it could be difficult to differentiate between AHOM and acute bone marrow infarct [9, 10].

AHOM can be limb- or life-threatening, and prompt diagnosis and treatment are crucial to minimize complications. AHOM can present either acutely with high fever and septicemia and with a localized distal limb tenderness or pain or as a more subacute gradual progression of symptoms and signs localized to the site of infection with concomitant loss of function due to bone pain. Since bone innervation is mainly restricted to the periosteum, the pain and tenderness with AHOM may be difficult for the patient or practitioner to precisely localize.

Neonatal osteomyelitis is more likely to be associated with septic arthritis of the joint adjacent to the metaphyseal infection, due to the vascularity of the epiphyseal growth plate, and, thus, may present with reduced range of motion (pseudoparalysis) [11].

AHOM in children should be differentiated from other pathologies such as nonaccidental trauma, toddler fracture, histiocytosis, Legg-Perthes disease, and tumors. Adult patients with suspected osteomyelitis may also present to the emergency department for evaluation. The clinical scenario in adults is almost always a patient with long-standing type II diabetes mellitus complicated by peripheral neuropathy and vascular disease, who presents with localized soft tissue infection and ulceration of the foot. Pedal osteomyelitis in this setting is virtually always from contiguous spread of soft tissue infection to bone [12].

Acute septic arthritis (SA) is a bacterial infection of a joint that typically affects young children. In this chapter we will concentrate on the

challenge of diagnosing hip septic arthritis in children presenting emergently with acute hip pain and in differentiating SA from transient synovitis, which is the more common cause of acute hip arthritis [13, 14]. Acute septic arthritis can also present in adulthood, but it is more apt to be associated with underlying chronic joint or systemic disease or prior joint arthroplasty, which can complicate the diagnosis. *Staphylococcus aureus* is the most common cause of bacterial infection of SA in children, and it usually arises from hematogenous seeding during bacteremia or contiguous spread of metaphyseal osteomyelitis. Prompt diagnosis of SA is crucial as prognosis worsens with increasing delay of treatment due to destruction of the physis and articular cartilage secondary to lytic enzymes. Increased pressure within the joint capsule reduces blood flow to the epiphyses and may lead to osteonecrosis [13–16]. The typical presentation includes acute limping with refusal to bear weight and systemic signs and symptoms of infection (fever, leukocytosis, elevated sedimentation, or C-reactive protein level). Children with low risk for septic arthritis can be observed clinically, while children with moderate or higher risk need a more definite diagnosis utilizing joint aspiration.

Cellulitis is an acute superficial bacterial infection spreading along subcutaneous and fascial planes with edema and hyperemia most commonly affecting the lower extremities. The typical presentation is acute swollen, erythematous, warm, and tender skin that may be associated with fever, leukocytosis, or other mild systemic manifestations. Uncomplicated cellulitis can be treated with antibiotics alone [17, 18]. Clinical assessment of severity of infection and response to treatment is crucial. The area of cellulitis should be clearly marked and reviewed daily for progression or regression to assess the efficacy of the antibiotic treatment. If cellulitis is complicated with an abscess, it should be drained [18].

Necrotizing fasciitis (NF) is a life-threatening, rapidly progressing type of necrotizing soft tissue infection. NF is most commonly polymicrobial (aerobic and anaerobic bacteria), but it can also be monomicrobial (typically *Streptococcus pyogenes* or *Staphylococcus aureus* species) [18–20]. There is often an identifiable underlying

predisposing risk factor such as trauma, surgical procedure, extension of focal skin wound, IV drug abuse, immunodeficiency, diabetes, arteriosclerotic vascular disease, or venous insufficiency [19–24]. The initial presentation of NF may mimic cellulitis or soft tissue abscess, and the early diagnosis can be challenging as the more definite signs and symptoms often appear later in the course of necrotizing infections. Necrotizing fasciitis should be suspected in patients who do not respond to antibiotic treatment and develop systemic toxicity, rapid progressive infection, constant severe pain disproportionate to the degree of cellulitis, physical findings of hard/wooden feel of the subcutaneous tissue, signs of skin necrosis (e.g., purple bullae, sloughing of skin), skin anesthesia, or gas/crepitus in the soft tissues [15–20]. Early surgical evaluation is crucial for accurate diagnosis and effective therapy. The definitive diagnosis of NF is based on the appearance of the subcutaneous tissues or fascial planes at operation. In the “finger test” a 2 cm incision is performed down to the deep fascia. If the index finger dissects the subcutaneous tissue off the deep fascia easily along the tissue plane, the test is positive [19, 20]. Other positive findings include foul-smelling brownish exudate, swollen and necrotic dull gray fascia, thrombosed vessels, and noncontracting muscles. Rapid surgical debridement is the mainstay and only definitive therapy for NF, as antibiotic treatment alone is insufficient, and thus surgery should not be delayed once the diagnosis is suspected or confirmed [15–20].

Epidemiology

There is an estimated incidence of AHOM and septic arthritis in developed world populations between 5 and 12 cases per 100,000 children per year. Half of the children with AHOM are under the age of 5, and boys are more likely (1.2–3.7 times) to be affected than girls [5, 6, 25, 26]. Fast-growing long bones such as the tibia and femur are the most affected regions, but approximately 20% of cases affect the flat bones including the pelvis [6]. A single bone is usually affected, and multifocal involvement is seen in less than 10%

of the children and more commonly in neonates [2, 5, 25, 27]. Children with septic arthritis have concomitant osteomyelitis in 17 to 68% of the cases [15, 16, 28].

In all, 14.2 million Americans visited primary care physicians, hospital outpatient departments, and emergency services with skin and soft tissue infections, i.e., 481 visits per 100,000 [17]. Cellulitis and erysipelas incidence is 200 cases per 100,000 patient-years [29]. Necrotizing soft tissue infection is rare, and necrotizing fasciitis has been reported to be 0.4 cases per 100,000 inhabitants in the United States (USA), while in Western Europe it is about 1 case per 100,000. This disease is more common in adults with an incidence increasing with age [19].

Overall Cost to Society

Musculoskeletal infections are a leading cause of patient morbidity and rising healthcare expenditures. The incidence of musculoskeletal infections, including soft tissue infections, periprosthetic joint infection, and osteomyelitis, is increasing. One of the main concerns is the increase in infections caused by drug-resistant strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA). Admission rate for osteomyelitis (OM) in children of 0–18 years of age was reported to range between 0.048 and 0.070 per 1000 child years [26]. There is no data on the overall cost to society from the diagnosis, treatment, and complications of acute hematogenous osteomyelitis or septic arthritis. Diabetic pedal infections are a major cost, with a US cost estimate in 2001 of \$10.9 billion [30]. Treatment of necrotizing fasciitis is particularly costly with a mean length of hospital stay of 26.3 ± 2.2 day with charges ranging from \$20,000 to \$866,000 (mean, \$154,000 \pm \$22,700) and an overall mortality rate $>10\%$ [31].

Goals of Imaging

The primary goal of imaging of acute musculoskeletal infection is to assist in early diagnosis and management to prevent mortality and long-term sequelae, which include growth arrest, limb

deformity, joint instability, joint destruction, ankylosis, and premature degenerative joint disease. In soft tissue infection, the primary goal is to detect deep soft tissue infection, tissue necrosis, and abscess formation to help prompt management and prevent spread of infection, sepsis, and death.

Methodology

The authors performed a MEDLINE search (January 2000 to December 2014). The search strategy used the following Medical Subject Headings: (1) osteomyelitis; (2) arthritis, infectious; (3) necrotizing fasciitis; (4) ultrasonography; (5) radionuclide imaging; (6) radiography; (7) tomography, x-ray computed; (8) magnetic resonance imaging; and (9) cost. We excluded animal studies and non-English articles. The abstracts were reviewed and selected based on relevance to the topic, methodology, and inclusion of accuracy measurements of the various imaging modalities. Additional relevant articles were selected from the references of reviewed articles.

Discussion of Issues

What Is the Best Imaging Modality in Diagnosis of Acute Hematogenous Osteomyelitis (AHOM)?

Summary of Evidence Imaging studies have a role in establishing the diagnosis and extent of AHOM. Initial imaging evaluation of AHOM usually begins with radiographs. Radiographs are neither sensitive nor specific in the diagnosis of early AHOM but can evaluate for other bone conditions, such as fractures and neoplasms. Bone rarefaction and periosteal reaction typically develop within 10 days. If the patient has clinical findings that are highly suggestive of AHOM and radiography shows metaphyseal rarefaction with periosteal reaction or a lytic are, no other imaging workup is necessary (insufficient evidence) [1, 3–5, 32].

Magnetic resonance imaging (MRI) and radionuclide bone scintigraphy have high sensitivity for detection of osteomyelitis (limited evidence). Bone scintigraphy can be used for whole-body imaging when symptoms cannot be localized or there is suspicion for multifocal AHOM (limited evidence) [4, 33, 34]. The experience with the use of whole-body MRI is limited [31].

WBC labeled with ^{111}In and $^{99\text{m}}\text{Tc}$ -hexamethylpropyleneamine oxime ($^{99\text{m}}\text{Tc}$ -HMPAO) is more specific than bone scan for diagnosis of osteomyelitis and may be considered when MRI is contraindicated or limited such as in patients with infected prosthesis (limited evidence) [35–37]. MRI is the preferred imaging method for evaluation of AHOM when symptoms are localized and when there is clinical suspicion for complications (limited evidence) [2–5].

Supporting Evidence

Radiography

Radiographs are often used as the first imaging in the evaluation of AHOM. Soft tissue swelling can be detected as early as 48 h. Osteopenia becomes visible on conventional radiographs after loss of approximately 30–50% of bone mineralization. The minimal period of time required for demineralization caused by inflammatory osteoclastic activity associated with infection to become visible is 10–14 days [1, 3, 5, 27].

Radiographic evidence for osteomyelitis includes bone destruction and periosteal reaction (Fig. 32.4a–c). Bone destruction may appear as an area of bone rarefaction, permeative destruction, and lucency that may be associated with surrounding bone sclerosis [1, 3, 5, 27]. The radiographic findings in AHOM are not specific, and the most important differential diagnoses include malignancy and Langerhans' cell histiocytosis. The sensitivity and specificity of plain radiographs depends on the duration of symptoms. The sensitivity and specificity have a range of 43–75% and 75–83%, respectively [5, 27]. If bone destruction is detected, no further imaging may be necessary in the appropriate clinical settings (insufficient evidence).

Magnetic Resonance Imaging

Magnetic resonance imaging has high soft tissue contrast resolution, which makes it the preferred imaging for evaluation of AHOM when symptoms are localized and whenever the patient does not respond to antibiotic treatment or there is clinical suspicion for complication [2–5]. The sensitivity and specificity for MRI are at the range of 82–100% and 75–96%, respectively (limited evidence) [5, 38–40]. MRI can detect complications such as subperiosteal and soft tissue abscesses, joint effusions, and soft tissue extension that would require surgical intervention (Fig. 32.5a, b). The disadvantages of MRI include higher cost relative to bone scintigraphy, and prolonged imaging time, which may require use of sedation.

There is insufficient evidence to determine if MRI is more sensitive than bone scintigraphy in the detection of AHOM. Some studies show that the sensitivity of MRI and bone scintigraphy is the same in the diagnosis of AHOM [33, 40]. In other studies MRI was found to be more sensitive than bone scintigraphy [38, 41]. Acute hematogenous osteomyelitis of the pelvis is associated with up to 55% of abscesses, and 6–26% require drainage [33, 42]. Therefore, MRI is especially advantageous in the evaluation of pelvic AHOM [33, 41, 42] (limited evidence).

There is controversy on the need of intravenous contrast material for increasing the sensitivity of MRI in the detection of AHOM and its complications [43–45]. It was shown that in infants, detection of osteomyelitis in the epiphyseal cartilage increases with intravenous contrast [44]. Whole-body MRI may be used as an alternative imaging to bone scintigraphy in the detection of multifocal AHOM. However, there is limited experience with the use of whole-body MRI [34].

Ultrasound

Ultrasound is a low-cost, easily available, non-ionizing diagnostic modality. The use of ultrasound in osteomyelitis has been reported in few small series [5, 32]. Ultrasound can detect subperiosteal and soft tissue fluid collections and can guide their aspirations [5, 32]. Color Doppler US

can show increased periosteal and adjacent soft tissue vascularity (Fig. 32.6) [46]. However, ultrasound cannot evaluate the bone marrow and may miss the diagnosis of osteomyelitis. The sensitivity to osteomyelitis increases with duration of symptoms with a range of 46–84% with a specificity range of 47–100% (limited evidence) [5, 46–48]. Ultrasound can be particularly useful in evaluation of AHOM in infants who are too fragile and unstable to withstand other cross-sectional studies.

Nuclear Medicine Imaging

Bone scintigraphy is the most common nuclear medicine used for the diagnosis of osteomyelitis. Scintigraphy usually does not require sedation, and the entire skeleton can be imaged which is ideal if symptoms cannot be localized or if there is multifocal disease (limited evidence) [2, 3, 5, 6, 32, 49]. It is usually performed with technetium-99m methylene diphosphate ($^{99m}\text{Tc-MDP}$), which binds to the hydroxyapatite crystals in bone inorganic matrix. Radiopharmaceutical uptake is increased with increased blood flow to bone and increased osteoblastic activity. A three-phase bone scan is the technique performed for evaluation of AHOM. The three phases consist of a dynamic perfusion phase followed by a static phase (blood pool) and a 2–4 h delayed phase (bone uptake phase). In osteomyelitis there is typically increased uptake in all three phases representing focal increased perfusion, hyperemia, and increased bone uptake (Fig. 32.7a, b). The overall sensitivity and specificity for radionuclide bone scanning are 73–100% and 73–79% (limited evidence) [2, 3, 5, 6, 32, 49]. The sensitivity of bone scintigraphy increases after 3 days of infection and decreases in neonates [2].

More than 90% of positive bone scans are “hot,” with increased uptake of $^{99m}\text{Tc-MDP}$. Less common reduced $^{99m}\text{Tc-MDP}$ uptake occurs, and “cold” foci are detected [4–6, 11, 25]. The specificity of the bone scintigraphy decreases when there are preexisting conditions that increase the rate of new bone formation such as fracture, orthopedic hardware, and postsurgical changes [49].

White blood cell scintigraphy can be performed with indium 111-labeled white blood cells

or $^{99m}\text{Tc-HMPAO}$ -labeled white cells. Uptake depends on intact chemotaxis, number and type of cells labeled, and cellular response. There is a need to take 20–40 mL of blood from the patient for white blood cell (WBC) scan, and this is one of the reasons why it is uncommonly used in pediatrics [5]. At least 2000 circulating WBC per microliter is required for an adequate study. Compared to bone scintigraphy, there is improved specificity (80–90%) [49–52]. White blood cell scintigraphy is useful in patients who have prostheses when artifact can interfere with cross-sectional studies and in patients after trauma or surgery, and increased uptake is expected in bone scan (limited evidence). Leukocytes accumulate both at the site of infection and in the active bone marrow. ^{99m}Tc -sulfur colloid bone marrow imaging can be performed with WBC scintigraphy as both accumulate in the bone marrow but only WBC accumulate in infection. The combined study is positive when there is an area of activity in the WBC scan not seen in the sulfur colloid scan. The combined study is especially useful when there are predisposition conditions that affect the bone marrow such as prosthesis. One limitation for the combined study in AHOM is that sulfur colloid scan may not become photopenic until about 1 week after the onset of infection, and this may lead to false-negative interpretation in the acute setting [36, 49].

The ^{18}F -fluorodeoxyglucose ($^{18}\text{F-FDG}$) positron emission tomography (PET) is increasingly being used for evaluation of musculoskeletal infections including osteomyelitis. It has a sensitivity of 94–100% [53] and specificities in the range of 75–99% in the evaluation of acute and subacute osteomyelitis (limited evidence) [49, 54, 55].

^{18}F -fluorodeoxyglucose enters the cells via glucose transporters and phosphorylated by hexokinase to ^{18}F -2- $^{18}\text{F-FDG}$ -6 phosphate that is not metabolized further. $^{18}\text{F-FDG}$ accumulates in the WBC when there is infection due to an increase in the number of glucose transporters in activated cells. Due to high costs and relatively high radiation, $^{18}\text{F-FDG}$ is not used routinely for evaluation of AHOM. However, $^{18}\text{F-FDG}$ PET has a role in special circumstances

such as in difficult to diagnose chronic osteomyelitis, spinal osteomyelitis, diabetic foot and post trauma, surgery, and metallic implant osteomyelitis [56, 57].

Special Cases

Diabetic Pedal Osteomyelitis

Type II diabetes mellitus foot infections are a major health burden [30, 58]. Diagnosis of diabetic pedal infection complicated with osteomyelitis is challenging because of underlying chronic skin infection, venous insufficiency, and changes related to peripheral neuropathy. Diabetic pedal osteomyelitis almost always arise via direct extension of skin ulceration [30], and hematogenous pedal osteomyelitis in diabetic adults is rare [59].

Determining the presence or absence of pedal osteomyelitis is a critical question for healthcare providers to answer when evaluating and managing a patient presenting emergently with a diabetic foot infection. While some clinical factors like large ulcer size, ability to probe to the bone, and elevated sedimentation rate may suggest the diagnosis, imaging may be necessary to substantiate the diagnosis of osteomyelitis [30].

Radiographs should be performed in the initial evaluation of infected diabetic foot when there is a clinical suspicion for osteomyelitis (limited evidence). Radiographs have low (60%) sensitivity but high specificity (80%) in diagnosis of diabetic pedal osteomyelitis [44]. Demonstration of bone resorption, periosteal new bone, or frank bone destruction suggest the diagnosis [30]. Radiographs provide useful ancillary information including the presence of foreign bodies, neuropathy, arthropathy, fractures, or amputations [30].

Magnetic resonance imaging is the most appropriate imaging modality for the initial evaluation of possible diabetic pedal osteomyelitis (limited evidence) [12, 30, 58–60]. In a meta-analysis of six studies, MRI has been shown to outperform radiographs and nuclear medicine bone scintigraphy and white blood cell scans [58]. In a meta-analysis of 16 studies, MRI was shown to have high sensitivity of 77–100% with a specificity range of 40–100% for diagnosing pedal osteomyelitis [58]. Using a diagnosis performance curve,

the specificity at a clinically relevant cut point of 90% sensitivity was 82.5% [58].

The hallmark MRI feature of osteomyelitis is hypointense signal on T1-weighted sequences replacing the typically fatty bone marrow and corresponding hyperintense signal on T2-weighted images [59, 60]. Post contrast image can show bone marrow enhancement that support the diagnosis of osteomyelitis, but the greater diagnostic value of enhancement is for assessing the soft tissues [60]. The use of nuclear medicine scintigraphy should be considered in patients that have contraindications for using MRI (limited evidence) [12].

Osteomyelitis in Sickle Cell Disease

Osteomyelitis is a common complication of sickle cell disease (SCD) with a prevalence of 12–18% [61, 62]. This is due to hyposplenism, impaired immune dysfunction, and infarction and necrosis of medullary bone. *Salmonella* species are the most common pathogen and *Staphylococcus aureus*, the second most common causal organism [9, 61, 62]. Osteomyelitis most commonly affects the long bones. Osteomyelitis often affects the diaphysis as compared to children without sickle cell disease where osteomyelitis is more often in the metaphysis. The clinical manifestations are pain, fever, swelling, and increased inflammatory markers in blood serum. These clinical features can be present in both acute osteomyelitis and infarction, and differentiation between them is difficult. Blood culture is positive in 30–76% of cases of acute osteomyelitis, and radiographic features are non-specific and initially are often normal [9].

Patients with SCD who present with bone pain and fever are initially treated empirically for possible osteomyelitis with broad-spectrum antibiotics. The antibiotics are discontinued at 48 h if the blood culture remains negative. However, in cases in which the patient's fever and pain are persistent despite negative blood, clinicians are often faced with the dilemma of whether to treat for osteomyelitis [9].

Magnetic resonance imaging is the imaging study of choice in diagnosis of osteomyelitis in patients with SCD who do not respond to antibiotics (limited evidence). Magnetic resonance

imaging is sensitive in detection of bone marrow abnormalities but is limited in differentiating between osteomyelitis and bone marrow infarction. There are findings that can be seen in both osteomyelitis and acute infarction such as bone marrow edema and edema and enhancement of adjacent soft tissue [62]. Decreased enhancement of the marrow is more suggestive of infarction, while subperiosteal fluid collection is more suggestive of osteomyelitis [62, 63]. Ultrasound findings of subperiosteal fluid collection (>4 mm) and fluid aspiration can also help in the diagnosis of osteomyelitis [64, 65]. However, there is no accepted imaging protocol for imaging of acute bone crisis in patients with sickle cell disease, and there is insufficient evidence on the best imaging modality [9, 62].

What Is the Diagnostic Performance of the Different Imaging Studies in Septic Hip Arthritis?

Summary of Evidence Radiography uncommonly detects other pathologies such as avascular necrosis of the femoral head, osteomyelitis, and tumor in children. As fluid has the same attenuation as soft tissue, the diagnosis of hip effusion is based on indirect signs such as asymmetric joint space and displacement of the fat planes. The sensitivity of plain radiograph for hip joint effusion is low (insufficient evidence) [66].

Children with moderate or high risk for septic hip arthritis can benefit from ultrasound of the hips. In children with effusion, an US-guided aspiration should be performed for the final diagnosis. Ultrasound is highly sensitive for the evaluation of hip effusion (moderate evidence) [67–69]. However, it cannot distinguish between septic arthritis and other noninfectious causes of joint effusions. The absence of hip effusion by ultrasound is reliable for exclusion of septic hip (moderate evidence) [67–69].

Magnetic resonance imaging is highly sensitive for joint effusion, and MRI can detect associated osteomyelitis or another source of infection or inflammation that present with limping and elevated inflammatory indices. However, due to cost,

availability, need for sedation in young children, and length of study, it is not used in most places as the primary imaging for the diagnosis of septic arthritis. There are some MRI findings, such as bone marrow changes and decreased perfusion of the hip joint, that suggest septic arthritis and are more commonly seen in children with septic arthritis as compared with transient synovitis. However, septic arthritis can occur without these secondary signs (limited evidence) [70–72].

Supporting Evidence

Pelvic Radiography

Pelvic radiograph is often obtained to evaluate children with suspected septic hip, but there is insufficient evidence to support this practice [73]. The yield of significant findings in pelvic radiograph is very low in a child presenting in the emergency department with acute non-traumatic hip pain [66]. The “joint space” seen on plain radiograph in the immature bone represents the non-ossified femoral head, articular cartilage, and the true joint space. Indirect signs for joint effusion include lateral displacement of the femoral head (distance of the ossified femoral head from the pelvis teardrop of >2 mm as compared to the contralateral side) and displacement or blurring of the fat pads. There are inconsistent results on the sensitivity and specificity of plain radiograph for the diagnosis of septic arthritis [73, 74]. However, compared to US, plain radiograph had a sensitivity of about 21–25% for the detection of hip effusion [75, 76].

Hip Ultrasound

Long view ultrasound of the anterior recess of the hip joint is accurate in the diagnosis of hip effusion with a reported sensitivity of 80–86% and specificity of 90–98% (moderate evidence) [69, 77–79]. In joint effusion, the capsule of the anterior hip joint recess changes its shape from concave to convex. Effusion thickness of greater than 5 mm between the femoral neck and outer capsule in a child, and greater than 7 mm in an adult, has been used as diagnostic criteria for a hip effusion. The fluid thickness should also be compared to the contralateral side (Fig. 32.8). A difference

of >2 mm in children and >1 mm in adults is considered positive for hip effusion [77].

No ultrasound characteristics, including complexity of the fluid, the quantity of fluid, or adjacent hyperemia on color Doppler imaging, have shown to be definitive in distinguishing septic arthritis versus other noninfectious causes of joint effusions. The absence of hip effusion by ultrasound is reliable for exclusion of septic hip (moderate evidence) [68, 69, 80]. There are only few reports of false-negative hip US, mainly in patients presented with pain less than 24 h [69, 81].

Pelvic MR Imaging

MRI is widely used in the evaluation of deep soft tissue infection and osteomyelitis. As discussed above, the diagnosis of septic arthritis in children is based on clinical evaluation with the use of hip US for guiding arthrocentesis for a definitive diagnosis. MRI is not routinely used for initial evaluation of septic arthritis [82]. However, in some children osteomyelitis can be associated with concomitant septic arthritis [15, 16]. In these cases, MRI could be useful in suggesting the diagnosis of septic arthritis rather than reactive effusion (insufficient evidence).

Magnetic resonance imaging is highly sensitive for hip joint effusion. Several studies demonstrated that associated bone marrow edema in the femur is associated with septic hip. An additional finding that was correlated with septic hip is decreased femoral hip enhancement. However, this is based on small series of patients [70–72, 83].

One potential advantage of MRI is the ability to diagnose concomitant septic arthritis and osteomyelitis, which has been reported in 17–68% of pediatric patients [15, 16, 28]. Septic hip is associated with osteomyelitis in 15–58% [15, 28]. The definition of osteomyelitis in these studies was based on imaging and not on pathology, and therefore it is possible that at least some of the bone marrow changes were related to reactive edema and not true marrow infection. Septic arthritis is an urgent medical condition, and drainage of the septic joint should be performed without delay to prevent complications. Magnetic resonance imaging study is associated with high costs and longer duration and is less available as

compared to US which can also guide drainage of the joint fluid when positive. In addition, MRI scans in children may involve sedation. For all these reasons, we believe that hip ultrasound should be the first imaging for evaluation of potential septic hip in children and MRI studies should be reserved for children that do not respond to treatment of septic hip or when the hip ultrasound is negative for joint effusion.

Special Case

Septic Arthritis in Adults

Acute septic joint in native joints of adults is uncommon. Large joints are most commonly affected, and the knee is infected in roughly half of the cases [84]. Septic hip arthritis is rare in the absence of prior arthroplasty or chronic joint disease [85]. It typically presents with joint pain and swelling, decreased range of motion, and fever. However, these symptoms are not specific, and it can be difficult to differentiate from other types of arthritis that are more common in adults such as acute flares of rheumatoid, reactive, neuropathic, crystalline arthritis, or osteoarthritis; depositional or neoplastic diseases; and periarticular fractures. Risk factors for septic arthritis (SA) in adults include age of >80 years, diabetes mellitus, rheumatoid arthritis, HIV infection, joint surgery, presence of a joint prosthesis, and skin infection [84–86]. Septic arthritis in a native joint is usually caused by hematogenous seeding, and *Staphylococcus* and *Streptococcus* species are the most common nongonococcal bacterial pathogens. Prompt diagnosis and treatment is crucial to prevent joint destruction [84]. The diagnosis of septic arthritis can be supported by abnormal serologic, hematologic, and imaging findings, but the definitive diagnosis can be confirmed or excluded only by joint aspiration with fluid analysis [84, 86, 87]. Treatment for septic arthritis includes prompt joint drainage or aspiration and antibiotics [88].

The role of imaging is primarily to evaluate for alternative diagnosis. Radiographs are usually the first study obtained to evaluate for acute joint pain and are important for exclusion for fracture or tumor (insufficient evidence). MRI with intravenous

contrast provides the most comprehensive means to assess for associated osteomyelitis, joint effusion, erosions, internal derangements, fracture, osteonecrosis, masses, and soft tissue inflammation or fluid collections (insufficient evidence) [86, 87]. In the presence of clinical suspicion of SA, detection of a joint effusion should be followed promptly by joint aspiration and synovial fluid analysis for definitive diagnosis.

What Is the Imaging Modality of Choice in the Evaluation of Complicated Soft Tissue Infection?

Summary of Evidence Cellulitis is a common soft tissue infection that is superficial and usually diagnosed clinically and treated medically without need for imaging [17, 18]. Ultrasound is the imaging modality of choice in the initial evaluation of cellulitis complicated with localized abscess formation (moderate evidence) [89–94].

The diagnosis of necrotizing fasciitis (NF) is based on clinical evaluation and surgical exploration. Patients with clinical suspicion of NF should be taken emergently to surgery [18–20, 22, 95]. In selected patients with low clinical suspicion, MRI or CT scan can assist to differentiate NF from other deep soft tissue infection [96–98] (insufficient evidence). The limited benefit of imaging in diagnosis of NF should be weighted with potential harm in delaying surgical exploration.

Supporting Evidence

Radiography

Radiography has no role in routine imaging soft tissue infections (insufficient evidence). Radiographs can be performed in selected cases when there is clinical suspicion for underlying radiopaque foreign body and in patients with palpation of crepitus on physical examination to confirm soft tissue gas (insufficient evidence) [18, 99].

Ultrasound

Ultrasound appearance of cellulitis is not specific as other conditions that cause noninfectious subcutaneous edema. Subcutaneous swelling appears

as increases in thickness of the subcutaneous fat with increased echogenicity. It may have cobblestone appearance and perifascial fluid. Hyperemia in color Doppler suggests an inflammatory process [100].

The main role of US is in the diagnosis and guidance of drainage of abscess formation (Fig. 32.9a, b). Detection of an abscess by physical examination can be difficult due to overlying edematous and indurated skin. The sensitivity and specificity of US in the diagnosis of cellulitis complicated with an abscess is 97–98% and 67–88%, respectively (moderate evidence) [89–92, 100, 101]. The use of elastography may have a role in increasing sensitivity in detection of echogenic fluid collection obscured by the surrounding inflammation [93].

A few prospective studies demonstrated increased accuracy of ultrasound performed by emergency department physicians as compared to physical examination in the diagnosis of an abscess. A study of 40 patients found that ultrasound scans were more accurate than physical examination with receiver operating characteristic curve of 0.85 by ultrasound as compared to 0.75 by physical examination. Ultrasound had a sensitivity and specificity of 97 and 67%, respectively, as compared to 76 and 83% by physical examination [89]. In a study of 65 patients, sensitivity increased from 78.7 to 97.5% and specificity from 66.7 to 69.2% when ultrasound was used as compared to physical examination for the diagnosis of an abscess [90]. In a prospective study of 126 patients, the use of ultrasound changed the management in about half of the patients. In the pretest group that was believed not to need further drainage, ultrasound changed the management in 39/82 (48%), with 33 receiving drainage and 6 receiving further diagnostics or consultation. In the pretest group in which further drainage was believed to be needed, ultrasound changed the management in 32/44 (73%), including 16 in whom drainage was eliminated and 16 who had further diagnostic interventions [92].

Magnetic Resonance Imaging

Magnetic resonance imaging is usually not required for evaluation of cellulitis not complicated by deep soft tissue extension. The MRI

findings in cellulitis are subcutaneous swelling and infiltration with low signal on T1- and high signal on T2-weighted sequences with post intravenous contrast enhancement. Abscess appears as well-defined fluid collection with low to intermediate signal on T1 and bright signal on T2 sequences and rim enhancement. Diffusion images show restricted diffusion and may increase sensitivity (92%) and specificity (80%) of MRI in the detection of soft tissue abscess (limited evidence) [82, 102].

The diagnosis of necrotizing fasciitis is suspected by clinical assessment of systemic signs, degree of pain, and physical examination of the affected area. The diagnosis is confirmed on surgical exploration. There is a limited role for imaging in most patients with clinically suspected NF as it may delay prompt surgical exploration [52, 59–62]. However, MRI is used in few cases to confirm presence of deep soft tissue infection and assess the extent of involvement. The most important criteria in MRI for the diagnosis of NF are edema and enhancement of the deep fascia (Fig. 32.10a, b) [96–98, 103]. There is, however, overlap in these findings between NF and non-necrotizing infectious fasciitis [97]. The sensitivity and specificity of MRI in the diagnosis of NF is 89–100% and 46–86%, respectively (limited evidence) [96, 98, 103].

Computed Tomography

There have been recent improvements in the CT technology including the use of multidetector CT (MDCT), improved detector sensitivity and spatial resolution, and use of noise reduction techniques such as iterative and model-based reconstruction. Together this allows for faster scanning, image acquisition during optimal post intravenous contrast material tissue enhancement,

decrease motion artifacts, volumetric acquisition, isotropic multiplanar reconstruction with better image quality, and less radiation dose [104–107]. These advancements made CT an alternative to MRI in the emergency setting with advantages such as increased availability, faster scan time, and no need for sedation or general anesthesia in the vast majority of patients [41, 42]. The main disadvantages of CT compared to MRI are the inferior soft tissue contrast resolution and ionizing radiation.

Computed tomography can be used selectively in the emergency setting as a rapid imaging for the diagnosis of extension and complications of soft tissue infection (limited evidence). Recent studies using MDCT show its ability to detect not only soft tissue gas but also differences in soft tissue enhancement, thickening of the deep fascia, edema of the muscles, and fluid collections (Figs. 32.11 and 32.12). The most specific CT findings of necrotizing fasciitis are fascial air, muscle and fascial edema, and fluid tracking. The reported sensitivity and specificity of MDCT are 86.3–100% and 81–91.5%, respectively [108].

Take-Home Tables and Figures

Tables 32.1, 32.2, and 32.3 highlight and summarize diagnostic performance characteristics of imaging studies for acute hematogenous osteomyelitis, septic arthritis, and cellulitis complicated with an abscess and necrotizing fasciitis, respectively. Figure 32.1 offers an algorithm for imaging suspected acute hematogenous osteomyelitis (AHOM). Figure 32.2 presents an algorithm for imaging suspected septic hip arthritis in the pediatric population. Figure 32.3 shows an algorithm for imaging of cellulitis.

Table 32.1 Diagnostic performance characteristics of imaging studies for acute hematogenous osteomyelitis (AHOM) based on studies in children and adults

	Sensitivity (%)	Specificity (%)	Level of evidence
Radiography	43–75	75–83	Insufficient
Ultrasound	46–84	47–100	Limited
^{99m} Tc bone scintigraphy	73–100	73–79	Limited
MRI	82–100	75–96	Limited

^{99m}Tc technetium-99M, MRI magnetic resonance imaging

Table 32.2 Diagnostic performance characteristics of imaging studies for septic arthritis

	Sensitivity (%)	Specificity (%)	Level of evidence
Radiography	0–100	0–77.3	Insufficient
Ultrasound for hip effusion	80–86.4	89.7–98	Moderate
MRI for septic hip	85.7–89	72.7–92	Insufficient

MRI magnetic resonance imaging

Table 32.3 Diagnostic performance characteristics of imaging studies of cellulitis complicated with an abscess and necrotizing fasciitis

	Sensitivity (%)	Specificity (%)	Level of evidence
Abscess			
Ultrasound	97–98	67–88	Moderate
MRI	92	80	Limited
Necrotizing fasciitis			
MRI	89–100	46–86	Limited
CT	86.3–100	81–91.5	Limited

MRI magnetic resonance imaging, *CT* computed tomography

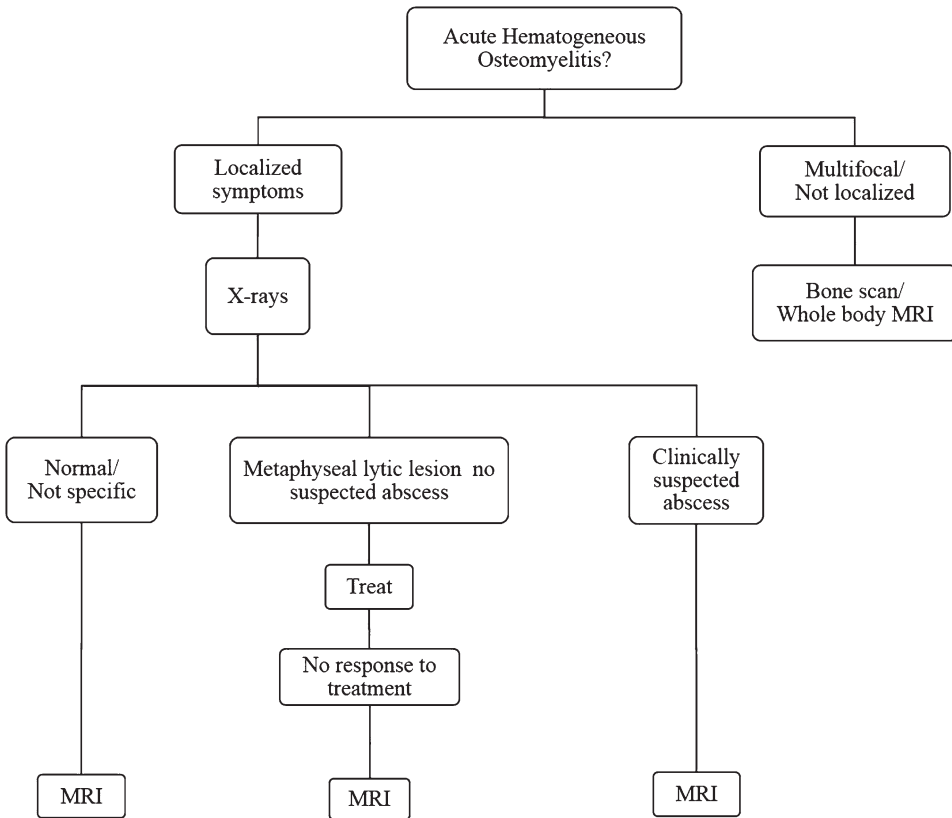


Fig. 32.1 Algorithm for imaging suspected acute hematogenous osteomyelitis (AHOM)

Fig. 32.2 Algorithm for imaging suspected septic hip arthritis in the pediatric population

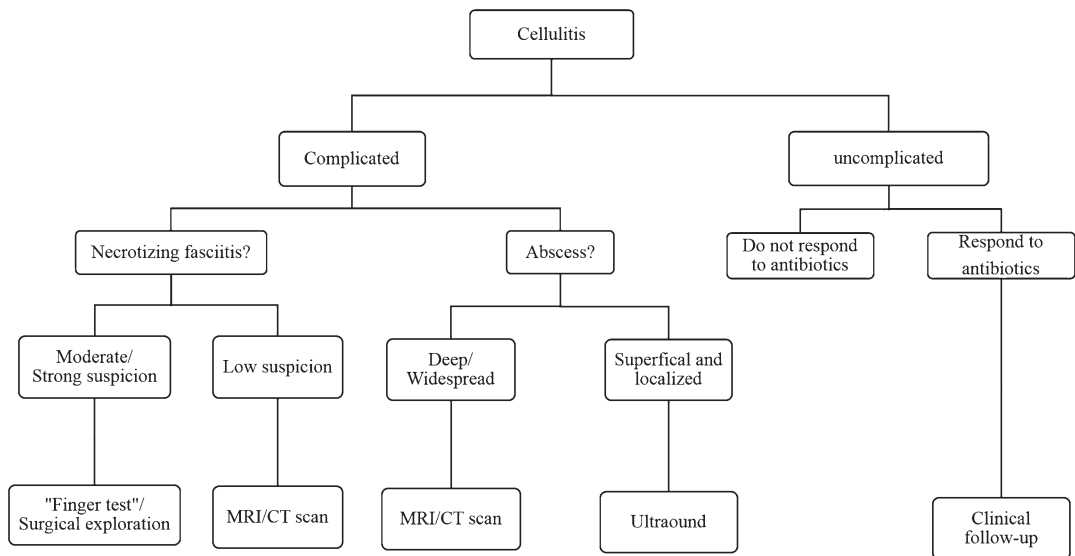
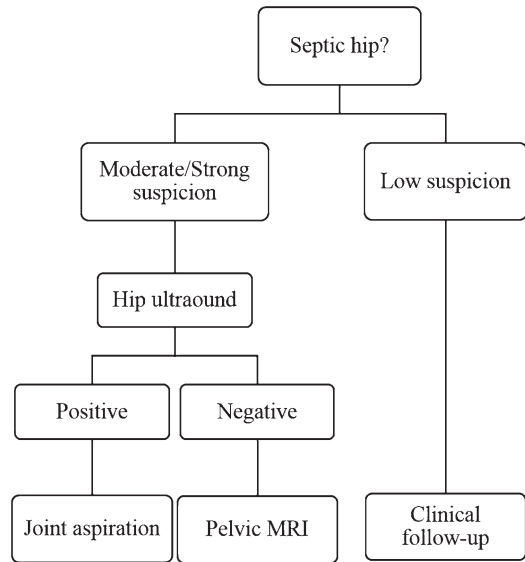


Fig. 32.3 Algorithm for the imaging of cellulitis

Imaging Case Studies

Case 1

In Fig. 32.4a–c, an 18-day-old male with distal left femoral osteomyelitis presents with refusal to move left leg.

Case 2

In Fig. 32.5a, b, a 10-month-old female with proximal left tibia osteomyelitis presents with refusal to crawl after fall off the couch 1 week earlier.

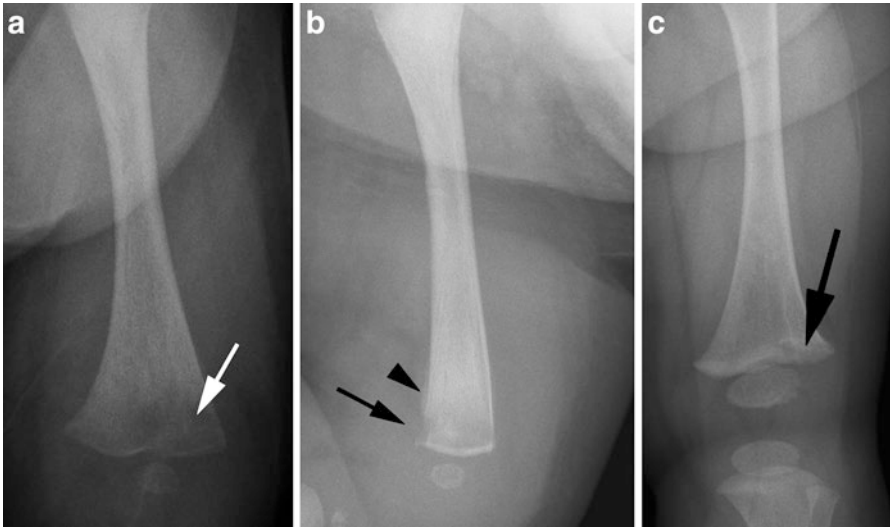


Fig. 32.4 An 18-day-old male with distal left femoral osteomyelitis presented with refusal to move left leg. AP and lateral radiographs (**a**, **b**) of the left femur demonstrate distal lateral and posterior metaphyseal lucency (*arrow*). Follow-up anteroposterior radiograph of the

left femur at the age of 10 months (**c**) shows irregularity and widening of the lateral physis with valgus angular deformity (*arrow*). The child was later treated with placement of medial tension plate and lateral bony bar resection

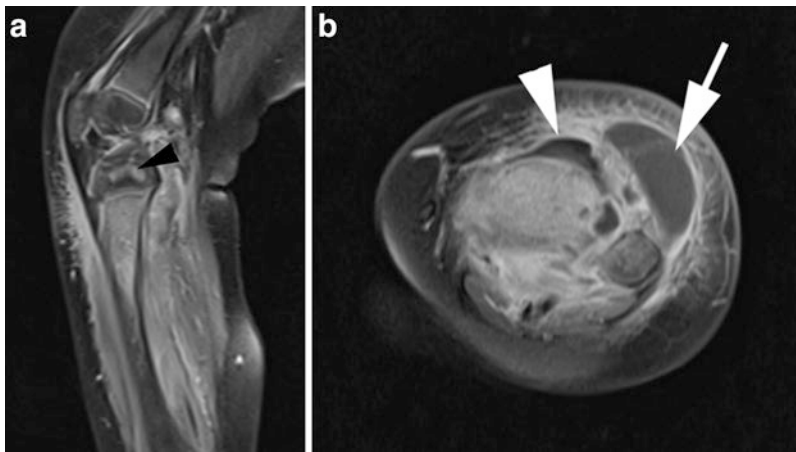


Fig. 32.5 A 10-month-old female with proximal left tibia osteomyelitis presented with refusal to crawl after fall off the couch 1 week earlier. On physical exam she had fever of 39.1 °C, and the proximal left tibia was tender and warm. Sagittal post contrast SET1 fat-suppressed image (**a**) shows extensive bone marrow enhancement

involving the proximal epiphysis (*arrowhead*), metaphysis, and diaphysis. Axial post contrast SET1 fat-suppressed image (**b**) shows subperiosteal fluid collection (*arrowhead*) and a large abscess (*arrow*). The abscess was drained and cultures were positive for *Staphylococcus aureus*

Case 3

Figure 32.6 presents a 3-year-old male with left proximal humerus osteomyelitis and pathological fracture.

Case 4

Figure 32.7a, b presents a 3-year-old female with *Bartonella henselae* multifocal osteomyelitis.

Case 5

Figure 32.8 presents a 15-month-old female with left septic hip.

Case 6

Figure 32.9a, b presents an 11-year-old male with left shin cellulitis and abscess.

Case 7

Figure 32.10a, b presents an 88-year-old female with necrotizing fasciitis of the left ankle.

Case 8

Figure 32.11 presents a 66-year-old man who died after rapidly progressive necrotizing fasciitis.

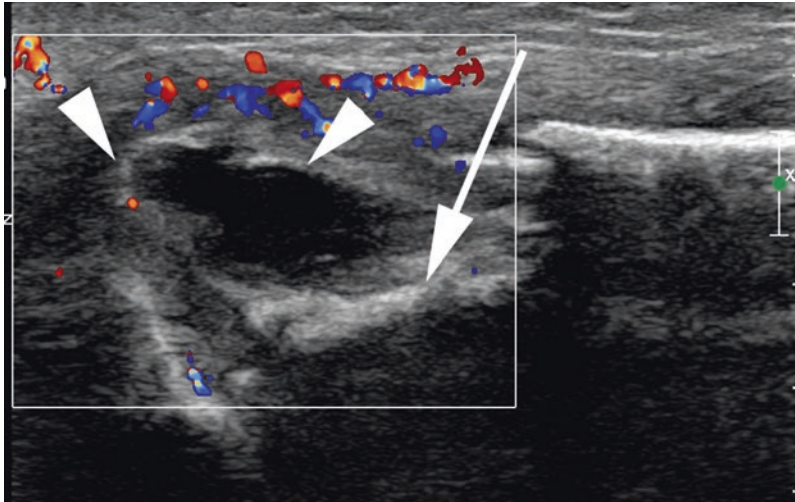


Fig. 32.6 A 3-year-old male with left proximal humerus osteomyelitis and pathological fracture. The child had a complex medical history due to extreme prematurity (23 +5 weeks premature), chronic lung disease, ventilator dependent, and post necrotizing enterocolitis presenting with persistent MRSA bacteremia. Chest radiograph

demonstrated an unsuspected left humerus fracture. Long view color Doppler ultrasound shows a proximal left humerus displaced fracture (*arrow*) and adjacent fluid collection (*arrowhead*) and increased soft tissue vascularity. The abscess was aspirated under ultrasound guidance

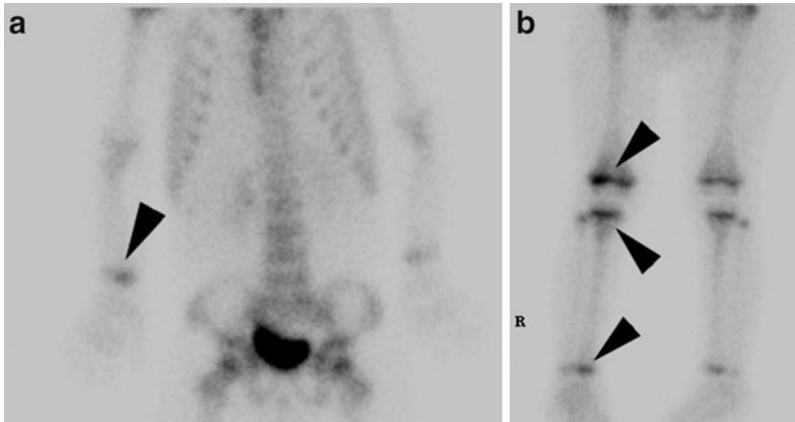


Fig. 32.7 A 3-year-old female with *Bartonella henselae* multifocal osteomyelitis. She presented with 10 days of fever, discomfort with movement and walking without any specific area of pain, and swelling and

erythema. Tc-99M MDP bone scan demonstrated increased uptake in the right distal radius (**a**, *arrow*), distal right femur, and proximal and distal right tibia (**b**, *arrows*)

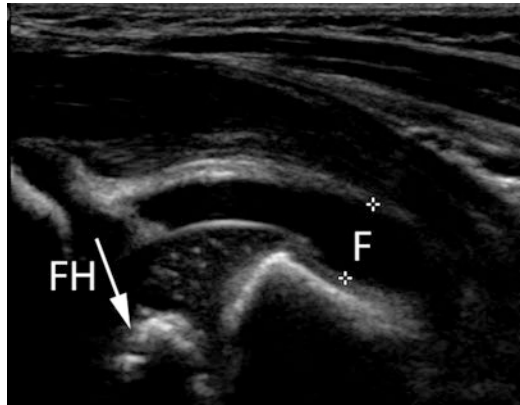


Fig. 32.8 A 15-month-old female with left septic hip. She presented with refusal to bear weight for 5 days, ESR (erythrocyte sedimentation rate) of 72 mm/h, and CRP (c-reactive protein) of 4.1 with no fever. Long view ultrasound of the

left hip demonstrates moderate effusion (F), femoral head ossification center (*arrow* FH). A cloudy fluid was drained with negative cultures. A follow-up MRI (not shown) demonstrated associated femoral epiphyseal osteomyelitis

Case 9

In Fig. 32.12, a 54-year-old female with necrotizing fasciitis presents with 2 days of malaise, fever, episode of hypotension, and progressive cellulitis in the left thigh involving the deep tissues.

Suggested Imaging Protocols

Radiographs

Two orthogonal views (at the very least) limited to the body part of interest should be performed: This should be done on all patients suspected of osteo-

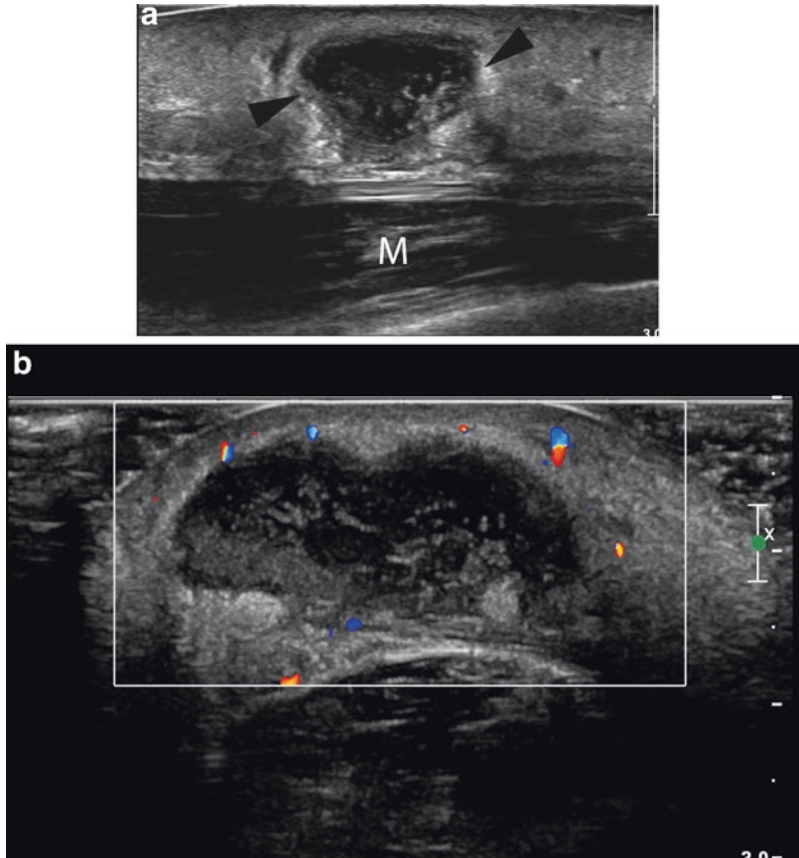


Fig. 32.9 An 11-year-old male with left shin cellulitis and abscess. The cellulitis did not respond to antibiotics with increased swelling and erythema. No fluctuation was felt. Long view ultrasound (a) at the cellulitis demonstrates subcutaneous soft tissue swelling with increased

echogenicity and an abscess (arrowheads). The muscles (M) appear normal. Transverse view color Doppler ultrasound (b) demonstrates a well-defined fluid collection (arrowheads) with surrounding increased vascularity compatible with an abscess

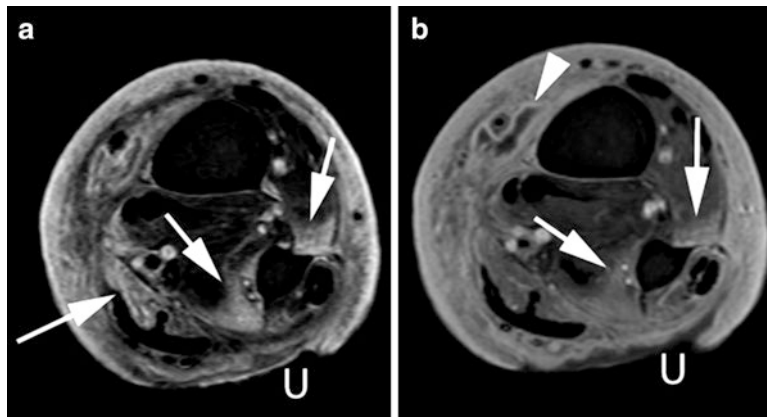


Fig. 32.10 An 88-year-old female with necrotizing fasciitis of the left ankle. She had underlying diabetic mellitus. She presented with cellulitis, severe pain, and skin ulceration that progressed under antibiotic treatment. Axial T2 fat suppression (a) shows the skin

ulceration (U) and edema and thickening of the deep fascia (arrows). Post contrast T1 fat suppression (b) shows the skin ulceration (U), subcutaneous fluid collection (arrowhead), deep fascia, and muscles enhancement (arrows)

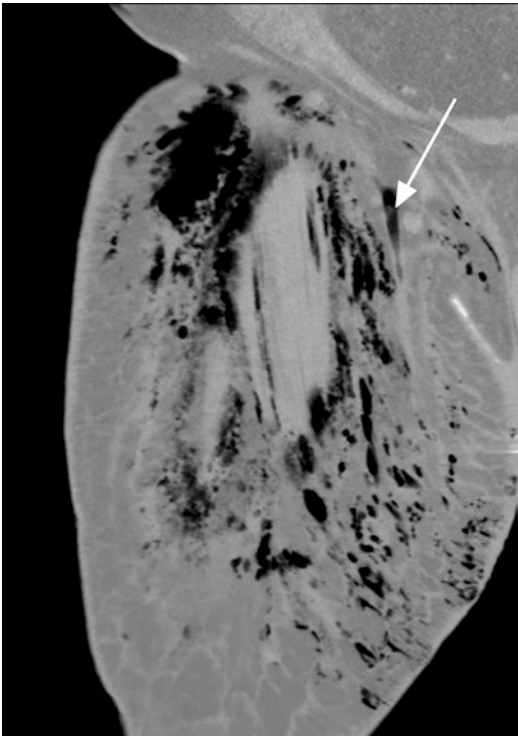


Fig. 32.11 A 66-year-old man who died after rapidly progressive necrotizing fasciitis. The patient presented with right thigh cellulitis that progressed, with development of respiratory distress and shock, and was resuscitated after cardiac arrest. He did not recover after emergent debriding surgery. Post IV contrast coronal CT scan shows extensive superficial and deep soft tissue emphysema and deep venous gas and gas in the femoral vein (*arrow*). Surgical exploration confirmed necrotizing fasciitis requiring extensive debridement

myelitis to evaluate for destruction and periosteal new bone, as well as to exclude other pathologies such as tumors or fractures.

Radionuclide Bone Scintigraphy

Three-phase radionuclide bone scintigraphy with Tc-99m-labeled MDP, planar images during blood flow and soft tissue phases, and planar images of extremities and SPECT images of the axial skeleton during bone phase: Imaging should be used if symptoms are non-

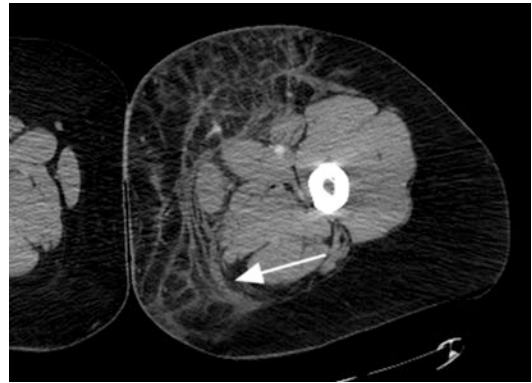


Fig. 32.12 A 54-year-old female with necrotizing fasciitis who presented with 2 days of malaise, fever, episode of hypotension, and progressive cellulitis in the left thigh involving the deep tissues. Post IV contrast axial CT scan shows extensive cellulitis extending to the deep tissue with fascia thickening (*arrow*). Surgical exploration confirmed necrotizing fasciitis requiring extensive debridement, and group A streptococcus grew on tissue culture

localizing or if suspicion of polyostotic disease arises.

Extremity MR Imaging

Axial T1 SE and T2 FSE with fat saturation, coronal STIR, and T1 SE, sagittal FSE T2 fat saturation and T1 SE, and axial and coronal T1 SE with fat saturation after intravenous gadolinium: Imaging should be performed if there are localizing symptoms of osteomyelitis and for evaluation of deep soft tissue infection.

Whole-Body MR Imaging

Three-dimensional coronal STIR with axial multiplanar reconstruction and coronal in-phase and out-phase gradient-echo T1 (this sequence can be helpful in differentiating red marrow hyperplasia from pathology): Imaging should be considered as an alternative to bone scan if symptoms are nonlocalizing or if there is suspicion for polyostotic disease.

Ultrasound Hip Joint

The patient should be placed in a supine position with the affected leg in abduction. Linear transducer high-frequency probe (7–18 MHz) should be used. Long views should be obtained. Long axis images of anterior recess of the joint should align the long axis of the femoral neck. Compare with opposite joint for symmetry. Any fluid should be measured. Imaging should be performed to evaluate for joint effusion and joint aspiration. Most commonly used for the hip joint.

Ultrasound for Soft Tissue

Use long and transverse gray scale images at the area of soft tissue swelling. Use gray scale and color Doppler. Use of elastography if available to detect an abscess with echogenic fluid collection that may be obscured by the surrounding inflamed echogenic tissue.

Future Research

- Investigate whether use of whole-body MR imaging technique obviates the need for radio-nuclide scintigraphy when evaluating of hematogenous multifocal osteomyelitis.
- Investigate whether ¹⁸F-FDG-PET increases sensitivity in detection of osteomyelitis versus ^{99m}Tc-MDP bone scan.
- Does US elastography increase accuracy of US in detection of soft tissue abscesses?

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Part VI

Pediatric Imaging



Evidence-Based Emergency Neuroimaging in Children and Adults with Sickle Cell Disease and Symptoms of Stroke

Jaroslaw Krejza, Michal Arkuszewski,
and Elias R. Melhem

Key Points

- Non-contrast CT imaging remains the initial test of choice for emergency brain assessment of patients with sickle cell disease (SCD) and symptoms of acute stroke (moderate evidence).
- MRI, especially with a use of gradient-echo sequences, may be as accurate as CT for the detection of acute hemorrhage in patients presenting with acute stroke symptoms and is more accurate than CT for the detection of ischemic stroke and chronic intracerebral hemorrhage (moderate evidence).
- MRI/DWI is recommended for better assessment of the extent of infarction and demonstration of cerebrovascular abnormalities (moderate evidence).
- CTA and CT perfusion can be added to emergency CT to detect large arterial

vasculopathy and perfusion defects (insufficient evidence).

- MRA/MRV can be added to standard MRI/DWI and is recommended to detect large arterial vasculopathy and cerebral venous thrombosis (insufficient evidence).
- PET/SPECT is not recommended in patients with acute stroke but can be useful to determine tissue viability in sub-acute settings (insufficient evidence).
- Ultrasound techniques such as transcranial Doppler (TCD), transcranial color-coded Doppler (TCCD), and carotid ultrasound are not recommended in patients with acute stroke; however, TCD/TCCD is useful in monitoring vasospasm after SAH (insufficient evidence).

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Definition, Pathophysiology, and Clinical Presentation

Definition and Etiology

SCD is the family of recessively inherited disorders of hemoglobin (Hb) [1], which have developed in response to strong evolutionary selection

by malaria [2, 3]. Sickle cell anemia (SCA), the most severe form of SCD, refers specifically to homozygosity for the HbS (β S), a variant of the HbB gene (which encodes β -globin), whereas people who inherit only one sickle gene are sickle cell carriers [4, 5]. HbS homozygotes suffer from SCD, but heterozygotes have a tenfold reduced risk of severe malaria [6, 7]. SCD also includes other variants of the HbB gene—namely, HbC and HbE [8–11], regulatory defects of HbA and HbB, which cause α - and β -thalassemia ($S\beta^+$ or $S\beta^0$) [12–14]. The evolutionary pressure has risen to high frequencies of HbS allele in malaria-exposed populations despite the fatal consequences for homozygotes (HbSS) [2]. Different populations have developed independent evolutionary responses to malaria at both the global and the local levels [15]. The most striking example is the Hb gene, in which three different coding single nucleotide points confer protection against malaria: Glu6Val (HbS), Glu6Lys (HbC), and Glu26Lys (HbE) [3]. The HbS allele is common in Africa but rare in Southeast Asia, whereas the opposite is true for the HbE allele [3, 15]. At the local level, not only the frequency of the HbC and HbS allele varies [8] but also their haplotypes; for instance, the HbS allele is found in four distinct haplotypes in West Africa region [16–18].

Pathophysiology

Sickle deoxyhemoglobin tends to polymerize to gel-like consistency, while the red blood cell (RBC) becomes more rigid and is deformed to a less pliable sickle shape [19–21], which increases blood viscosity and mechanical stress on RBCs during their passage through microcirculation, resulting in hemolytic anemia [22, 23], chronic inflammation with elevated levels of biologic mediators, and ongoing activation of the coagulation system, even when they are in “steady state” [23–25]. As a result, the viscosity of the oxygenated sickle blood is about 1.5-fold that of normal at equal shear rates, but blood viscosity increases tenfold in the deoxygenation state [26].

In anemia, O_2 transport is optimized at lower hematocrit and higher blood volume to counterbalance abnormal rheological behavior of sickle RBCs and higher blood viscosity saturated with deoxygenated HbSS [27–30]. Cerebral blood flow (CBF) and systemic circulation adapt to the altered rheological conditions [31], especially by recruiting vasodilatation to reduce resistance to flow and increase flow velocity, which decreases apparent blood viscosity [32–34]. Blood vessels by adjusting their radius keep returning shear stress on their walls toward “normal” levels [35] via NO (nitric oxide)-dependent mechanism, which causes vasodilation and/or vascular remodeling. The upper limit of cerebral dilatation corresponds to a tissue perfusion rate of approximately 200 ml/100 g/min, and this limit is clearly approached in many anemic patients [36]. Very short mean transit time (MTT) and high flow velocities in capillaries may reduce oxygen extraction fraction (OEF), regardless of lower O_2 affinity to HbSS [37]. The central point is that O_2 transfer from capillaries to the surrounding tissue depends nonlinearly on blood flow [38]. Thus, if capillary oxygenation is close to the arterial level as in hyperemic flow regime in anemia, small increases in tissue-oxygen delivery occur only when there are very large increases in CBF, because the RBCs have less time to lose their oxygen [38]. In many patients, additional CBF increase to meet brain demand can be prohibitive [39, 40].

The alternate hemolytic pathway that leads to brain ischemia can begin with intravascular destruction of RBCs and the release of free Hb and arginase into the plasma with subsequent disturbances of cerebral autoregulation [41, 42]. Free Hb binds and inactivates NO, and, concomitantly, free arginase converts L-arginine into ornithine, a NO substrate, reducing the production of NO [43, 44]. Reduced levels of NO cause vasoconstriction and may interfere with vasodilation needed to maintain brain functions [43, 44]. Severe systemic hemodynamic disturbances might further compromise reduced CBF and oxygen delivery leading to ischemic brain injury [36].

Clinical Symptoms

There is a wide range of values for all RBC indices in chronic SCA [45]. The reduction in volume of RBC restricts the oxygen-carrying capacity of Hb, leading to chronic oxyhemoglobin desaturation [46]. Children with HbSS are more vulnerable to frequent episodes of pain, chest crisis, stroke [47–50], and delayed growth [51] than those with HbSC or HbS β^0 -thalassemia, who usually have less severe neurological complications in later life [21].

Stroke in Patients with SCD

Stroke is a major cause of morbidity in SCD, typically defined as a cerebral vascular accident (CVA) of sudden onset with focal neurological deficit persisting after 24 h, developed either spontaneously or in the context of an acute illness such as infection [52]. There is a high risk of CVA recurrence—particularly for patients presenting spontaneously—that is reduced but not eliminated by regular blood transfusion [52, 53].

Both ischemic and hemorrhagic strokes may be encountered as well as common subclinical strokes called “silent infarcts” [47, 54, 55]. The typical areas of infarction are the frontal and parietal lobes, particularly in boundary zones of territories supplied by the internal carotid and middle and anterior cerebral arteries, whereas the posterior circulation is affected less frequently [54]. There is a broad spectrum of acute presentations with CVA and other neurological complications in patients with SCD [56–59]. Patients with SCD also can have transient ischemic attacks (TIAs) with symptoms and signs resolving within 24 h [56–58], although many of these individuals are found to have had recent cerebral infarction or atrophy on imaging [47]. The insidious onset of “soft neurological signs,” such as difficulty in tapping quickly, is an indicator of associated cerebral infarction [60, 61]. Melek et al. observed that in over 95% of SCD patients with silent infarcts, at least one soft sign was present [60]. In addition, seizures (20–48%) [62, 63], decreased levels of consciousness [64], and headache

(6.9%) [65, 66] are also indicators of stroke and CVA in children with SCD. Altered mental status—with or without reduced level of consciousness, headache, seizures, visual loss, or focal signs—can occur in numerous contexts, including infection, shunted hydrocephalus [67], acute chest syndrome (ACS) [68, 69], aplastic anemia secondary to parvovirus [70], after surgery [65], transfusion [71], or immunosuppression [72, 73], and apparently spontaneously [74]. In one large series of 538 patients with ACS, 3% of children had neurological symptoms at presentation, and such symptoms developed in a further 7–10% in association with ACS [68]. These patients are classified clinically as having had a CVA [47], although there is a wide differential of focal and generalized vascular and nonvascular pathologies—often distinguished using acute magnetic resonance techniques [74]—with important management implications [63, 67, 71, 75–78]. Sixty-seven percent of those who have had an initial stroke and are not transfused will develop another, most likely within 36 months [79]. With each episode, the child is usually left with greater neurological deficits including some degree of mental retardation [80].

Epidemiology

Epidemiology of SCD

SCD is a global, chronic, noncommunicable disease affecting millions of people in Africa, the Mediterranean region, Middle East, India, the Caribbean, the Americas, and, in recent decades, much of Western Europe [81–91]. The incidence of SCA in the African-American population is 0.2–0.3%, that of HbSS trait is 9–11%, and that of HbSC disease is 3% [86, 92–95]. The sickle gene is present in about 20% of the indigenous black population in Africa [88, 96, 97]. Approximately 72,000 African-Americans in the USA have SCD [98]. About 1 in 12 African-Americans and about 1 in 100 Hispanic Americans are carriers of the disease [99]. This prevalence has remained constant primarily because the trait provides partial protection

against malarial infection from *Plasmodium falciparum* [88, 100, 101]. The malaria parasite has a complex life cycle and spends part of it in red blood cells. In a carrier, the presence of *Plasmodium* causes the RBC with defective Hb to rupture prematurely, making the plasmodium unable to reproduce. Further, the deoxygenation that leads to polymerization of Hb affects the ability of the parasite to digest Hb in the first place. The parasites by themselves lower the pH and cause the cells to sickle faster. Therefore, in areas where malaria is a problem, people's chances of survival actually increase if they carry sickle cell trait (selection for the heterozygote). Such protection has become irrelevant in the USA where malaria is no longer endemic.

While early childhood mortality and life expectancy of people with SCD have improved significantly over the past 30 years in the USA and other developed countries, no such improvement has been seen in poor African countries where most young children with SCD die before 5 years of age, even without proper diagnosis of SCD [102]. SCD contributes to the equivalent of 5% of deaths in children under 5 years of age on the African continent, more than 9% of such deaths in West Africa, and up to 16% of under-five deaths in individual West African countries [102].

Epidemiology of Stroke

The overall prevalence of stroke in all forms of SCD is 4% and 5% in those with SCA. First stroke occurs in all age groups, except for children under 1 year of age. The annual incidence of first stroke is approximately 0.6 per 100 patient-years or 600/100,000/year in SCA children. However, the highest incidence occurs in the first decade of life, with rates of 1.02 per 100 patient-years in 2–5-year-old SCA patients and 0.8 in those 6–9 years old [47]. The cumulative risk of first stroke in SCA patients is 11% by age of 20 years, 15% by age 30, and 24% by age 45 [47]. The combined incidence of hemorrhagic and ischemic strokes in a general sample of American children 14 years of age was reported as 3.3 per

100,000 yearly or 0.0033 per 100 patient-years [103]. The types of stroke differ between adults and children with SCD. The Cooperative Study of Sickle Cell Disease (CSSCD), a prospective cohort study of over 4000 children and adults, identified a history of stroke in 3.8% of the participants; 9.6% of first strokes in SCD patients under age 20 were hemorrhagic, while 52% of all strokes in those over 20 years were hemorrhagic. In the CSSCD, stroke occurred less frequently in the other common genotypes of SCD. Age-adjusted prevalence rates of stroke at study entry were 2.43% for $S\beta^0$ thalassemia (SCD- $S\beta^0$), 1.29% for SCD- $S\beta^+$, and 0.84% for SCD-SC. Twenty-one percent of SCD-SC patients who had a stroke were less than 10 years old compared to those with SCD-SS (31% under age 10).

Overall Cost to Society

Expenditures of children with SCD were 6 and 11 times higher than in those without SCD enrolled in Medicaid and private insurance, respectively [104]. Total health-care costs generally rise with age, from \$892 to \$2562 per patient-month in the 0–9- and 50–64-year age groups, respectively, on average \$1389 [104]. The estimated cost of medical care for the 70,000 individuals with SCD in the USA exceeds \$1.1 billion [105]. Overall, 51.8% of care is directly related to SCD, the majority of which (80.5%) is associated with patients' hospitalizations [104]. Non-SCD-related costs were substantially higher than those reported for the general US population [106]. Non-SCD-related costs were estimated at \$9428 per patient annually, compared to reported average total medical expenses of \$3917 in 2005 [104, 107]. On an annualized basis, the total care cost of health care for patients with SCD ranged from \$10,704 ($\pm 24,696$) for individuals aged 0–9 years to \$34,266 ($\pm 52,224$) for those aged 30–39 years [104]. For an average patient with SCD reaching age 45, total undiscounted health-care costs were estimated to reach \$953,640 [104]. This estimated cost does not include direct and indirect non-health-related costs, patient's and

family member's time lost from school, lost workdays and reduced productivity of the patient, lost earnings of unpaid caregivers, transportation expenses, and income lost from premature death. In a report from the UK [108] based on 6077 admissions in years 2010–2011 associated with SCD with crisis as primary diagnosis, the total cost for these admissions was 18,798,255 GDP (about 27,300,000 USD). The cost of admissions increases with age (children admissions cost 50% less than adults). Patients between 10 and 19 years old are more likely to stay longer in hospital compared with others. Taken together the full burden of SCD worldwide is quite higher than the figures reported above [109].

Goals of Imaging

The goal of neuroimaging in acute stroke is to document whether the stroke is ischemic or hemorrhagic, to assess the extent of parenchymal abnormalities, to determine presence of cerebrovascular lesions, and to monitor cerebral blood flow disturbances. However, initiation of neuroprotective therapy, including exchange transfusion therapy to minimize secondary brain damage and neutralize "ischemic cascade," should not be delayed by arrangement for imaging studies.

Methodology

We conducted a systematic review of the literature using a database search of MEDLINE (PubMed, National Library of Medicine, Bethesda, MD) and of Web of Science® (Institute for Scientific Information, Philadelphia, PA) to identify studies dealing with sickle cell disease and stroke and relevant to neuroimaging. The search covered the time period January 1990 to November 2015, using the key terms (1) sickle cell disease and (2) stroke and one of the following: "exp cerebral ischemia," "cerebral infarction," "cerebrovascular disorders" or "cerebrovascular accidents," "epidemiology," "cost," "ultrasound," "TCD or transcranial Doppler sonography," "TCCS or transcranial

color-coded sonography," "TCCD or transcranial color-coded duplex sonography," "MRI or magnetic resonance imaging," "MRA or magnetic resonance angiography," "angiography," "DSA or digital contrast angiography," "CT or computed tomography," "PET or positron emission tomography," and "SPECT or single-photon emission computerized tomography." There was one randomized controlled trial, no meta-analyses, and no cost analysis of neuroimaging diagnostic options. We expanded our retrieval to include also clinical trials, cohort studies, multicenter studies, comparative studies, case-control studies, and case reports having more than five subjects for the key question of the age-specific natural history of ischemic stroke. Reviews, letters, hospital bulletins, and single case reports were excluded.

Discussion of Issues

What Is the Imaging Modality of Choice to Detect Intracranial Hemorrhage in Patients with SCD?

Summary of Evidence CT imaging is the initial test of choice for emergency assessment of patients with SCD and acute hemorrhagic stroke (moderate evidence). However, there is ongoing debate if MRI can replace CT in emergency stroke settings, because there is no evidence based on randomized or non-randomized controlled trials that suggests diagnostic superiority of CT over MR imaging on outcome of emergency management of children or adults with SCD and stroke. If the sequences of the MRI of the brain are optimized to detect cerebral hemorrhage and the MR study can be done promptly, an MRI/DWI of the brain can be a preferred strategy over CT to detect both hemorrhage and cerebral infarct (insufficient evidence). Currently, many stroke centers obtain both CT and MRI in the initial evaluation of patients with stroke. The use of both modalities can be time-consuming and expensive.

Advantages of using CT in emergency settings lie in its widespread immediate 24/7 availability, relative ease of interpretation, speed of scans

acquisition, and ability to reliably detect or exclude hemorrhagic causes (moderate evidence), which are more often fatal in patients with SCD compared to ischemic causes. The American Heart Association stresses the importance of emergency CT imaging of the head within 25 min after admission of a patient with symptoms of acute stroke. Taking this time aspect into account, MRI is limited by its relatively long duration, higher vulnerability to motion artifacts, and patients' contraindications such as claustrophobia, cardiac pacemakers, patient confusion, or metal implants. Additionally, in $\approx 10\%$ of patients, an inability to remain motionless may affect the quality of MRI, especially in uncooperative and unstable patients, who require sedation and anesthesiological support as in most pediatric cases. In acute intraparenchymal hemorrhage (ICH), the accuracy of MRI seems to be similar to the accuracy of CT, especially when gradient-echo sequences are used (insufficient evidence). In patients with subarachnoid hemorrhage (SAH), CT is superior (moderate evidence).

Compared with CT, advantages of MRI include the ability to distinguish acute, small cortical, small deep, and posterior fossa infarcts; the ability to distinguish acute from chronic ischemia; identification of subclinical satellite ischemic lesions that provide information on stroke mechanism; the avoidance of exposure to ionizing radiation; and greater spatial resolution (moderate evidence).

Supporting Evidence About 9.6% of first strokes in SCD-SS patients younger than 20 years were hemorrhagic, compared to 52% of first strokes in those over 20 years old [47], in whom there is nearly a 250-fold increase in the risk of hemorrhagic stroke compared with children [58]. In the CSSCD study, almost all fatal cases (24%) were due to hemorrhagic stroke. In the first published series, the mortality rate associated with hemorrhagic stroke was over 50% [110], similar to the rate (40%) reported by Strouse et al. [71]. The typical clinical presentation of hemorrhagic stroke in SCD includes focal neurological deficits, severe headache, nuchal rigidity, and coma.

No etiology for hemorrhagic stroke is identified in most cases. Among those with an etiology,

subarachnoid hemorrhage is the most common and is often associated with intracranial aneurysm [111, 112]. The presence of hemorrhagic stroke does not exclude the possibility of ischemic stroke [113]. The ratio of ischemic to hemorrhagic risk was not modified with modern management compared with historical series [114]. If a concomitant ischemic stroke is identified, there should be consideration for regular blood transfusion therapy [115]. Intracranial aneurysm in children with SCD had specific characteristics, similar to intracranial aneurysms described in adults with SCD. Data favored concurrent development of intracranial SCD-associated anterior stenosis and posterior dilation, suggesting common pathophysiology and management strategies [116, 117]. The risk of hemorrhagic stroke increases along with decreasing steady-state Hb concentration (RR 1.61 per 1 g/dL decrease) and increasing leukocyte count (1.94 per $5 \times 10^9/L$ increase) [47]. Associations with hypertension, recent blood transfusions, treatment with corticosteroids, previous ischemic stroke, moyamoya, cerebral aneurysms, or acute chest syndrome (ACS) were also reported [71, 78, 118–122].

Computed Tomography (CT)

In the emergency setting, non-contrast CT (NCCT) is adequate and the most cost-effective strategy in diagnosing acute hemorrhagic stroke [123]. NCCT also enables quantification of intracranial hematoma volume and monitoring hemorrhage evolution [124]. In patients with hemorrhagic stroke, both initial hematoma volume and hematoma growth are independent predictors of clinical outcome and mortality [125, 126]. Hematoma volume can be calculated by using the readily available ABC/2 method [127, 128] derived from an approximation, according to the formula for ellipsoids, where A is the greatest hematoma diameter; B, the diameter at 90° to A; and C, the approximate number of CT slices with hematoma multiplied by slice thicknesses [128].

CT imaging enables estimation of age of a hematoma based on its density measured in Hounsfield units. At onset, hematoma is commonly seen as uniform, smooth hyperdense

lesion on CT. Over the course of the first 48 h, large hematomas tend to show fluid levels, indicating that they are not solidified yet [129]. To this regard, fluid blood levels have been defined as a horizontal interface between hypodense bloody serum layered above hyperdense settled blood. Fluid blood levels in acute ICH are moderately sensitive (59%) to the presence of coagulopathy (i.e., abnormal prothrombin time and partial thromboplastin time) and highly specific (98%) for this condition [130]. Over the first 72 h, a hypodense region can be detected around lesions, as a result of the edema that surrounds the brain tissue; a noteworthy mass effect can be detected as well. Three to twenty days after onset, the lesion area tends to shrink and becomes less intense, losing ≈ 1.5 Hounsfield units per day. The periphery of the lesion tends to take on an uneven profile, which acquires a pseudo-abscess (ringlike) appearance, as seen on contrast.

Detection of intracranial hematoma and determination of its volume and age enable to make decisions as to further testing with vascular imaging modalities to detect a source of bleeding and/or performing neurosurgical interventions such as craniectomy in cases of large ICH and/or aneurysm coiling/clipping, ventricular drainage, and/or aggressive management of vasospasm.

The complete CT protocol, therefore, increasingly includes not only plain CT but also optional perfusion CT and CT angiography, which can be performed as a single CT examination with separate contrast material boluses. The examination is frequently completed and analyzed within 15 min in a real clinical setting using new-generation multi-detector CT scanners. In addition, correlation of all the imaging findings with the vascular anatomy and clinical findings can be crucial in diagnosis of hyperacute stroke [131, 132]. Nevertheless, the use of perfusion CT and CT angiography to achieve a more precise vascular diagnosis should be consulted with the neurologist because these studies expose patients to the risks of radiation, as well as risks associated with contrast-induced nephropathy and allergic reaction, which can lead to death. Furthermore, the risk of contrast on blood-brain barrier permeabil-

ity has unknown effects on bleeding risks and the worsening of vasogenic edema [133–137].

A typical protocol of plain non-enhanced CT protocol on 32 detectors CT scanner includes axial scanning at gantry angle along meatus-orbital plane, with section thickness 5 mm, rotation time 0.8 s, 120 kVp, and 250 mA [138, 139].

Magnetic Resonance Imaging (MRI)

Multimodal MRI has been proposed as an alternative to CT imaging in the emergency stroke setting. A prospective, multicenter study in the general population showed that MRI, especially with the use of gradient-echo sequences, may be as accurate as CT for the detection of acute hemorrhage in patients presenting with acute focal stroke symptoms and is more accurate than CT for the detection of chronic intracerebral hemorrhage [140–142]. The accuracy of MRI relative to CT for the detection of acute intracerebral hemorrhage, however, has not been demonstrated in patients with SCD. If the sequences of the MRI of the brain are optimized to detect cerebral hemorrhage and the MR study can be done promptly, an MRI of the brain can be preferred over CT to detect both hemorrhage and cerebral infarct [140, 143]. Further, using an MRI/DWI scan can determine whether the ischemic event occurred within the last 10 days [144–146]. In a patient with focal neurologic deficit, distinguishing acute cerebral infarcts from old infarcts with an MRI is clinically relevant because the decision to perform acute exchange transfusion may require central line placement, multiple units of blood, and other associated risks, including the possibility of a stroke [115, 147]. In rare instances, children and adults with focal neurologic deficits may have a negative MRI/DWI scan, specifically negative DWIs, within 24 h of the onset of symptoms [148, 149]. If MRI changes are absent, other diagnostic considerations include hemiplegic migraine, Todd's paralysis following seizures, PRES, and central sinus venous thrombosis (CSVT) [68, 150–152]. If a hemorrhagic stroke is identified, magnetic resonance venography (MRV) should be added to the initial MRI as 10% of hemorrhages in children are due to CVST [153].

Considering MRI as the sole modality to evaluate acute stroke patients, the MR protocols should include T1, T2, T2*, or gradient-echo (GE), fluid-attenuated inversion recovery, contrast-enhanced, diffusion-weighted, and perfusion-weighted images, as well as MRV and MR angiography [154]. The appearance of parenchymal hemorrhage on MR is primarily affected by the age of hematoma, as well as the type of MR contrast used. The substrate responsible for early hemorrhage identification on MR scan is deoxyhemoglobin, a blood degradation product with paramagnetic properties, because of its unpaired electrons. On GE images, a few areas of hyperintensity can be detected in the lesion core, and, of these, most are usually surrounded by hypointense boundaries. Hyperintense signals are commonly found bordering the central lesion on T2-weighted and GE images, whereas a hypointense signal is commonly observed on T1-weighted images, thereby indicating perifocal vasogenic edema [154]. There is strong evidence supporting the diagnostic accuracy of MRI/DWI in the hyperacute setting [155, 156], even after only 20 min of symptom onset [157]. A randomized trial investigating the role of MR in detecting ICH has reported that hyperacute ICH is detectable with excellent accuracy even when the raters had only limited experience [140]. Moreover, GE is as sensitive as NCCT in the detection of acute ICH, whereas a complete MR in patients with acute stroke has higher sensitivities for IS (diffusion-weighted imaging sequences) and chronic hemorrhage [142, 158]. However, in the case of minor bleeding, GE MR may not be sufficient to distinguish acute bleeding from chronic bleeding (i.e., microbleeds [MBs]), and for this, NCCT should be performed [142].

MRI is also a neuroradiological tool for distinguishing between hemorrhagic transformation and primary ICH. In fact, most HTs are smaller than their fields of ischemic infarct; thus, MRI can provide information on nonhemorrhagic regions and evidence whether blood is within the larger ischemic infarct [159]. A primary hematoma tends to be round and have a larger surrounding edema than would be seen on IS. Furthermore, hematomas do not necessarily

respect vascular territories [159]. In case of hemorrhagic transformation of IS, MR angiography can identify the location of vascular occlusion.

MRI is sufficiently accurate in detecting underlying causes of secondary hemorrhages, including vascular malformations, tumors, and cerebral vein thrombosis, as well as a high diagnostic yield for young patients having lobar ICH and no history of hypertension [160]. Thus, MR is a sensitive tool for detecting cerebral venous thrombosis in the acute, subacute, and chronic phases [161]. Contrast-enhanced MR venography is able to show the thrombosed segment of the venous sinus and is generally well correlated with conventional angiographic findings [162]. It also assists in distinguishing anatomic variants, such as a hypoplastic sinus, from cerebral venous thrombosis [163].

Also, MRI is a sensitive and specific neuroradiologic modality for detecting cavernomas, the abnormal capillary-like vessels with intermingled connective tissue whose rupture can lead to ICH [164]. Cavernoma has a hyperintense popcorn ball-like appearance at T2-weighted imaging. The central component, hyperintense, indicates subrecent bleeding; the hypointense halo consists of hemosiderin and is the outcome of remote bleeding.

With MRI, it is possible to detect previously existing and clinically silent cerebral infarcts and microbleeds (MBs) that are not detectable on CT [165].

What Are the Imaging Modalities of Choice to Detect Brain Ischemia and Determine Tissue Viability?

Summary of Evidence Stroke centers highlight the importance of timely neuroimaging to establish the diagnosis of ischemic stroke and rule out intracranial hemorrhage in emergency care settings. A primary stroke center should have the ability to perform CT of the head within 25 min after admission and the availability of this imaging modality 24 h a day, 7 days a week. The high frequency of stroke mimics in children makes confirmation of stroke especially important. A

CT scan, however, will often miss early signs of ischemic infarction and thus is not sufficient for ruling out ischemic stroke in a child with SCD (insufficient evidence). MRI with diffusion-weighted imaging (DWI), along with magnetic resonance angiography (MRA) of the head and neck, should be performed in all children with SCD and suspected acute ischemic stroke (moderate evidence). Some centers do not have MRI capability 24 h a day, 7 days a week; in these instances, head CT to rule out hemorrhage, admission for observation and neuroprotection, and treatment is indicated until MRI can be performed (moderate evidence).

Compared with CT, advantages of MRI include the ability to distinguish acute, small cortical, small deep, and posterior fossa infarcts; the ability to distinguish acute from chronic ischemia; identification of subclinical satellite ischemic lesions that provide information on stroke mechanism; the avoidance of exposure to ionizing radiation; and greater spatial resolution (moderate evidence). Limitations of MRI in the acute setting including higher cost; relatively limited availability of the test; relatively long duration of the test; increased vulnerability to motion artifact, especially in children, who tend to remain motionless; and patient's contraindications such as claustrophobia, cardiac pacemakers, patient confusion, or metal implants may obviate the ability to obtain a good quality MR study.

Supporting Evidence

CT

CT is relatively insensitive in detecting acute and small cortical or subcortical infarctions, especially in the posterior fossa [166]. Despite these limitations, its widespread immediate availability, relative ease of interpretation, and acquisition speed make CT the most common modality used in acute ischemic stroke imaging.

A sign of cerebral ischemia within the first few hours after symptom onset on CT is loss of gray-white differentiation [167–171]. This sign may manifest as loss of distinction among the nuclei of the basal ganglia (lenticular obscuration) or as a blending of the densities of the cor-

tex and underlying white matter in the insula (insular ribbon sign) [171] and over the convexities (cortical ribbon sign). Another sign of cerebral ischemia is swelling of the gyri that produces sulcal effacement. The more rapidly these signs become evident, the more profound is the degree of ischemia. However, the ability of observers to detect these early infarct signs on CT is quite variable and occurs in $\leq 67\%$ of cases imaged within 3 h. Detection is influenced by the size of the infarct, severity of ischemia, and the time between symptom onset and imaging [172, 173].

Another useful CT sign is that of increased density within the occluded artery, such as the hyperdense middle cerebral artery (MCA) sign, indicative of large-vessel occlusion [174]. The hyperdense MCA sign, however, is seen in only one third to one half of cases of angiographically proven thromboses [175, 176]; hence, it is an appropriate indicator of thrombus when present. Another CT sign is the hyperdense MCA “dot” sign [177] that represents a clot within a branch of the MCA [178]. The hyperdense basilar artery sign has been described with similar implications as the hyperdense MCA sign [179, 180].

MRI

Diffusion-weighted imaging (DWI) has emerged as the most sensitive and specific imaging technique for acute infarct, far better than NECT or any other MRI sequence, whereas standard MRI sequences (T1 weighted, T2 weighted, fluid-attenuated inversion recovery [FLAIR]) are relatively insensitive to the changes of acute ischemia [181]. DWI has a high sensitivity (88–100%) and specificity (95–100%) for detecting infarcted regions within minutes of symptom onset [182–189]. DWI allows identification of the lesion size, site, and age. DWI can detect relatively small cortical lesions and small deep or subcortical lesions, including those in the brainstem or cerebellum, areas often poorly or not visualized with standard MRI sequences and NECT scan techniques [190–193]. DWI can identify subclinical satellite ischemic lesions that provide information on stroke mechanism [185, 187, 194–206]. There are a few articles describing negative DWI studies when cerebral perfusion is decreased

enough to produce infarction [207, 208] and the reversal, partial or complete, of DWI abnormalities with restoration of perfusion [209]. Thus, early after ischemia onset, the visible diffusion lesion will include both regions of irreversible infarction with more severe apparent diffusion coefficient changes and regions of salvageable penumbra with less severe apparent diffusion coefficient changes.

The *artery susceptibility sign* is the MR correlate of the hyperdense MCA seen on NCCT. A direct comparison of NCCT and MRI in patients with occlusion of the proximal MCA found that 54% of patients demonstrated this sign on NCCT, whereas 82% of the same patients had clot demonstrated on MRI using a gradient-echo sequence [176]. Vascular hyperintensities on fluid-attenuated inversion recovery sequences can indicate slow-flowing blood passing through leptomeningeal collaterals [210]. Conventional MRI is more sensitive than standard NCCT in identifying both new and preexisting ischemic lesions in patients with 24 h time-defined TIAs [211–227]. DWI-positive lesions tend to be smaller and multiple in TIA patients [166]. There does not appear to be a predilection for cortical or subcortical regions or particular vascular territories. Recently, several studies have demonstrated that DWI positivity in TIA patients is associated with a higher risk of recurrent ischemic events [228–230].

Perfusion CT and MRI

Information about the nature and severity of the ischemic insult may be just as important as the “time” of the ischemic event for predicting outcome and making therapeutic judgments. Ischemic, potentially salvageable “penumbral” tissue is an ideal target for reperfusion and neuroprotective strategies but requires proper patient selection [231–239]. However, in the acute stroke setting, there is a trade-off between the increased information provided by perfusion imaging and the increased time needed to acquire additional imaging sequences. Brain perfusion imaging provides information about regional cerebral hemodynamics in the form of such parameters as cerebral blood flow, cerebral blood volume, and

mean transit time. Perfusion CT and perfusion-weighted MRI have been widely incorporated into acute multimodal imaging protocols. Combined with parenchymal imaging, both permit delineation of the ischemic penumbra [221, 223–225, 240–244]. Perfusion imaging can also indicate areas that are severely and probably irretrievably infarcted. A current technical challenge is that methods for processing of perfusion data to derive perfusion parameters vary, and the most biologically salient perfusion parameters and thresholds for acute decision making have not been fully defined [225]. On MRI, the ischemic penumbra is roughly indexed as the area of perfusion-weighted imaging–DWI mismatch [185, 212, 214, 222]. On perfusion CT imaging, the penumbra is indexed as the area of mean transit time–cerebral blood volume mismatch [211, 218, 220, 226]. “Core” ischemia can be defined accurately by perfusion CT depending on equipment and programming. Various studies have used different hemodynamic parameters, such as mean transit time, cerebral blood volume, and cerebral blood flow [245–264], different thresholds for determining hemodynamic abnormality (e.g., degree of reduction in cerebral blood volume and absolute versus relative threshold), and different thresholds for the amount of penumbral tissue that warrants treatment (e.g., 20, 100, or 200% the size of the infarct core) [215, 221, 223, 224, 242–244].

Advantages of the multimodal CT approach over MRI include wider availability of emergency CT imaging, more rapid imaging, and fewer contraindications to CT versus MRI [265–267]. Perfusion CT parameters of cerebral blood volume, cerebral blood flow, and mean transit time can be more easily quantified than their perfusion-weighted MRI counterparts, owing in part to the linear relationship between iodinated CT contrast concentration and resulting CT image density, a relationship that does not hold for gadolinium concentration versus MRI signal intensity. Disadvantages of the CT approach over MRI include the use of ionizing radiation and iodinated contrast, which carries a small risk of nephrotoxicity. Another disadvantage of perfusion CT is limited brain coverage, typically a

4-cm-thick slab per contrast bolus [268–271]. The latest generations of the 256- and 320-slice CT scanners afford whole-brain coverage but are limited in availability.

The major advantages of perfusion MRI over perfusion CT include its inclusion in a package of imaging sequences that effectively evaluate many aspects of the parenchyma, including the presence of infarction with DWI and the avoidance of ionizing radiation. Of note, the whole-brain coverage offered by perfusion MRI comes at the cost of a limited spatial resolution (matrix size or interslice gap) or temporal resolution. Disadvantages of perfusion MRI include limited availability in emergency settings, duration of the study, and patient's contraindications. Gadolinium reactions are uncommon but can be dangerous [267, 272]. Arterial spin labeling (ASL MRI) is a relatively new MRI method that assesses brain perfusion without the need to inject gadolinium contrast material but is not yet widely available [273]. This technique allows quantification of regional CBF using magnetically labeled water molecules in arterial blood, without the need for exogenous agents [274, 275].

There is growing evidence that studying brain perfusion in SCD may provide more insight into the effect of microcirculatory abnormalities, which are typically invisible to MRI of the brain and MRA of the intracranial arteries, on brain function [65]. These apparently paradoxical results may be explained based on brain injury secondary to microcirculatory vaso-occlusion (direct correlation) and brain injury secondary to exhaustion of cerebrovascular reserve (inverse correlation). The ASL MRI studies were performed in stable children with SCD and controls showing substantial differences in perfusion; hence, the interpretation of perfusion data in patients with SCD should include disease-specific pathophysiological CBF disturbances (hyperemia) [65, 276, 277].

Nuclear Imaging: PET and SPECT

PET and SPECT are indicated if CT and MRI are negative in patients with clinical stroke to detect the neuronal tissue viability by using radioactive tracers to indicate glucose metabolism 2-deoxy-2

[18F] fluoro-D-glucose (FDG) and evaluate microvascular perfusion ([15O]H₂O) [278, 279] (Limited Evidence). PET studies [278–280] that have been done in patients with SCD have shown a variety of abnormalities including hypometabolism in frontal areas of the brain and areas of low perfusion that appear normal on MRI [281]. The study of Powars et al. [279] suggested that few patients with SCD have normal PET studies and that areas of hypometabolism in brain regions with normal MR appearance are not uncommon. The authors suggest that PET could be used to select patients for treatment as four patients showed improvement in metabolism and perfusion with transfusion treatment. The most powerful predictor of ischemia in other applications of PET is an increased oxygen extraction fraction, but this application, as well as metabolism measurements, remains to be established in children with SCD. The application of PET and SPECT in emergency settings is limited. PET and SPECT imaging, additionally to MRI, identified abnormalities in children with SCD and particularly contributed to the identification of higher number and more extensive ischemic lesions, often bihemispheric. PET is considered useful to evaluate metabolic improvement after therapeutic interventions; however, correlation of PET abnormalities to subsequent stroke or progressive neurologic dysfunction requires further study [278, 279, 282].

SPECT was used to estimate cerebrovascular reserve, which can be an independent variable to determine cerebrovascular status in patients with SCD and potentially would provide insight into tissue at risk of infarction; however, there is no sufficient evidence to justify the use of this method in emergency settings [283].

What Is the Role of Neuroimaging in Patients with SCD and Symptoms of Recurrent Stroke?

Summary of Evidence Recurrent stroke is observed in children and adults with SCD despite proper regimen of transfusion therapy. Arterial stenosis is the main risk factor for recurrent

stroke. There is very limited data on emergency neuroimaging of patients with SCD and recurrent stroke. NCCT is the emergency modality of choice to search for an acute hemorrhage; however, it can also be detected by MRI (moderate evidence). Early MRA also gives the opportunity to noninvasively evaluate intracranial and extracranial vasculature. MRI with MR angiography, MR venography, and diffusion-weighted imaging is the preferred modality for evaluating ischemic recurrent stroke and eliminating diagnosis of dural cerebral sinus venous thrombosis (CSVT) and large artery dissection as the etiology of the event (insufficient evidence). CSVT is a less common neurologic complication in SCD when compared with ischemic strokes. Despite the low frequency, detecting the presence of CSVT is important because its presence may alter the treatment strategy. Children and adults with SCD and CSVT can present with symptoms that mimic a stroke, such as seizures, coma, cranial nerve palsies, headaches, nausea, and vomiting. MRV can be included in initial imaging study because it only adds a maximum of 7 min to the total time of an MRI study (insufficient evidence). MRI techniques that include T1, T2, FLAIR, diffusion imaging, and susceptibility imaging and MRA protocols that include 3D time-of-flight techniques and reconstruction provide accurate, non-invasive, high-quality images of the cerebral vasculature. Functional imaging techniques, such as PET or single-photon emission computed tomography, are being studied in pediatric patients with SCD as they may be able to detect perfusion deficits in subacute settings predicting the development of infarcts (insufficient evidence).

Supporting Evidence

CT

The multifactorious symptoms and the difficulties in diagnosis point to the importance of neuroimaging not only for diagnostic purposes but also for evaluation of etiology and outcome. Computed tomography has the advantage of being readily available in emergency settings but has the disadvantage of missing out on early, small, or infratentorial ischemia [139, 158, 279].

MRI/MRA

MRI of the brain is the preferred strategy over a brain CT scan to detect both hemorrhage and recurrent cerebral infarct [140, 143]. Further, using an MRI/DWI scan can determine whether the ischemic event occurred within the last 10 days [144, 145, 284]. In a patient with focal neurologic deficit, distinguishing acute cerebral infarcts from old infarcts with an MRI is clinically relevant because the decision to perform acute exchange transfusion may require central line placement, multiple units of blood, and other associated risks, including the possibility of a stroke [285]. In rare instances, children and adults with focal neurologic deficits may have a negative MRI/DWI scan, specifically negative DWIs, within 24 h of the onset of symptoms [148, 149]. If MRI changes are absent, other diagnostic considerations include clinical symptoms [68, 150, 152] and presence of CSVT [151, 286]. To decrease the likelihood of failing to diagnose CSVT, an MRV with the initial MRI can be recommended.

Assessment of intra- and extracranial vasculature is important in patients with recurrent stroke in view of recent data showing that 53% of children with arterial ischemic stroke show arteriopathies [287]. Inclusion of the neck vessels for imaging is also recommended, as 25% of the children show lesions of cervical vessels [246]. Best sequences for detection of dissections are a combination of (contrast-enhanced) MRA and nonfat- and fat-suppressed T1-weighted images of cervicocranial vessels [288]. In view of the frequency of arteriopathy, CT angiography might be equal to MR angiography, but both are known to miss the information from fat-suppressed images [289, 290]. Although conventional angiography is still the gold standard for detecting dissections and vasculitis, it is rarely performed in childhood stroke and has its indication for specific questions or in cases of endovascular treatments.

MRI techniques that include T1, T2, FLAIR, diffusion imaging, and susceptibility imaging and MRA protocols that include 3D time-of-flight techniques and reconstruction provide accurate, noninvasive, high-quality images of the cerebral vasculature [291].

Nuclear Imaging: PET and SPECT

Functional imaging techniques, such as PET or single-photon emission computed tomography, are being studied in pediatric patients with SCD and recurrent stroke as they may be able to detect perfusion deficits in subacute settings predicting the development of further infarcts [220, 279, 282].

What Is the Role of Vascular Investigations?

Summary of Evidence Cerebrovascular imaging is an important aspect of the workup of patients with SCD and stroke because the majority of large ischemic strokes are caused by severe stenosis and/or occlusion in ≥ 1 -mm-large vessel. Noninvasive intracranial vascular imaging greatly improves the ability to establish as soon as possible the mechanism of ischemia and make appropriate clinical decisions in emergency settings (moderate evidence). Large-vessel occlusion can be suspected on NCCT as described above (hyperdense MCA sign, etc.). Adding CTA to NCCT can allow for rapid evaluation of the intracranial and extracranial vasculature and therefore provide potentially important information about the presence of vessel occlusions or stenoses (insufficient evidence). Also, MRA can be performed in combination with brain MRI in the setting of acute stroke to guide therapeutic decision making. However, it cannot reliably identify distal or branch occlusions (insufficient evidence). DSA remains the “gold standard” for the detection of many types of cerebrovascular lesions because the resolution, sensitivity, and specificity of DSA exceed those of the noninvasive techniques (moderate evidence). However, if noninvasive imaging provides firm diagnostic findings, DSA may not be required for solely diagnostic purposes (limited evidence).

It is also important to evaluate the *extracranial vasculature* in patients with SCD and symptoms of acute cerebral ischemia to exclude significant stenoses, thrombosis, and arterial dissection. The carotid and vertebral vessels can be imaged by several noninvasive techniques, such as CTA, MRA, ultrasound, and DSA. Although each tech-

nique has certain advantages in specific clinical situations, the noninvasive techniques show general agreement to DSA in 85–90% of cases (moderate evidence). For evaluation of the degree of stenosis and for determination of patient eligibility for interventional procedures, however, DSA is the “gold standard” imaging modality (moderate evidence).

DSA and multimodal MRI are complementary in detection of vascular dissections. A very high-grade stenosis (“string sign”) is most accurately detected by DSA, followed closely by CTA and contrast-enhanced MRA (limited evidence). Ultrasound techniques are seldom used to evaluate carotid arteries in emergency settings in patients with SCD (insufficient evidence).

Supporting Evidence

CT Angiography (CTA)

CTA allows for rapid evaluation of the intracranial and extracranial vasculature in acute, subacute, and chronic stroke settings and can therefore provide potentially important information about the presence of vessel occlusions or stenoses [245, 268]. The accuracy of CTA for the evaluation of large-vessel intracranial stenoses and occlusions is very high [246–249], and in some cases, its overall accuracy approaches that of digital subtraction angiography (DSA) [246, 250]. The sensitivity and specificity of CTA for the detection of intracranial occlusions range between 92 and 100% and between 82 and 100%, respectively, with a positive predictive value of 91–100% [251, 252, 268, 269]. Because CTA provides a static image of vascular anatomy, it is inferior to DSA for the demonstration of flow rates and direction [292].

Direct comparisons of CTA source images (CTA-SI) and MRI/DWI have demonstrated very similar sensitivity of these two techniques for detecting ischemic regions, with DWI being better at demonstrating smaller abnormalities (reversible or irreversible) and those in the brainstem and posterior fossa [237, 293]. Improved stroke detection explains the greater predictive value for final infarct size by use of CTA-SI [292]. For early strokes (<3 h), CTA-SI has a

greater sensitivity to ischemic changes and more accurately identifies the volume of tissue that will ultimately become infarcted than NCCT alone [235, 292]. CTA-SI is more an estimate of cerebral blood volume than the expression of cytotoxic edema seen on NCCT. CTA requires administration of intravenous contrast agent and, thus, is associated with risk of nephrotoxicity and other adverse reactions. The utility of CTA in children with SCD and stroke therefore remains to be established.

CTA is a sensitive, specific, and accurate technique for imaging the *extracranial vasculature*. CTA is clearly superior to carotid ultrasound for differentiating a carotid occlusion from a very high-grade stenosis [294] and has been reported to have an excellent (100%) negative predictive value for excluding >70% of stenoses compared with catheter angiography and is thereby functioning well as a screening test [295]. A large meta-analysis found it to have a sensitivity of >90% and specificity of >95% for detecting significant lesions compared with DSA [296–298].

MR Angiography (MRA)

MRA is performed in combination with brain MRI in the setting of acute stroke to guide therapeutic decision making [253]. There are several different MRA techniques that are used for imaging intracranial vessels. They include two-dimensional time of flight (TOF), three-dimensional TOF, multiple overlapping thin-slab acquisition, and contrast-enhanced MRA [254]. Intracranial MRA with non-enhanced TOF techniques has a sensitivity ranging from 60 to 85% for stenoses and from 80 to 90% for occlusions compared with CTA or DSA [246, 251]. Typically, TOF MRA is useful in identifying acute proximal large-vessel occlusions but cannot reliably identify distal or branch occlusions [255]. In a study of 22 SCD patients, an MRA abnormality in a long segment (6 mm) with reduced distal flow correlated with subclinical infarction, while short focal areas of abnormal MRA most commonly in branching regions showed no associated MRI infarction [299].

More recent data from adults showed that MRA has 70–86% sensitivity in detecting intra-

cranial stenosis on DSA, while the sensitivity of CTA is 98% [246, 300, 301]. MRA does not need a contrast agent, while CTA requires intravenous contrast, and its toxicity can exacerbate symptoms in acute stroke [302]. MR spectroscopy can distinguish an ischemic lesion from other non-ischemic changes, but the utility of MRS in acute stroke is limited in children with SCD.

Two-dimensional and three-dimensional TOF MRA used for the detection of *extracranial* carotid disease (threshold stenosis typically 70%) showed a mean sensitivity of 93% and a mean specificity of 88% [254]. Contrast-enhanced MRA is more accurate than non-enhanced TOF techniques, with specificities and sensitivities of 86–97% and 62–91%, respectively, compared with DSA [303–305]. Craniocervical arterial dissections of the carotid and vertebral arteries can often be detected with MRA [306–308]. Contrast-enhanced MRA may improve the detection of arterial dissections [309, 310], although there are few large, prospective studies to prove its accuracy versus catheter angiography. Non-enhanced T1-weighted MRI with fat-saturation techniques can frequently depict a subacute hematoma within the wall of an artery, which is highly suggestive of a recent dissection [309, 310]. However, an acute intramural hematoma may not be well visualized on fat-saturated T1-weighted MRI until the blood is metabolized to methemoglobin, which may require a few days after ictus. MRA is also helpful for detecting other less common causes of ischemic stroke or TIAs such as arterial dissection, fibromuscular dysplasia, venous thrombosis, and some cases of vasculitis [311].

Digital Subtraction Angiography (DSA)

DSA remains the “gold standard” for the detection of many types of cerebrovascular lesions and diseases. For most types of cerebrovascular disease, the resolution, sensitivity, and specificity of DSA exceed those of the noninvasive techniques, including for arterial stenoses [312–314]. However, if noninvasive imaging provides firm diagnostic findings, cerebral angiography may not be required for solely diagnostic purposes.

Emergency intracerebral evaluation of large-vessel occlusion in stroke can be performed with CTA or MRA, especially because it requires only additional 2–4 min during initial stroke evaluation (in a multimodal evaluation process), and can obviate the need for catheter angiography.

DSA is not part of the initial acute ischemic stroke imaging in children with SCD and is performed when endovascular therapy is anticipated, usually in case of hemorrhagic stroke. DSA is accurate in detecting intracranial vascular abnormalities (AVM, aneurysm, dissection, occlusion) and quantifying arterial narrowing.

DSA is an invasive test and can cause serious complications such as stroke and death, although recent advances in high-resolution rapid-sequence digital subtraction imaging, digital image reconstruction with three-dimensional techniques, catheter technology, and nonionic contrast media have made cervicocerebral angiography easier and safer. Most large series have reported rates of stroke or death in <1% of DSA procedures [315–317].

DSA remains the most informative technique for imaging the *cervical carotid and vertebral arteries*, particularly when making decisions about invasive therapies. In addition to providing specific information about a vascular lesion, DSA can provide valuable information about collateral flow, perfusion status, and other occult vascular lesions that may affect patient management [312–314]. Catheter angiography can be particularly useful in cases of carotid dissection, both to image the dissection and to delineate the collateral supply to the brain.

Ultrasound Techniques: Transcranial Doppler (TCD), Transcranial Color-Coded Doppler (TCCD), and Carotid Ultrasound

There are two techniques of transcranial Doppler (TCD) ultrasonography—conventional TCD and color-coded duplex TCD; both have been used to detect intracranial vessel abnormalities [318–320]. TCD has been used to evaluate occlusions

and stenoses in intracranial vessels [318, 321]. TCD accuracy is less than that of CTA and MRA for steno-occlusive disease, with a sensitivity and specificity of TCD ranging from 55 to 90% and from 90 to 95%, respectively [257, 259, 261]. TCD can detect microembolic signals, which are seen with extracranial or cardiac sources of embolism [322].

The usefulness of TCD is limited in emergency settings in patients with SCD. This is also due to the long time needed to perform the study and, regarding the overall accuracy, the dependence on the experience of the technician, the interpreter, and the patient's vascular anatomy. For posterior circulation stroke, Doppler ultrasound is not helpful. In intensive care units, TCCD can be useful for detecting and monitoring of vasospasm in SCD patients with intracranial hemorrhage [323, 324].

Carotid ultrasound is a safe and inexpensive screening technique for imaging the carotid bifurcation and measuring blood velocities [325–327] but has limited usefulness in emergency settings. Doppler measures that have been correlated with angiographic stenosis include internal carotid artery peak systolic velocity and end-diastolic velocity, as well as ratios of internal carotid artery and common carotid artery peak systolic velocity [318, 328, 329]. Doppler test results and diagnostic criteria are influenced by several factors, such as the equipment, the specific laboratory, and the technologist performing the test [330, 331]. Sensitivity and specificity of carotid ultrasound for detecting lesions are less than for other modalities, in the range of 83–86% for sensitivity and 87–99% for specificity [248, 296].

Take-Home Figure

Figure 33.1 presents an algorithm for the imaging of patients with SCD and symptoms of stroke.

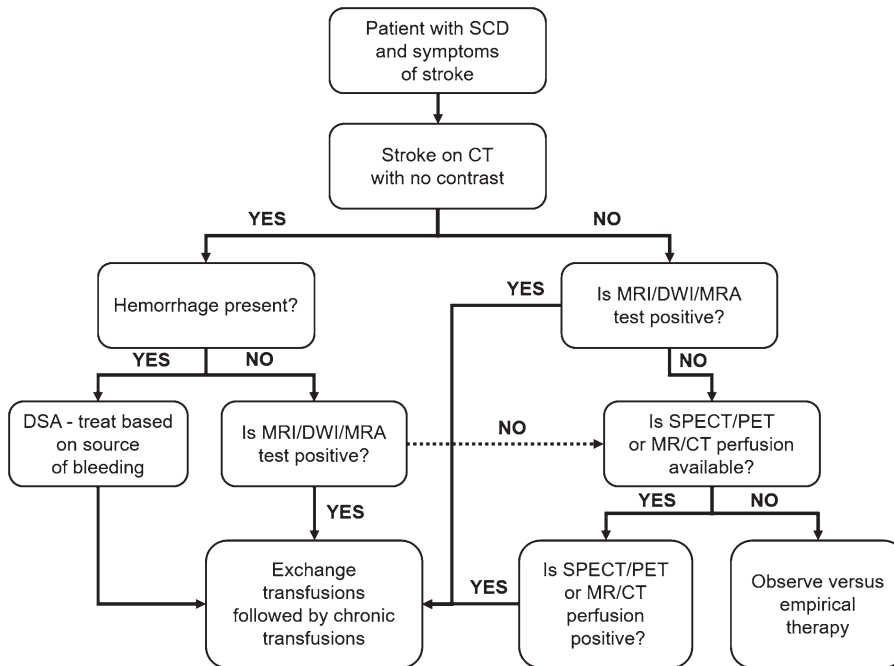


Fig. 33.1 Decision tree shows the role of neuroimaging in emergency management of a patient with sickle cell disease (SCD) and neurological symptoms of stroke. *CT* Computed tomography, *MRI* magnetic resonance imaging,

DWI diffusion-weighted imaging, *MRA* magnetic resonance angiography, *SPECT* single-photon emission CT, *PET* positron emission tomography, *DSA* digital subtraction angiography

Take-Home Points

- NCCT remains the first-line imaging modality in emergency settings of patients with SCD and symptoms of stroke.
- Centers that have emergency access to MR studies increasingly use MRI as modality of choice in acute ischemic stroke; however, the duration of the study and quality of image acquisition in motionless patients, especially children with SCD, limit the utility of MRI as first-line imaging in patients with SCD and acute stroke.
- CTA, CT perfusion, and MRA/DWI MR perfusion are increasingly used in combination with standard NCCT and anatomical MRI to evaluate cerebrovasculature and neuronal tissue viability in emergency settings.
- DSA is the modality of choice in the evaluation of cerebrovasculature if emergency endovascular treatment is anticipated.
- PET and SPECT imaging are not used in emergency settings and are employed to eluci-

date mechanism of ischemia in patients with symptoms of stroke and negative CT and MR findings.

- Ultrasound techniques, including transcranial Doppler and carotid Doppler ultrasound, are not used in emergency settings in patients with SCD and stroke.

Imaging Case Studies

Case 1

Figure 33.2a–c presents a patient with hemorrhagic stroke and a patient with ischemic stroke.

Case 2

Figure 33.3a–e presents imaging comparing ischemic versus hemorrhagic stroke.

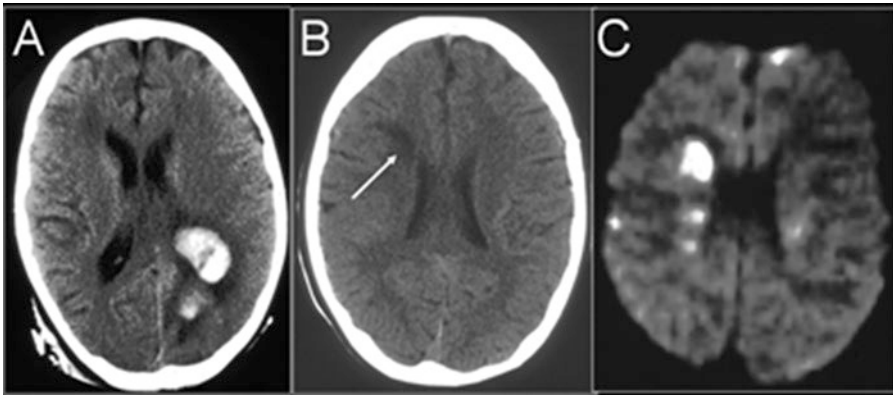


Fig. 33.2 Imaging in ischemic versus hemorrhagic stroke in a patient with sickle cell disease. (a) Patient with hemorrhagic stroke and (b, c) patient with ischemic stroke. (a) shows intraparenchymal high-density hematoma on CT image. (b) CT image shows area of slightly lower periventricular density on the right (*arrow*) suggesting ischemic

lesion. (c) DWI image shows clearly in the same patient as on (b) several ischemic high-intensity infarcts. CT is the imaging modality of choice for detection of hemorrhagic stroke but is not very good for detection of ischemic stroke

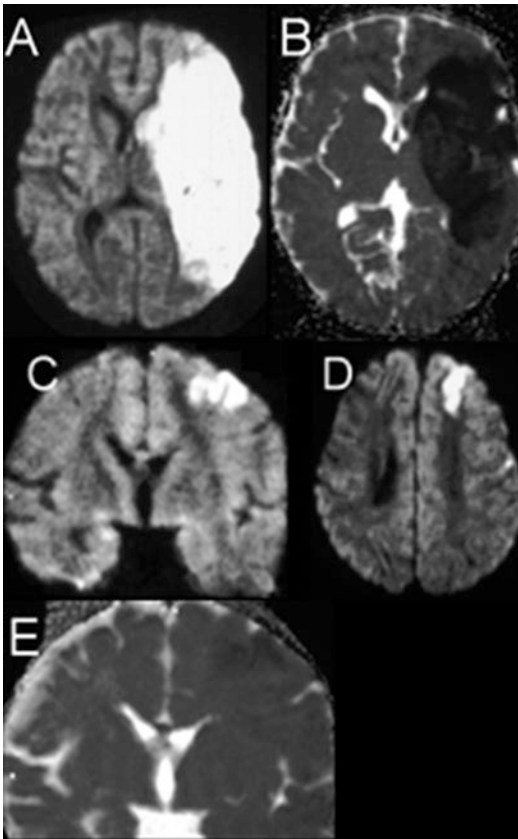


Fig. 33.3 Imaging in ischemic versus hemorrhagic stroke. MRI (DWI) is the imaging modality of choice for territorial and interterritorial ischemic stroke. (a, b) show DWI axial images of hemispheric ischemic stroke. (c, d, and e) show DWI images of focal infarcts

Case 3

Figure 33.4a–d presents types of “silent” infarcts in patients with SCD.

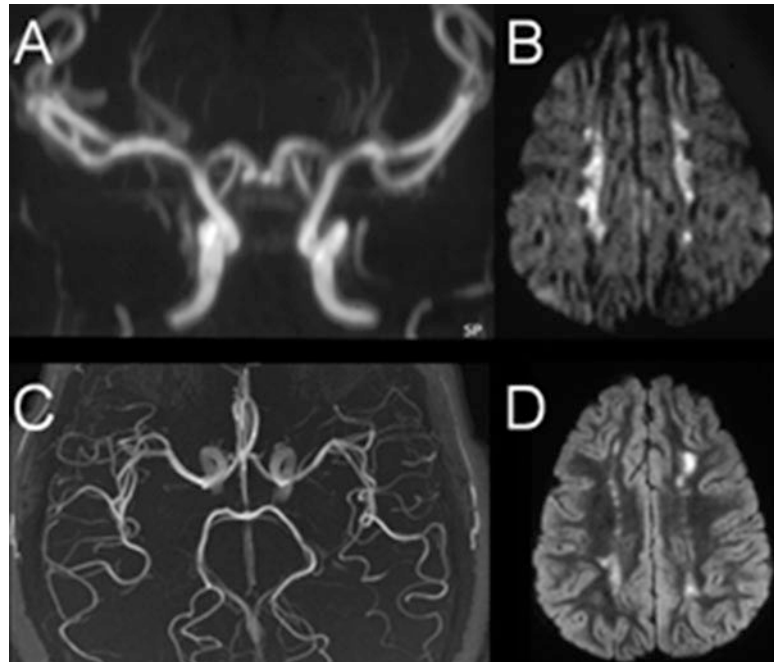
Suggested Imaging Protocols

Anatomical MRI of the Brain

Gradient-echo-based three-plane localizer followed by whole-brain MRI with sagittal three-dimensional isotropic T2-weighted fast spin-echo, fast FLAIR (fluid-attenuated inversion on recovery), and magnetization prepared isotropic high-resolution T1-weighted fast gradient-echo (MPRAGE). Three-dimensional isotropic MPRAGE provides exquisite gray-white matter contrast and will be used to facilitate registration of inherently lower-resolution images, such as perfusion MRI, to the brain atlases. Total acquisition time is approximately 16 min.

Parameters for the 3D isotropic T2-weighted sequence are TR, 3200 ms; TE_{eff} , 444 ms; 1 mm slice thickness with no gap; field of view, $256 \times 256 \text{ mm}^2$; matrix, 256×256 ; and number of slices, 192, with resultant voxel size of $1.0 \times 1.0 \times 1.0 \text{ mm}^3$. Parameters for the 3D iso-

Fig. 33.4 Types of “silent” infarcts in patients with SCD. (a, b) Infarcts showed on DWI image (b) associated with abnormalities on image (a) from MRA (prevalence 85%). (c, d) Infarcts not associated with abnormalities on MRA (prevalence 15%), considered microvascular disease



tropic fast FLAIR sequence are TR, 6000 ms; TE_{eff} , 355 ms; TI, 1800 ms; 1 mm slice thickness with no gap; field of view, $256 \times 256 \text{ mm}^2$; matrix, 256×256 ; and number of slices, 144, with resultant voxel size of $1.0 \times 1.0 \times 1.0 \text{ mm}^3$. Parameters for the 3D magnetization prepared high-resolution T1-weighted fast gradient-echo sequence are TR, 1760 ms; TE, 3.87 ms; field of view, $256 \times 256 \text{ mm}^2$; matrix, 256×256 ; and number of slices, 192, with resultant voxel size of $1.0 \times 1.0 \times 1.0 \text{ mm}^3$. Note all 3D sequences are obtained with a parallel imaging factor of 2 (iPAT = 2).

MR Angiography

Time-of-flight (TOF) three-dimensional gradient-echo sequence covering the intracranial internal carotids arteries, vertebrobasilar arteries, and the circle of Willis should be performed in the axial plane. Acquisition time is approximately 6.5 min.

Parameters are TR, 28 ms; TE, 3.58 ms; flip angle, 20° ; 100 0.9-mm-thick partitions; field of view, 220 mm; and matrix, 224×512 , with resultant in-plane resolution of $0.40 \times 0.80 \text{ mm}$. Off-

resonance magnetization transfer pre-pulses and ramped RF pulses should be used to improve contrast-to-noise ratio between the vessel lumen and stationary tissue.

Diffusion Brain MRI

Diffusion-weighted MRI is used to detect and differentiate acute silent white matter infarcts from chronic ones. It should be performed in the axial plane using a single-shot spin-echo echo-planar readout (TR, 5800 ms; TE, 93 ms), diffusion-sensitizing gradients ($b\text{-value} = 1000 \text{ s/mm}^2$ will be applied in three orthogonal directions (D-WIx, D-WIy, D-WIz), and a reference image with low diffusion weighting ($b\text{-value} = 33 \text{ s/mm}^2$ will also be recorded). The in-plane resolution for DWI is $2.25 \times 0.90 \text{ mm}^2$, and the slice thickness is 5.0 mm (1 mm gap).

Perfusion Brain MRI

Brain MR perfusion imaging should be performed using the continuous arterial spin label-

ing (CASL) method originally described by Alsop et al. [275]. To help with the image registration process, slice orientation will be parallel to the anterior commissure—posterior commissure (AC-PC) plane. Fifty pairs of labeled and control volumes are acquired consecutively to enhance signal-to-noise ratio for a total acquisition time of 10 min.

Perfusion sensitization is obtained using a single send-receive head coil. A 2.4-s-long RF pulse is applied simultaneously with gradient at the level of the cervicomedullary junction to achieve flow-driven, adiabatic electromagnetic labeling of arterial spins in both carotid and vertebral arteries. The amplitude of the RF pulse is $3.5\mu\text{T}$ and the gradient strength is 2.5 mT/m. To control for magnetization transfer (MT) effects, a reference image is acquired with sinusoidal modulation of the RF envelope with a frequency of 250 Hz, thereby achieving the simultaneous inversion of two parallel planes leading to a net zero degree on the labeled arterial water spins. This method allows for control of MT artifacts throughout the entire brain, thus enabling to perform whole-brain perfusion imaging. In order to reduce the sensitivity of the method for arterial transit time, the acquisition is delayed by 1.2 s after the labeling pre-pulse. Flow-compensated single-shot spin-echo echo-planar (TR, 5000 ms; TE, 36 ms) readout is used to obtain 15 8-mm-thick axial slices separated by a 1 mm gap with an in-plane resolution of $3.75 \times 3.75 \text{ mm}^2$. The slices are acquired in ascending order to reduce the remaining intravascular labeled spins by its natural crushing effect. Fifty pairs of labeled and control volumes are acquired consecutively to enhance signal-to-noise ratio.

Conventional TCD

TCD should be performed according to the STOP protocol. MCAs, terminal ICAs, ACAs, and PCAs should be insonated through transtemporal windows using a 2 MHz probe. The time-averaged maximum velocity (V_{mean}) should be

measured over several (at least three) complete cardiac cycles.

TCCD

Transcranial color Doppler imaging should include M-1 segment of MCA, A-1 segment of ACA, and P1 segment of PCA, the intracranial portion of the ICA. The angle-corrected blood flow velocities should be measured. The sample volume should be placed on the point of the highest velocity acceleration of a particular segment determined by color aliasing artifact. The peak systolic ($V_{\text{peak systolic}}$), mean (V_{mean}), and end-diastolic ($V_{\text{end-diastolic}}$) velocities should be obtained by tracing of the maximum frequency envelope of the waveform.

Future Research

Future research in this field should address the following:

- Utility of multimodal advanced MR techniques in detection of acute hemorrhagic and ischemic stroke and determination of tissue viability in emergency settings
- Utility of CT perfusion and CT angiography in patients with SCD and symptoms of stroke
- Utility of ultrasound techniques in preadmission settings
- Emergency employment of DSA for treatment of cerebrovascular causes of stroke

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Non-Accidental Injury in Infants and Children: Evidence-Based Emergency Imaging

34

Wouter A. Karst and Rick R. van Rijn

Key Points

- Child abuse is a world-wide problem and the emergency department (ED) is one of the first places where a diagnosis can be made (strong evidence).
- Child abuse is a recurrent problem, i.e. if the diagnosis is missed there is a significant risk to the child for new incidents of abuse (strong evidence).
- Certain radiological findings in young children, e.g. subdural hematoma and posterior rib fractures, are strong indicators for child abuse and should lead to additional evaluation (strong evidence).
- Timely detection of physical child abuse can prevent further harm to the child in question (strong evidence).

Definitions and Pathophysiology

The World Health Organization defines child abuse as “*Child maltreatment, sometimes referred to as child abuse and neglect, includes all forms of physical and emotional ill-treatment, sexual abuse, neglect, and exploitation that results in actual or potential harm to the child’s health, development or dignity. Within this broad definition, five sub-types can be distinguished—physical abuse; sexual abuse; neglect and negligent treatment; emotional abuse; and exploitation*” [1]. One form of physical abuse which can be encountered in the ED and may be overlooked or downplayed as being part of parenting is corporal punishment. With respect to this, UNICEF states that “*corporal punishment is any punishment in which physical force is used and intended to cause some degree of pain or discomfort, however light*” [2]. Therefore, this should be seen as a form of child abuse. The focus of this chapter is physical abuse, although sexual abuse and neglect can certainly be encountered in the emergency department.

Epidemiology

Given that not all epidemiology studies of child abuse use the same definitions, and that local and socio-economic factors play a significant role in child abuse, it is difficult to give clear figures on the

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epidemiology of child abuse. Based on a meta-analysis, reporting on a total of 9,698,801 children, Stoltenborgh et al. estimated that the prevalence of child abuse was 0.3% for studies using informants, e.g., teachers and healthcare personnel, and 22.6% for studies using self-report [3].

Several studies, with variable results, have been published on the incidence of child abuse in the emergency department. The incidence varies from 0.2%, in a Dutch general ED population study, to 8%, in a selected population of severely injured children [4, 5]. The variance in reported incidences can, besides differences in study population and definitions, also be explained by differences in screening methods [6]. A US study showed that of 16,897 ED visits, that were the result of physical child abuse, 5182 (30.7%) required admission into the hospital [7]. Estroff et al. demonstrated that the mortality rate in trauma resulting from child abuse was significantly higher compared to accidental trauma [8.9 vs. 1.4% ($p < 0.001$)] [8]. These studies show that child abuse is a serious medical problem with a potential severe outcome.

The importance of timely detection of physical child abuse has been well documented in the pediatric radiological literature. Carty and Pearce estimated that 12% of children visiting the ED with injuries due to physical abuse, which initially were not identified as such and were sent home, return later with significant injuries and a mortality rate of 12% [9]. More recently, Sieswerda et al. showed that in a population of 89 children with severe abusive head trauma in 81%, earlier signs of child abuse were present [10].

Overall Cost to Society

The costs of child abuse to society are difficult to calculate. Total costs include direct medical costs related to the presenting incident and the long-term costs of child abuse. The latter, has been shown by Felitti et al., to lead to a significant increase in social and medical problems later in adult life due to adverse childhood experiences [11, 12].

A study from the United States of America showed an estimated total cost of child abuse to be in the range of \$585 billion for 2008 [13]. This analysis included both fatal and nonfatal cases, and in the analysis, costs for childhood health care, child welfare, adult medical care, productivity loss, criminal justice, and special education were accounted for.

Goals of Imaging

In the majority of cases imaging in the ED will be performed to enable immediate medical care. However, imaging can also reveal findings which may indicate child abuse and which should lead to further investigation. All ED personnel involved in acute patient care should consider the possibility of child abuse when caring for children.

Methodology

A comprehensive Medline search (United States National Library of Medicine database) for original articles using the Pubmed search engines was performed using a combination of the following keywords and Medical Subject Headings: *Child abuse, abusive head trauma, dating, fractures, bone, abdomen, liver, spleen, bowel.*

The search was limited to English-language articles and human studies in children up to 18 years. Additional relevant articles were selected from the references of reviewed articles and published guidelines. The website of the Cardiff Child Protection Systematic Reviews—CORE INFO was used to review the latest systematic reviews in the field of child abuse [14].

Discussion of Issues

What Is the Association Between Subdural Hematoma and Abusive Head Trauma?

Summary of Evidence In very young children, the presence of a subdural hematoma (SDH),

especially of an interhemispheric SDH, is significantly suggestive of abusive head trauma (AHT) (strong evidence). So are multiple, bilateral or infratentorial SDH's (moderate evidence). In case of a subarachnoid SDH, the risk of AHT is about 50% (strong evidence). Due to the large variability in findings, dating SDH's may not be reliable (moderate evidence).

Supporting Evidence One of the most severe forms of physical child abuse is AHT. This is relatively common in childhood with an estimated incidence of 14–41 cases per 100,000 children under the age of 1 year [15]. Approximately 15–23% of these children die within days after the incident. One-third of the survivors have a good clinical outcome, one-third are mildly handicapped, and one-third become severely handicapped [16]. With respect to neuro-imaging findings, a systematic review by Maguire et al. showed that in children predominantly below 3 years, the presence of a subdural hematoma was significantly associated with AHT [17]. The odds ratio (OR), of the combined studies was 9.18 (95% confidence interval 7.12–11.83, $I^2 = 0\%$; $p < 0.00001$). The anatomical location of the SDH was also studied in this meta-analysis. The presence of interhemispheric SDH, based on seven studies, is significantly associated with abusive head trauma OR 8.03 (95% confidence interval 5.58–11.56, $I^2 = 0\%$; $p < 0.00001$). Multiple SDHs (OR of 6.01, 95% confidence interval 2.52–14.35, $I^2 = 0\%$; $p < 0.0001$), SDH along the convexity (OR 4.93, 95% confidence interval 1.25–19.42, $I^2 = 75\%$; $p = 0.02$), bilateral SDH (OR 3.36, 95% confidence interval 1.10–10.27, $I^2 = 77\%$; $p = 0.03$), and infratentorial SDH (OR 2.55, 95% confidence interval 1.06–6.13, $I^2 = 0\%$; $p = 0.047$) are also related to AHT [17]. This is, however, based on a smaller study sample (2–4 included studies. In case of a subarachnoid haemorrhage there was an equal distribution between accidental trauma and AHT (OR 1.28, 95% confidence interval 0.67–2.44, $I^2 = 77\%$; $p = 0.95$; $p = 0.45$).

Radiologists are often requested to date an SDH. The basis for this dating is found in parenchymal brain haemorrhages. Recently, a study by

Postema et al. showed a wide variability in dating as performed by Dutch neuroradiologists and paediatric radiologists [18]. Based on their findings, the authors concluded that there is a lack of uniformity among experts and that thus dating in a legal environment, e.g. a court of law, is not to be advocated. In a meta-analysis by Sieswerda et al. the authors showed a lack of evidence for dating SDH based on signal intensity or density on MRI or CT [19]. Even outcomes such as polycystic encephalomalacia, which historically have been described as an end stage finding in traumatic brain injury can be found after approximately 1 week [20, 21]. This illustrates the extreme caution that should be taken in dating SDH in AHT.

Which Skeletal Bone Injuries Are Suggestive of Physical Child Abuse?

Summary of Evidence Multiple and/or bilateral skull fractures and fracture lines crossing sutures are seen more often in child abuse than in accidental trauma (moderate evidence). In a young child with a skull fracture, child abuse cannot be excluded, and a skeletal survey should be obtained (limited evidence). Rib fractures are more commonly found in physically abused children than in accidentally injured young children (moderate evidence). Many young children with abusive head trauma also show rib fractures (strong evidence). Metaphyseal corner fractures in children up to an age of 2 years are highly specific for child abuse (strong evidence). Long bone fractures as a result of child abuse are more probable in children who are not independently mobile (moderate evidence). Dating fractures is, up to a certain level, possible for radiologists (moderate evidence).

Supporting Evidence

Skull Fractures

In children, skull fractures can be the result of accidental injuries, abusive head trauma, birth injury or underlying diseases such as osteogenesis imperfecta. For the purpose of this chapter, only the first two causes will be addressed.

Isolated skull fractures as a single presenting factor in the ED are relatively rare. Children, especially those who are starting to mobilise, tend to fall frequently, and given the limited value of a radiograph of the skull on treatment strategies, the use of radiography has been abolished in most countries. However, if a skull fracture is encountered, it is important to be aware that linear and even complex skull fractures can occur from a fall of a height of 80 cm or more [22]. This implies that, a fall from the arm of a parent/ caretaker—an often reported trauma mechanism—can certainly lead to a skull fracture. Several studies have shown that multiple and/or bilateral fractures, and fracture lines crossing sutures are seen more often in child abuse cases compared to accidental trauma (moderate evidence) [23, 24]. With the increasing quality of three-dimensional reconstructions of CT data, these are increasingly used to evaluate such cases [25].

Two publications have focussed on the value of a skeletal survey in young children presenting with an isolated skull fracture [26, 27]. Wood et al. found an incidence of 1.4% of additional fractures in a retrospective study in a population under the age of 1 year [27]. Laskey et al. reported an incidence of 6% of additional fractures in a retrospective chart review in a population less than 18 months old [26]. Although the overall yield of the skeletal survey in both studies is low, it is advised to obtain a skeletal survey in a child with a skull fracture and child abuse cannot be excluded.

Rib Fractures

Rib fractures have a high specificity for child abuse. Prevalence of rib fractures among children with suspected or confirmed abuse ranges from 8.7 to 14% [28]. In a large case-control study by Pandya et al., rib fractures in children less than 4 years of age were more commonly found in abused children (94/500, 18.8%) than in accidentally injured children (11/985, 1.1%) ($p < 0.001$) [29]. In the same study, in children less than 18 months old with rib fractures, the OR for abuse was 23.7 (95% CI = 9.5–29.2, $p < 0.001$). In children over 18 months with rib fractures, the OR for abuse was 9.1 (95% CI = 3.3–25, $p < 0.001$). Multiple rib fractures and posterior rib fractures are significantly

associated with abuse. On the other side, lateral rib fractures are more common in non-abused children than in abused children [30]. Maguire et al. demonstrated in a meta-analysis the strong association between rib fractures in young children and abusive head trauma (OR was 45) [31].

Metaphyseal Corner Fractures

Metaphyseal corner fractures, also known as classic metaphyseal lesions, are planar fractures through the primary spongiosa of the metaphysis. These fractures are caused when torsional and tractional shearing strains are applied across the metaphysis, as may occur with vigorous pulling or twisting of an infant's extremity [32].

Metaphyseal corner fractures are highly specific for child abuse, and very uncommon in children 2 years of age and older. Metaphyseal corner fractures are the most common long bone fractures found in infants who die with evidence of inflicted injury [33]. Fractures resembling metaphyseal corner fractures radiographically have been reported after breech delivery and as a result of treatment of clubfoot [32].

Kleinman et al. performed a retrospective study and compared 42 infants considered low risk for abuse because of skull fractures associated with falls and no risk factors for abuse, with 18 infants considered high risk for abuse because of significant intracranial injury, retinal haemorrhages, and skeletal injuries (excluding metaphyseal corner fractures and skull fractures). They found no metaphyseal corner fractures in the low risk group, whilst 9 out of 18 infants in the high risk group had metaphyseal corner fractures (50%, $p < 0.0001$) [34].

Long Bone Fractures

Children who are not independently mobile are far less likely to sustain an accidental long bone fracture [32]. In a systematic review by Kemp et al., the overall estimate of the probability of suspected abuse, given a humeral fracture, in a child under 3 years of age, was 0.54 (95% CI = 0.20–0.88) [30]. In one small study, in children with radial and ulnar fractures, overall 25% were the victims of abuse [35]. The overall estimated probability of abuse given a femoral fracture,

excluding children who were involved in a motor vehicle crash or violent trauma, was 0.43 (95% CI = 0.32–0.54) [30].

Dating Fractures

A systematic review published in 2005, showed that at that time there was insufficient evidence to exactly date fractures [36]. Based on their data, the authors only concluded that “*radiologists can clearly differentiate recent from old fractures*”. In a subsequent study, researchers from the same group showed that, based on 228 radiographs of 82 fractures in 63 children, dating up to a certain level is indeed possible [37]. This study showed that sub-periosteal new bone formation was first visible at day 5, soft callus was first visible at day 12, hard callus and bridging was first visible at day 19, and remodelling first at day 45. In a study by Halliday et al. it was shown that radiologists use criteria to date fractures that, with the exception of sub-periosteal new bone formation, are not reproducible [38].

Which Organ Injuries May Be a Result of Child Abuse?

Summary of Evidence Abdominal injuries are a common result of child abuse, especially in young children (moderate evidence). Liver injuries occur with equal frequency among accidentally and abused children (limited evidence). Abusive spleen injuries are less common, and little is known about abusive bowel injuries (insufficient evidence).

Supporting Evidence Abusive abdominal injuries in children are a significant cause of morbidity and mortality [39]. The cause of traumatic abdominal trauma requiring hospitalization in children aged 0–4 years is non-accidental in almost 40% of cases [40]. Mortality rates range from 9 to 45%, making intra-abdominal trauma the second most common form of fatal child abuse, after head injury [41]. Symptoms of abdominal injuries are often non-specific and, especially in young children, recognition can therefore be challenging. Injuries to solid organs

and hollow organs are equally common [42]. Children with abusive abdominal injuries are significantly younger than children with accidental abdominal injuries (mean ages of less than 3 years vs. greater than 7 years) [43].

In 2013, Maguire et al. published a systematic review of abusive visceral injuries in childhood [43]. The authors concluded that liver injuries occurred with equal frequency among accidentally and abused children. Liver injuries included laceration, contusions, subcapsular hematomas, and involved each lobe of the liver. Splenic injuries are less common compared to liver injuries. They are noted equally prevalent in accidental and abusive cases [44, 45], while another study recorded splenic injuries only among accidentally injured children [46]. Amongst fatal cases, motor vehicle collisions are the most common cause of pancreatic injuries, while abuse is the second most common cause [47]. Co-existent additional abdominal injuries and other injuries like burns and fractures are common.

The most common bowel injuries are perforations or transections of the duodenum. The junction of the third and fourth part is most commonly involved [43]. Transections of the duodenum are more common in abused children, while perforations have an equal frequency among accidentally and abused children [48]. Duodenal injuries are rare in accidental trauma and have not been recorded in children less than 4 years of age due to a fall [44, 45]. Accompanying bruising to the upper abdomen is relatively uncommon, even in abused children. A gastric rupture is only described in a single case report of a 2 year old girl, due to a forceful blow to the abdomen [49]. Finally, colonic contusions, rectal perforations and serosal tears of the colon in abused children are only described in conjunction with other injuries and not as single indicators of child abuse [43].

Imaging Case Studies

Case 1

Fig. 34.1a, b presents CT scan and MRI scans of a young child found unresponsive in its crib.

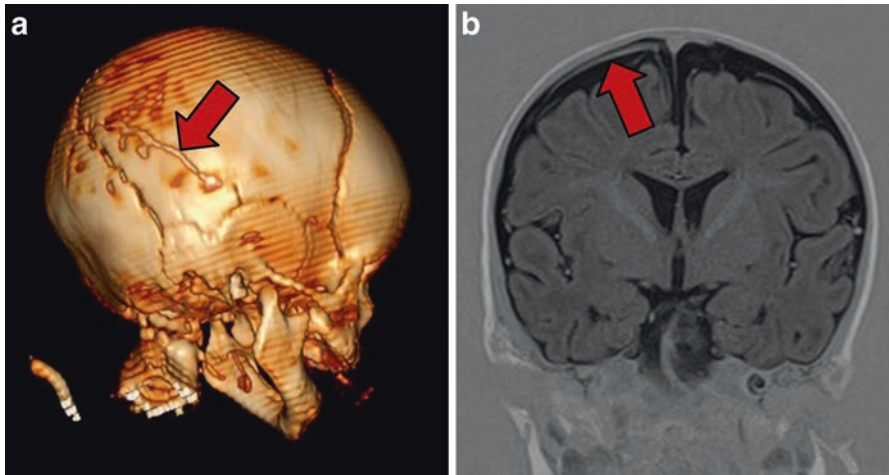


Fig. 34.1 Young child found unresponsive in its crib. According to the clinical history no trauma was known. Three dimensional reconstruction of the CT-scan shows a

linear skull fracture (*arrow*) (a). Coronal T1 weighted MRI shows a thin subdural hematoma along the right convexity (*arrow*) (b)

Case 2

Figure 34.2 presents radiographs of a young child who after being picked up from its crib seemed to be in pain.

Suggested Imaging Protocols in Suspected Child Abuse

Head Trauma

Ultrasonography (US)

Cranial US plays no role in the work-up of suspected AHT. A meta-analysis, based on a total of 21 children, showed that cranial US missed 5 out of 20 SDH [50]. Given the impact of the test, this high false negative rate is not acceptable.

Computed Tomography (CT)

CT has become the standard imaging technique in daily trauma care. The standards for radiological investigations of suspected non-accidental injury of the Royal College of Radiology and Royal College of Paediatrics and Child Health specifically state that in the acute situation CT is the modality of choice [51].

Magnetic Resonance Imaging (MRI)

In most cases, MRI is second line imaging. MRI should be performed if the CT is abnormal or equivocal. If MRI is performed, diffusion weighted imaging should be a routine part of the study. The use of susceptibility weighted imaging is encouraged as this has shown to increase the conspicuity of small haemorrhagic foci, e.g. in diffuse axonal injury and thus leads to a better prognosis of the neurological outcome [52, 53].

Skeletal Trauma

Skeletal Survey

The skeletal survey should be performed according to the American College of Radiography [54] or The Royal College of Radiologists and the Royal College of Paediatrics and Child Health [51] guidelines. In 2014, the European Society of Paediatric Radiology adopted the RCR-RCPH guidelines, meaning which apply throughout Europe [55]. According to these guidelines, a set of radiographs should be performed, including spot radiographs of the large joints. It is important that the skeletal survey is supervised by a radiologist and that the child is

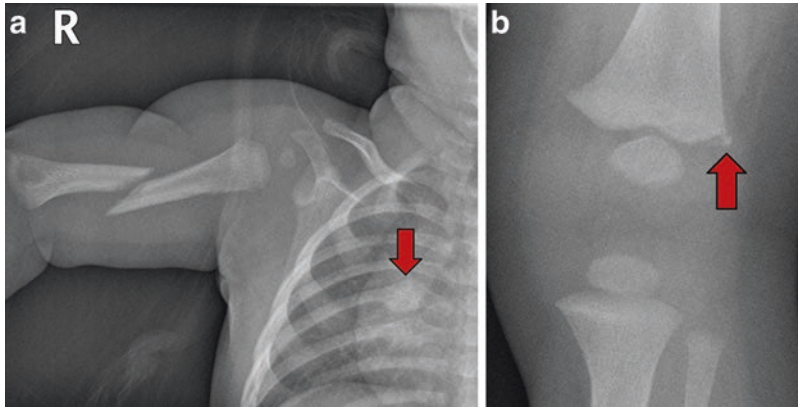


Fig. 34.2 Young child who after being picked up from its crib seemed to be in pain. On physical inspection the child did not move its right arm. A radiograph of the arm shows a fracture of the right humerus, in the same radiograph

healing posterior rib fractures were noted (*arrow*) (a). A skeletal survey showed the presence of a metaphyseal corner fracture of the distal left femur (*arrow*) (b)

not allowed to leave the room before all radiographs are reviewed and, additional radiographs obtained as required.

From a legal point of view it is mandatory that the radiological technician's initials are clearly visible on the radiographs.

Value of Follow-Up Skeletal Survey

Several studies have examined the value of follow-up skeletal survey. Anilkumar et al. assessed follow-up chest radiographs in a series of 59 children and found additional information in 7 children (12%) [56]. In two cases rib fractures were only found on the follow-up chest radiograph, in the other five cases additional information was obtained. Bennett et al. specifically addressed children in whom the initial skeletal survey was negative [57]. In their study of 47 children, four children (8.5%) showed healing bone injury, one a humerus fracture and three rib fractures.

Based on the 'Examining Siblings To Recognize Abuse' study, Harper et al evaluated 796 cases with a follow-up skeletal survey. Of these, 174 (21.5%) follow-up skeletal surveys showed additional relevant findings and in 124 (15.6%) at least one additional fracture was diagnosed. In a smaller study, Kleinman et al. showed that the follow-up skeletal survey showed new information in 14

(61%) of 23 cases [58]. In their series the total number of fractures increased significantly from 70 to 89.

In summary, there is strong evidence that a follow-up skeletal survey has a significant impact on patient care.

Value of Imaging Siblings

In the 'Examining Siblings To Recognize Abuse' study, an observational, multicentre cross-sectional study, siblings of physically abused children with serious injuries underwent a skeletal survey if they were <24 months of age [59]. Based on this protocol the study found in 16 of 134 cases (11.9, 95% confidence interval 7.5–18.5) at least one abusive fracture. In none of these cases physical examination showed any signs of abuse (moderate evidence).

Abdominal Trauma

US (FAST)

In case of blunt abdominal trauma the first imaging modality should be "Focused Assessment with Sonography for Trauma" [60]. In a study performed in a major London trauma centre the positive predictive value of FAST for intra-abdominal

trauma in children was 0.96 (0.81–0.99) and Negative Predictive Value of 0.39 (0.26–0.54) (moderate evidence) [61].

Computed Tomography

In case of a positive FAST the use of CT should be considered. The decision to perform CT should be based on the overall clinical condition of the patient and the fact if additional imaging would alter the treatment of the patient [60].

Future Research

- There is a strong need for proper training of ED personnel, both physicians and nurses, in the detection of child abuse.
- There is a strong need for a validated screening tool for child abuse in the emergency department.
- There is a strong need for clinical prediction rules for the detection of abusive head trauma.

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Infantile Hypertrophic Pyloric Stenosis (IHPS) in Infants and Children: Evidence-Based Emergency Imaging

Marta Hernanz-Schulman

Key Points

- The presentation of infants with IHPS is not always typical and, particularly in early cases, may be confused with other causes of non-bilious vomiting, such as reflux (limited evidence).
- Clinical examination by palpation of the pyloric mass (olive) is effective in diagnosis but may be time-consuming (moderate evidence).
- UGI diagnosis is based on inference of the pyloric muscle from its effect on the lumen, as the external portion of the pylorus is not visible. Thus, gastric emptying must occur, and this may be quite delayed, thus leading to prolonged fluoroscopy. Because the child needs to drink contrast, there is also potential for aspiration (limited evidence).
- US visualizes pyloric length and pyloric thickness and does not require gastric

emptying or intake of contrast for diagnosis. However, it is an exam that is not performed in adult patients and requires special operator and diagnostic expertise (strong evidence).

Definition, Clinical Presentation, and Pathophysiology

IHPS is an enigmatic condition of unknown cause which causes gastric outlet obstruction in infants, typically between the second and twelfth weeks of postnatal life. The condition is associated with failure of relaxation and hypertrophy of the antropyloric portion of the stomach and thickening of the mucosa in its lumen, leading to protracted, forceful vomiting of gastric contents, typically described as “projectile.” When diagnosis is delayed, the infant suffers from dehydration, electrolyte imbalance, and eventually emaciation. If untreated, death may be the final outcome, and in fact prior to the development of today’s treatment algorithms and diagnostic tools, this was often a fatal disease [1, 2]. The infant may have manifested signs of reflux initially, and the onset of IHPS may be unrecognized and thought secondary to worsening reflux. Initially intermittent, vomiting increases in severity and frequency; the loss of gastric contents

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results not just in dehydration, but also in loss of acid leading to hypochloremic alkalosis, with paradoxical aciduria as the kidney attempts to conserve sodium at the expense of hydrogen ion. The infant is voraciously hungry, often gnawing his fists, and as weight loss and starvation follow, the distended stomach and vigorous peristaltic waves may be visible through the emaciated body habitus. This “classic” presentation is the exception today, when the diagnosis is typically made much before emaciation, and even severe dehydration have ensued.

Despite the frequency with which IHPS occurs, its pathophysiology remains elusive. The hypertrophied muscle begs investigation, and indeed multiple abnormalities have been identified. When compared to control specimens, the muscular layer has been found to have increased expression of insulin-like growth factor-I messenger RNA, increased platelet-derived and insulin-like growth factors. Further, it is deficient in interstitial cells of Cajal, in the quantity of nerve terminals and markers for nerve-supporting cells, in peptide-containing fibers, and in messenger RNA production for nitric oxide synthase as well as in nitric oxide synthase activity [3–12]. Genetic studies have identified genetic heterogeneity, and cases have been mapped to loci on chromosomes 3p25.1, 5q35.2, 16q-24, 16p12-p13, and 11q14-q22, the latter affecting ion channels with a potential role in smooth muscle control and hypertrophy [13–16]. Simple nucleotide polymorphisms (SNPs) have been identified mapping to 3p25.1, 3p25.2, and 5q35.2 in patients with IHPS compared with controls; these map to the vicinity of genes controlling muscle and gut development as well as regulation of alternative splicing, some of which show differential activity levels in the early postnatal period; the authors hypothesize that such temporal differentials might be involved in the temporal boundaries in which IHPS develops in infants, i.e., typically between 2 and 8 weeks of age [17].

An additional hypothesis suggests that a genetically influenced increase in the parietal cell mass initiates a cycle of increased acid production, repeated pyloric contraction, and decreased gastric emptying, with histopathologic muscle

and mucosal abnormalities as secondary events. The proliferation of mucosa in turn acts as an obstructive element, leading to further muscular hypertrophy [1, 2, 18, 19]. Data supporting these contentions include induction of IHPS in puppies with pentagastrin infusion [20], with very rare exceptions, the development of IHPS after inception of feeding [21], the development of IHPS with prokinetic agents such as erythromycin [18], and the resolution of the lesion and histopathologic and myoelectrical abnormalities after obstruction is surgically relieved [22, 23]. Thus, despite impressive advances, etiologic factors remain heterogeneous and confusing, with uncertainty as to which of these epiphenomena are the cause and which the result of the disease and further research is needed to extricate the etiology and pathophysiology of this intriguing condition from the multiplicity of associated findings and confounding variables.

Epidemiology

The epidemiology of IHPS is variable, influenced by genetics and dependent on racial and geographic extraction. Among white populations of northern European extraction, the incidence of IHPS is approximately 2–5 per 1000 births; this incidence falls by 20–30% among Caucasians in India and among Black and Asian populations, even those residing in the United States. Probandwise concordance in monozygotic and in dizygotic twins is 0.25–0.44 and 0.05–0.10 respectively [24]. As noted earlier, presentation is typically between 2 and 8 weeks of life. There is a male predominance, with male/female ratio ranging from 2.5:1 to 5.5:1. Male and female children of affected mothers carry a 20 and 7% risk of developing IHPS, respectively, while male and female children of affected fathers carry a 5 and 2.5% risk, respectively. IHPS occurs more commonly in firstborns; other associations that have been inconsistently identified include breast feeding, formula feeding, maternal smoking, prone sleeping position, and seasonal variations with increased incidence in summer months [25–29]. Interestingly, testosterone levels in fetal cord

blood have been lower in infants who developed pyloric stenosis, although the differences failed to reach statistical significance [30].

Overall Cost to Society

The costs to society of caring for infants with IHPS vary with the decision tree for diagnosis, with the type of surgery performed, with the skill of the physicians involved, and with the rate of complications. In a retrospective study of 234 patients suspected of IHPS, White and colleagues [31] determined that the mean total charges for their patients with IHPS were \$2454, with a potential savings of \$100.00 per patient in a model in which diagnostic imaging was applied after surgical evaluation, so long as the surgeon's sensitivity to palpate the olive was at least 38%, and a positive examination was followed by surgery. However, this study does not address the potential delays in obtaining outpatient clinic appointments with pediatric surgeons and might presuppose an ED visit, which would carry additional cost and inconvenience, particularly if the patient does not have pyloric stenosis.

Goals of Imaging

In patients with IHPS, the goal is to diagnose the condition as quickly and noninvasively as possible, so that treatment may be begun before the onset of clinical deterioration with dehydration, electrolyte abnormalities, and weight loss.

Methodology

The author performed a MEDLINE search using PubMed (National Library of Medicine, Bethesda, MD) for data relevant to the diagnostic performance and accuracy of both clinical and radiographic examination of patients suspected of IHPS, as well as the surgical and medical therapy for this condition. The diagnostic performance of the clinical examination (history and physical exam) and surgical outcome was based

on a systematic literature review performed in MEDLINE (National Library of Medicine, Bethesda, MD) during the years 1966–2015. The search strategy used the following statements: (1) pyloric stenosis, (2) US (ultrasound), (3) UGI (upper gastrointestinal imaging), and (4) clinical examination.

Discussion of Issues

What Are the Clinical Findings that Raise the Suspicion for IHPS and Direct Further Investigation?

Summary of Evidence The clinical presentation of IHPS is that of non-bilious vomiting. Although the color of the emesis may be yellow-tinged, if it is green, the differential shifts radically to malrotation and its emergent complications, such as midgut volvulus. There is one study which reports that bilious vomiting may be present in 1.4% of infants with IHPS [32]; however, this is a retrospective study, based on chart notes, and the basis of the information or the level of expertise of the person who entered the information is not stated. In patients with IHPS, forceful vomiting sometimes described as “projectile” develops acutely, or as an exacerbation of preexistent reflux, which represents the major differential diagnosis. The episodes of vomiting are initially intermittent but progress to follow all or nearly all meals. Unlike patients with gastroenteritis, patients with IHPS are voraciously hungry and may be seen sucking at their fists. Starvation can exacerbate the low activity of hepatic glucuronyl transferase, and indirect hyperbilirubinemia may be present in 1–2% of patients. Gastritis may lead to blood-tinged vomitus. The distribution of electrolyte abnormalities is characteristic; protracted vomiting results in depletion of hydrochloric acid, sodium, and potassium, which in turn leads to hypochloremic alkalosis with absolute deficits of sodium and potassium, which may be masked by the infant's dehydration on initial blood tests. Renal mechanisms supervene to maintain intravascular volume by conservation of sodium at the expense of hydrogen ion, leading to “paradoxical

aciduria," i.e., excretion of hydrogen ion despite systemic alkalosis; sodium may also be conserved at the expense of potassium, exacerbating potassium deficits. If the course is protracted, the infant becomes emaciated, with a distended stomach and visible gastric peristalsis in the hypochondrium; this previously characteristic presentation is thankfully rare today.

Supporting Evidence In the vomiting infant, measurement of serum electrolyte levels could help differentiate the child with IHPS from the child with vomiting secondary to reflux; however, these findings are seen late in the course of the development of IHPS, are correlated with more severe dehydration, and therefore are less helpful in the early stages, when ideally the diagnosis should be made. In a 1983 retrospective study of 65 infants with IHPS [33], investigators found that bicarbonate levels were normal in 29%, moderately elevated in 33.8%, and markedly elevated in 24.6%, for a total of 62% presenting with alkalosis. Patients with elevated bicarbonate levels showed the most severe dehydration, the lowest chloride levels, and the highest percentage of low urinary pH and had the longest duration of symptoms. In a subsequent 1989 study of 216 infants [34], the authors found that the alkalotic and hypochloremic infants had a significantly longer duration of illness, sodium, potassium, and chloride deficits. These sicker patients also had a higher percentage of palpable olives, and overrepresentation of female and black infants, likely because of a lower initial suspicion of IHPS in these populations, leading to a more delayed diagnosis. More recently, investigators reviewed 118 infants who presented with IHPS between 2006 and 2008 at The Hospital for Sick Children; they found that only 8% presented with clinical signs of dehydration; only 21% were reported with metabolic alkalosis, although the degree of alkalosis is not stated or compared to prior reports; these numbers contrast with those in the earlier publications, demonstrating that the diagnosis is made earlier and in healthier infants today [35].

Therefore, the patient with IHPS will present with new onset or exacerbation of postprandial

non-bilious vomiting, with more advanced cases demonstrating dehydration; elevated serum bicarbonate, with chloride, sodium, and potassium deficits; and paradoxical aciduria. The evidence indicates that the typical electrolyte disturbances of IHPS occur later in the evolution of this condition, that heightened clinical suspicion and further investigation before the full constellation of findings has appeared will aid in reaching the goal of early treatment, and that this is increasingly the case today.

What Is the Diagnostic Performance of the Clinical and Imaging Examinations in IHPS?

Summary of Evidence The clinical examination in IHPS refers to the ability to palpate the pyloric mass or olive. In the mid-twentieth century, the mainstay imaging examination for IHPS was the UGI or barium meal, standardized in 1932 by Meiweissen and Sloof. In 1977, US was first reported as a tool in the correct diagnosis of IHPS in five patients, published in the *New England Journal of Medicine* [36]. After considerable literature discussing specific numerical cutoff values and initially variable success rate, ultrasound has now become the preferred imaging modality for the diagnosis of IHPS. The diagnostic performance of the clinical and the imaging examinations varies with the skill of the examiner, particularly for clinical palpation and for US; yet, since it was first reported, the success rate of US has continued to increase, and with increased reliance on US, the success rate of clinical palpation has declined, while the UGI is now seldom performed for this purpose, particularly in pediatric-focused practices.

Supporting Evidence

Clinical Palpation

Success in palpating the enlarged pylorus is not easy in most circumstances, is only possible if the infant is calm or lethargic, and is more difficult in the well hydrated well-fed infant presenting early in the course of the disease. The use of

a pacifier or a small feeding (such as 5% dextrose in water) may be helpful and has been advocated by various investigators. Passage of a feeding tube to decompress the stomach and allow the pylorus to rise and approximate the anterior abdominal wall has also been advocated, although this adds an invasive element to the procedure. Per the literature, the examiner should be willing to commit 10–20 min of time in order to successfully palpate the pylorus, and repeat examinations may be required [37]. The frequency of diagnosis of the pyloric mass by successful palpation has decreased over the past two decades; this is believed to be due in part to the time commitment needed for successful physical examination, to the earlier referral of these patients for diagnosis, and particularly to the ease and reliability of the noninvasive US study, addressed later in this section.

In a 1996 prospective investigation of 116 infants with vomiting, the physical examination was successful in 80% of 75 patients with proven IHPS. In this study, the physical examination had a sensitivity of 72%, specificity of 97%, positive predictive value of 98%, and negative predictive value of 61% [38].

In one retrospective study of 212 patients seen between 1974 and 1977 and of 187 patients seen between 1988 and 1991, Maccessi and Oates [39] found that the pyloric mass was successfully palpated by the surgeons in 99% of patients in the earlier group and in 79% of the patients in the later group; among the non-surgeons to whom the patients initially presented, the pyloric mass was palpated in 47% of patients in the earlier group and in just 33% of patients in the later group.

In another retrospective study of 234 patients, 150 of whom had pyloric stenosis, the pyloric mass was successfully palpated in 111 patients with one false-positive examination, for a sensitivity of 74% and a specificity of 99%. However, the sensitivity ranged between 31 and 100% among the five surgeons in the group [31].

More recently, in a series of 118 patients seen in a tertiary referral pediatric hospital between 2006 and 2008, a palpable olive was recorded in only 13% of patients, while ultrasound was performed in 100% of the infants [35].

UGI Examination

The UGI examination is performed by introduction of a positive oral contrast agent, typically barium, into the stomach, and observation of the abnormal antropylic channel during passage of the contrast. The UGI as a diagnostic tool in infants with IHPS was introduced in 1932 by Meuwissen and Sloof, with proponents such as Rigler in the United States [40]. In 1964, Currarino advocated double-contrast examination with compression spots [41]. Since the diagnosis depends on passage of contrast through the abnormal channel, which can be markedly delayed, the fluoroscopic examination can be lengthy. In addition, the contrast will be diluted by the fluid within the stomach, and drinking additional contrast will further distend and compromise an already distended stomach. Passage of an orogastric tube to decompress the stomach, which allows improved visualization by eliminating dilution of the contrast by the gastric contents, adds invasiveness to the procedure.

When performed by an experienced radiologist, the UGI is considered to be accurate in the diagnosis and exclusion of IHPS, although there are few studies today that specifically address the sensitivity and specificity of UGI in IHPS. Extending the search back several decades, a 1967 publication of a study of 46 patients with surgically proven IHPS but without an initially palpable olive, reported that UGI was diagnostic in 44 (95.5%), with 2 false negatives [42]. These authors found the double-track sign and string sign to be present in more than one-half the patients, while beak, shoulder, and pyloric tit signs were present in slightly less than half. Seven percent of the patients had complete obstruction, with no passage of contrast from the stomach 30 min after completion of the fluoroscopic examination; although the abnormal channel was not demonstrated, these were considered true positive. By selection of the study group as only patients with proven IHPS, there could be no false positives in this report; nevertheless, there were two false-negative UGIs, for a sensitivity of 95% in this biased, highly selected group of patients. In another study, the UGI was tangentially addressed; in one patient who had both UGI

and US, findings on the UGI were diagnostic of IHPS; however, surgery was not performed because the US was normal, and follow-up confirmed that the infant did not have IHPS. Since in that study 44 UGIs were performed, the calculated specificity would be 98% [43].

Ultrasound Examination

The US examination, similar to abdominal palpation, requires a skilled and experienced examiner. Unlike the clinical examination, US is not time-consuming, and diagnosis by an experienced examiner can be made very quickly, even in a hungry, crying infant, without need to empty the stomach with an orogastric tube or any other maneuver. Unlike the UGI examination, US diagnosis is not dependent upon gastric emptying, and both the lumen and the outer muscle are directly visualized. The child does not need to drink further contrast, and there is no radiation exposure.

Uncertainty in the US diagnosis arises when absolute reliance is placed upon measurements of the antropyloric channel. The measurements most often used include muscle thickness, length of the hypertrophied pyloric channel typically termed pyloric length, and pyloric diameter. Analysis of the literature on this subject must be viewed with the realization that the technique has evolved in unison with the equipment and with our ability to visualize increasing details of the antropyloric junction.

The initial and seminal report of US for the diagnosis of IHPS, reported in the *New England Journal* in 1977 [36], consisted of five patients examined with a static B-scanner, and used the pyloric diameter as a diagnostic criterion; the diameter ranged between 1.8 and 2.8 cm, with a mean of 2.3 cm. With the advent of real-time scanners and improved resolution soon thereafter, muscle thickness began to be reported as an important component of this diagnosis.

In a prospective study of 200 infants with vomiting [44] scanned with a mechanical sector transducer operating at 7.5 MHz, Stunden et al. found a mean muscle thickness of 3.4, with a range of 3–5 mm, a mean pyloric length of 22.3 with a range of 18–28 mm, and a pyloric diame-

ter of 13.3, with a range of 9–19 mm. In their work, these investigators found the pyloric length the most discriminatory criterion, with a cutoff value at 18 mm. They additionally identified the importance of real-time evaluation, the lack of relaxation and opening of the channel in patients with IHPS (not necessarily lack of any passage of contents), and the variability in size of the normal channel secondary to normal muscular contractions. Using these criteria, these authors were able to discriminate between patients with and without IHPS with 100% success rate, without false-positive or false-negative results. In their patient population, a pyloric mass was palpated in two patients who had normal US examinations and subsequently were proven not to have IHPS.

In a subsequent study including 323 sonographic examinations, scanned at 5.0 or 7.5 MHz, Blumhagen and colleagues [45] reported an accuracy of 99.4% for US, despite classifying as false negatives a positive case initially diagnosed as “suspicious” and a case diagnosed by sonography 4 days later. There were no false positives. In 8% of the normal patients, clinical examination had been false positive (specificity 91%). The authors found a mean muscle thickness of 4.8, with a range of 3.5–6.0 mm, and a mean pyloric length of 17.8 with a range of 11–25 mm. They found some overlap in the pyloric length and identified muscle thickness as the criterion with the higher discriminatory value.

Graif et al. [46] examined a control group of 22 infants with gastrointestinal symptoms, and 22 patients suspected of IHPS, of whom 17 were shown to have IHPS. These investigators found a mean muscle thickness of 4.5, with a range of 3–6 mm, and pyloric length of 22.1 with a range of 16–26 mm. In the control group, mean muscle thickness was 2.3 with a range of 1.9–3.5, and pyloric length was 12 with a range of 8–16 mm.

In a retrospective study of 145 consecutive infants with vomiting, O’Keefe et al. [47] determined that a muscle thickness of 3 mm or greater is diagnostic of IHPS, while muscle thickness was <2 mm in all normal patients and <1.5 mm in 98% of these.

These results were validated in a study of 152 consecutive patients scanned with linear trans-

ducers at 7.5 MHz, with non-palpable olive on initial physical examination. Hernanz-Schulman et al. [43] found that in the 66 patients with IHPS, a muscle thickness of 3 mm or greater was diagnostic of IHPS in their patient population, with no false-positive examinations. In the 77 normal patients, muscle thickness was evaluated only during the time when the pyloric antrum was relaxed and measured 1 mm or less in all the patients. There were no false-negative studies. These investigators identified seven patients in whom the muscle thickness ranged between 1.3 and 2.7 mm; these patients were observed and did not develop IHPS. Although the muscle thickness in these patients did not reach 3 mm, the length of the abnormal canal overlapped with that of patients with IHPS. These authors also described thickening of the mucosa within the channel lumen, and protrusion into the gastric antrum (termed the antral nipple sign), variability in the thickness of the muscle of the normal antrum during antropyloric contraction, as well as occasional variability (within the abnormal range) in the muscle thickness and pyloric length in patients with IHPS.

Thus, the weight of the evidence indicates that muscle thickness consistently ≥ 3 mm over a period of observation; failure of the antropyloric channel to relax and open; mucosa filling, obstructing, and protruding from the antropyloric canal; and a length of non-relaxing antropyloric muscle of >13 – 14 mm are diagnostic of IHPS on US.

What about small infants? Are the numerical criteria different in these smaller patients? In a retrospective investigation of pyloric dimensions in 51 patients with IHPS younger than 21 days and 149 older than 21 days, investigators found a roughly linear relationship between patient age on the one hand and muscle thickness and abnormal canal length on the other hand. However, in all patients the measurements were greater than 3.5 mm for muscle thickness and 1.6 mm for abnormal channel length [48]. By the same token, in 2012 Iqbal et al., in a study of 304 infants, utilizing 3 mm muscle thickness and 15 mm abnormal channel length, confirmed the relationship between age and pyloric size; however, utilizing

these same criteria, all patients were diagnosed with 100% sensitivity and specificity [49].

Is There a Role for Repeat Imaging in the Management of IHPS?

Summary of Evidence Initially described as congenital hypertrophic pyloric stenosis, IHPS is now known to be a condition that develops after birth. The rate at which pyloric stenosis evolves in all patients or in specific individuals is not known, nor is it known whether pylorospasm, or reversible contraction of the antropyloric musculature, is typically a self-resolving condition or whether it is one of the initial steps in the development of pyloric stenosis in some patients. Therefore, in the small minority of patients with equivocal findings, i.e., findings which are neither normal nor diagnostic of IHPS, if symptoms do not resolve, a repeat examination is important to assess for the development of IHPS. This is particularly pertinent if the equivocal examination occurs in a child at the lower end of the age spectrum of presentation.

Supporting Evidence In the retrospective evaluation of 145 consecutive patients, O'Keefe et al. [47] found 6 (4%) patients with equivocal findings and borderline muscle measurements of >2 and <3 mm. In two of these patients, IHPS developed, with follow-up examination demonstrating a change in muscle thickness from 2 to 4 mm 2 weeks later. The findings resolved in two patients who probably had transient pylorospasm that resolved; of the other two patients, one patient had milk allergy and one had eosinophilic gastroenteritis.

In a prospective Doppler study of vascularity of the pyloric muscle and mucosa, Hernanz-Schulman [43] identified one child who was referred at 2 weeks of age for US evaluation of vomiting secondary to family history and heightened clinical suspicion. The initial examination found a muscle thickness of 2.8 mm with intermittent widening and opening of the canal; the muscle thickness increased to 3.5 mm at 5 weeks of age without canal opening, at which time the

diagnosis of IHPS was made and confirmed at surgery. More recently, a group of three patients whose initial US examinations were either completely normal, or falling in a gray area of muscle thickness between 2 and 2.5 mm, were documented as progressing to fully developed IHPS in persistently symptomatic infants [50].

Is There a Role for Two Different Studies (US and UGI) to Be Performed?

Summary of Evidence In infants suspected of IHPS, the evidence indicates that sonography is the most expedient examination with extremely high accuracy in experienced hands. In patients who have a normal pylorus, an UGI, pH probe or scintigraphy can be done to evaluate reflux, if a presumptive diagnosis of gastroesophageal reflux is not viewed as sufficient by the referring physician for decisions regarding therapy.

Patients who have borderline measurements by US should be observed, with repeat sonography if symptoms do not abate, to identify the small minority of patients with developing IHPS, as noted in the above section. Performing an UGI in those patients will add radiation exposure and will not shed additional light on the morphology of the pylorus. Occasionally, a patient with pre-ampullary duodenal stenosis presenting with non-bilious vomiting is identified by US revealing a normal pylorus and a distended duodenal bulb [51]; UGI in such patients is useful in confirming the diagnosis prior to surgical correction.

On the other hand, occasionally an UGI will be done in a patient with IHPS. In those patients, if there is delay in gastric emptying (as would be expected in patients with IHPS), prolonged fluoroscopy can be obviated by switching to US to establish the diagnosis.

Supporting Evidence In a study of 152 consecutive patients suspected of IHPS [43], 66 patients (43%) had IHPS and required no fur-

ther imaging. Seventy-seven patients (51%) had normal pylorus, and of these 47 (31% of original group) had a second study to assess for reflux (UGI, 43; radionuclide, 3; pH probe, 2), although empiric treatment could have been instituted, as was the case in the rest of the group. Of seven patients with equivocal muscle thickness of >2 mm and <3 mm, two had UGI, with the erroneous diagnosis of pyloric stenosis suggested in one of these. In a more recent, 2011 report on 118 infants with IHPS, 100% received US examination, and UGI was performed in none [35].

Take Home Figure and Table

Figure 35.1 is an algorithm for diagnosis of infants suspected of IHPS. Table 35.1 shows performance of diagnostic imaging in IHPS.

Imaging Case Studies

Case 1

Figure 35.2 presents a sonogram of a 2-month-old boy with vomiting and IHPS.

Case 2

Figure 35.3 presents a sonogram of an infant without IHPS.

Case 3

Figure 35.4 presents an UGI of an infant with IHPS.

Case 4

Figure 35.5 presents an ultrasound of a patient with non-bilious vomiting suspected of IHPS.

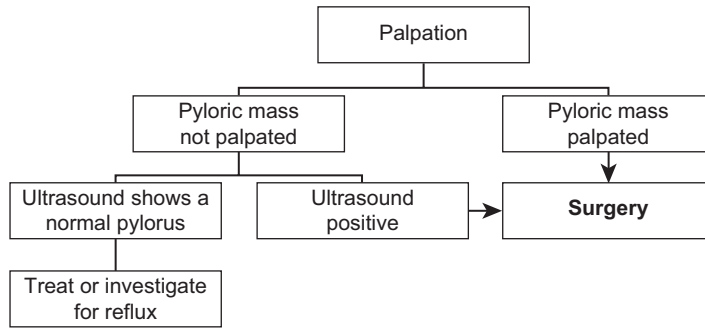


Fig. 35.1 General algorithm for diagnosis of infants suspected of IHPS (Adapted with kind permission of Springer Science+Business Media from Hernanz-Schulman M, Berch BR, Neblett III WW. *Imaging of Infantile Hypertrophic Pyloric Stenosis (IHPS)*. In Medina LS,

Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science + Business Media, 2010)

Table 35.1 Performance characteristics of diagnostic examinations in IHPS

	Sensitivity (%)	Specificity (%)
Palpation	24–99	92–99
Ultrasound	98–100	99–100
UGI	95–100	98

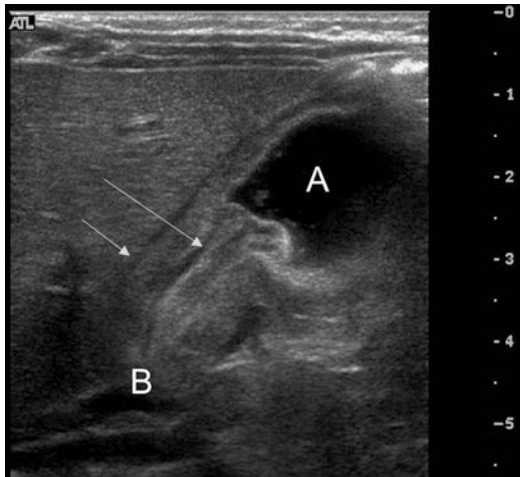


Fig. 35.2 A 2-month-old boy with vomiting and IHPS. The antropylic portion of the stomach shows non-relaxing, abnormally thickened muscle (5 mm), and the lumen is filled and obstructed by hypertrophied mucosa, which protrudes into the fluid-filled antrum (A). B= duodenal bulb. The *short arrow* points to the outer edge of the muscle, the *longer arrow* to the mucosa

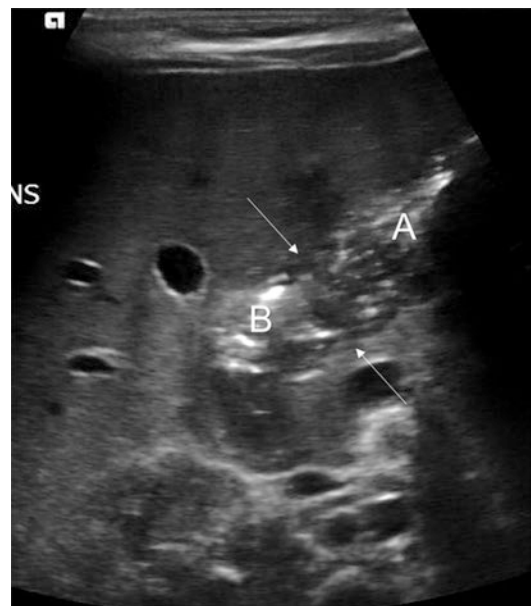


Fig. 35.3 US of infant without IHPS, normal pylorus. The widely open antrum (a) leads to the duodenal bulb. (b) Arrows point to the level of the pyloric membrane. The second portion of the duodenum is fluid filled and courses about the head of the pancreas

Suggested Diagnostic Protocols

In assessing the utility of various diagnostic examinations for IHPS, the clinicians’ overarching goals in caring for their patients are early diagnosis, diagnostic accuracy, and noninvasive

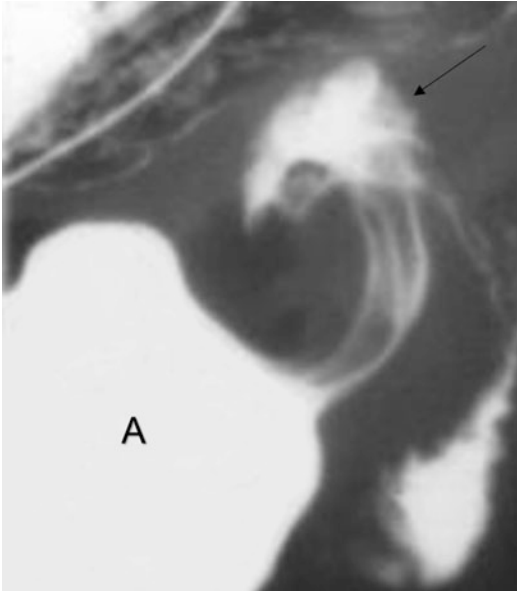


Fig. 35.4 UGI of infant with IHPS. The antropyloric portion of the stomach is narrowed by the thickened muscle, and contrast is seen coursing between the interstices of the thickened and compressed mucosa. A = antrum; arrow points to the duodenal bulb

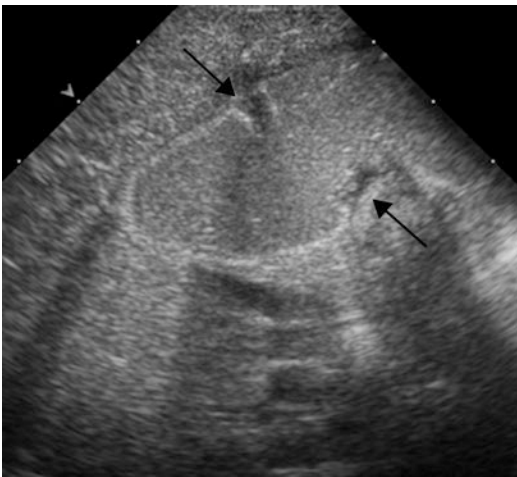


Fig. 35.5 Ultrasound of patient with non-bilious vomiting, suspected of IHPS. The ultrasound reveals a widely open antropyloric canal and pylorus (arrows) with a dilated duodenal bulb. The diagnosis of duodenal stenosis was confirmed at subsequent surgery

methodology. This then allows treatment to occur in the safest manner with the most expeditious recovery. The decision tree in Fig. 35.1 outlines

the role of each diagnostic examination in the evaluation of IHPS. Plain radiographs are not routinely obtained, although if requested for other reasons, a distended stomach with paucity of more distal bowel gas is characteristic, often with a peristaltic wave visible in the stomach.

Palpation of the olive is the first diagnostic examination by the physician to whom the child presents. In doing this, consideration should be given to the time investment required for success with this method, including the relative invasiveness of inserting an orogastric tube to evacuate the stomach, and further time in calming the infant. However, once the pyloric mass is palpated with confidence, there is no need for further diagnostic investigation.

If a pyloric mass is not palpated by the primary caregiver or ED physician, consideration should be given either to a direct surgical referral or to a diagnostic imaging examination. The cost and time delay to obtain a surgical consultation or a surgical clinic visit vs. the cost and time delay of an imaging procedure can be taken into consideration, which may differ in various clinical settings, in various institutions, and at various times. If the pyloric mass cannot be palpated by the surgeon, again consideration should be given to a diagnostic imaging examination; waiting and reexamining the patient may not be practical in an ED or clinic setting, while prolongation of inpatient care is not cost-effective and leads to delay in diagnosis and treatment. Sedating an infant at high risk for vomiting in order to increase sensitivity in palpating the olive, as suggested by some [52], does not seem appropriate, particularly in a setting in which noninvasive and accurate imaging is available.

US is an imaging technique which, like abdominal palpation, requires an appropriate learning curve. When this is achieved, US is diagnostic within a few minutes and does not require insertion of orogastric tubes or further ingestion of contrast material to distend the stomach. If US expertise is not available, referral of the child to a center where the expertise is available should be a primary consideration; if this is not possible, UGI should be considered if there is persistent clinical concern and the pyloric mass remains palpable.

Future Research

- Further research on the etiology of IHPS may prevent the condition or allow more effective and rapid medical management.
- Further evaluation of the learning curve and skills necessary for the laparoscopic procedure and of its relative value vs. open surgical procedure may allow a more definite definition of the specific selection of patients that will benefit most from each procedure.

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Intussusception in Infants and Children: Diagnostic Evidence-Based Emergency Imaging and Treatment

Kimberly E. Applegate and Gelareh Sadigh

Key Points

- Children with clinically suspected intussusception should undergo enema reduction after surgical consultation. The only absolute contraindications to enema are signs of peritonitis on clinical exam or free air on abdominal radiographs. Air enema has better overall reduction rates than liquid enema, but the outcome depends on the experience of the radiologist (strong evidence).
- Ultrasound (US) should be the primary imaging modality in the initial diagnosis of intussusception because it is a noninvasive test with high sensitivity and specificity. US also plays a role in the evaluation of reducibility of intussusception, presence of a lead point mass, potential incomplete reduction after

enema, and of intussusception limited to small bowel (limited evidence).

- Barium should not be used due to the poorer outcomes compared with iodinated liquid contrast in those children who perforate (moderate evidence).
- Abdominal radiographs have poor sensitivity for the detection of intussusception but may serve to screen for other diagnoses in the differential diagnosis, such as constipation, and for free peritoneal air. For evaluating children with a low probability for intussusception, sonography is the preferred screening test (limited evidence).
- The use of delayed repeat enema for the reduction of intussusception shows promise, but there are few data on the appropriate methods or time (limited evidence).
- For recurrence of intussusception, including multiple recurrences, enema is the preferred method for reduction (limited evidence).

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Definition and Pathophysiology

Intussusception is an acquired invagination of the bowel into itself, usually involving both small and large bowel, within the peritoneal cavity.

The more proximal bowel that herniates into more distal bowel is called the intussusceptum, and the bowel that contains it is called the intussusciens. It is an emergent condition where delay in diagnosis is not uncommon and leads to an increased risk of bowel perforation, obstruction, and necrosis. There may be an accompanying pathologic lead point (PLP) mass in approximately 5% of children [1]. Intestinal intussusception may occur along the entire length of the bowel from the duodenum to prolapse of intussuscepted bowel through the rectum. It can also range from classic clinical presentations to asymptomatic transient intussusception seen increasingly on multichannel CT studies of the abdomen for other indications [2]. Most cases are “idiopathic” in that the etiology of the intussusception is due to hypertrophied lymphoid tissue in the terminal ileum which results in ileocolic intussusception. Some reports have suggested a viral etiology, most commonly adenovirus but also enterovirus, echovirus, and human herpes virus 6 [3]. The clinical signs and symptoms of intussusception are often nonspecific and overlap with those of gastroenteritis, malrotation with volvulus, and, in older children, Henoch–Schonlein Purpura (HSP). The large majority of clinically symptomatic cases occur in the infant and toddler, with a peak age of 5–9 months, although it has been reported on prenatal imaging and may occur in children who present without the typical clinical presentation of vomiting, bloody stools, palpable abdominal mass, and colicky abdominal pain [4]. The classic triad of colicky abdominal pain, vomiting, and bloody stools is present in less than 25% of children [5–7].

Epidemiology

Intussusception is the most common cause of small bowel obstruction in children and occurs in at least 56 children per 100,000 per year in the USA [8]. It is second only to pyloric stenosis as the most common cause of gastrointestinal tract obstruction in children. It occurs in boys more than girls at a ratio of 3:2. Several papers have reported associations with viruses, particularly

adenovirus, although lack of seasonality suggests more than one pathogen [4, 8, 9] and, in developing nations, parasites [9–11]. Delay in diagnosis and treatment is not uncommon, making enema reduction less successful, bowel resection more likely, and death due to bowel ischemia possible [1, 4, 12, 13]. There were 323 intussusception-associated deaths in American infants reported to the Centers for Disease Control (CDC) between 1979 and 1997. In a review of administrative discharge data of intussusception-associated hospitalizations and deaths in the USA, Parashar and colleagues [8] noted a peak age of 5–7 months, with two-thirds of patients under the age of 1 year, no consistent seasonality, hospitalization rates of approximately 56 per 100,000 children, and a general trend toward fewer hospitalizations over the past two decades. The mortality rates also decreased over this time period, from 6.4 per 1,000,000 to 2.3 per 1,000,000 live births. They also reported an increased risk of intussusception-related deaths among infants whose mothers were <20 years old, unmarried, nonwhite, and had less than a grade 12 education. The authors concluded that these data suggest reduced access or delay in seeking care contributed to the risk of death. They did not investigate costs or rates of surgical versus enema reductions.

In another paper comparing worldwide data, Meier and colleagues noted that the most important difference between industrialized and developing countries’ outcomes was the delay in presentation for treatment and consequent lower rates of enema reduction and higher rates of surgical mortality (18%) from bowel necrosis [13].

Rotavirus Vaccine

Shortly after the first and only rotavirus vaccine was introduced in the USA in 1998 for routine vaccination of infants at ages 2, 4, and 6 months, several reports to the CDC suggested an association between the vaccine and intussusception. This was noted particularly within 2 weeks after vaccination with the first dose. The vaccine was removed from the world market in 1999 [14]. Although under some debate, subsequent sys-

tematic reviews and investigations have either not found higher rates of intussusception after rotavirus vaccination [15–17] or a very low rate of increased cases [18]. Two new rotavirus vaccines are on the global market.

Overall Cost to Society

No data have been identified detailing the total cost to society of intussusception. Three recent surveys have documented practice patterns for the evaluation of intussusception [4, 19, 20]. In centers without pediatric radiologists, the enema is the initial and often only imaging test performed for both diagnosis and treatment. In contrast, at the 2004 SPR annual meeting, a survey of pediatric radiologists showed that 57% now use sonography for initial diagnosis prior to enema [19]. Overall, the total hospital cost for children with intussusception treated with surgery is approximately four times that of those treated with enema [21–23].

Goals of Imaging

The goal of initial bowel imaging is early detection of intussusception to enable enema reduction of the intussusception. Additional imaging studies may be performed to further characterize indeterminate results. The ultimate goal that radiologists should strive for is nonoperative reduction for all children with idiopathic intussusception (approximately 95% cases), but delay in presentation and diagnosis makes this goal elusive.

Methodology

A MEDLINE search was performed using PubMed (National Library of Medicine, Bethesda, Maryland) for original research publications discussing the diagnostic performance and effectiveness of imaging strategies in intussusception. Clinical predictors of intussusception were also included in the literature search. The search covered the years 1966 to June 2016. The

search strategy employed different combinations of the following key terms: (1) *intussusception*; (2) *children, ages under 18 years or pediatric*; (3) *diagnosis or etiology*; (4) *reduction or reduce or therapy or surgery or surgical procedures or treatment or perforation or rupture*; and (5) *enema*. Additional articles were identified by reviewing the reference lists of relevant papers, identifying appropriate authors, and use of citation indices for MeSH terms. This review was limited to human studies and the English language literature. The author performed an initial review of the titles and abstracts of the identified articles followed by review of the full text in articles that were relevant.

Discussion of Issues

What Are the Clinical Predictors of Intussusception?

Summary of Evidence At this point there are no reliable clinical prediction models that can accurately identify all patients with intussusception (limited evidence). Determination of children who should undergo imaging and who should not undergo imaging has not been studied in formal prospective trials.

Supporting Evidence

What Are the Clinical Predictors of Intussusception?

Ideally, children with intussusception should be diagnosed early to avoid bowel necrosis and surgery. However, one report found that only 50% of children were correctly diagnosed at initial presentation to a healthcare provider [24]. The classic triad of colicky abdominal pain (58–100% cases), vomiting (up to 85% cases), and bloody stools is present in less than 25% of children [5, 25]. Guaiac positive stool is present in 75% of children with intussusception [7, 26]. Vomiting or diarrhea may lead to dehydration, which exaggerates lethargy. The mixture of stool, blood, and blood clots has been described as “currant jelly stools” and is suggestive of intussusception.

Kupperman and colleagues published a cross-sectional study that evaluated the clinical factors that might predict intussusception in 115 children (limited evidence) [27]. Using multivariate logistic regression and bootstrap sample analysis, they not only found that the presence of highly suggestive abdominal radiographs, rectal bleeding, and male sex was independent predictors of intussusception but also noted that these factors were not specific. Harrington and colleagues investigated the positive and negative clinical predictors of intussusception in a prospective cohort study (moderate evidence) [5]. They recorded signs and symptoms in 245 children and correlated them with sonographic and enema findings. Significant positive predictive factors for intussusception were the presence of right upper quadrant mass, gross blood in stool, guaiac positive stool, and the triad of colicky abdominal pain, vomiting, and right upper quadrant mass. They were unable to identify significant negative predictors. Klein and colleagues reviewed clinical history, physical exam, and radiographic findings to develop a prediction model of children with possible intussusception (moderate evidence) [28]. Their univariate analysis identified several known factors associated with intussusception, including vomiting, abdominal pain, palpable abdominal mass, guaiac positive stool, and rectal bleeding. However, they concluded that they were “unable to develop a prediction model that would reliably identify all patients with the diagnosis of intussusception. Previously identified predictors of intussusception remain important in increasing suspicion of this important diagnosis. At this point there is no reliable prediction model that can accurately identify all patients with intussusception.”

What Are the Clinical Predictors of Reducibility and Bowel Necrosis?

The most important factor that decreases the reduction rate of enema is a longer duration of symptoms. This finding is supported by multiple case series. A significant delay is typically 48 h, but some reports suggest 24 or 72 h as either one of several factors or the single factor predicting unsuccessful enema reduction [4, 29]. Other fac-

tors associated with lower reduction rates include age less than 3 months, dehydration, small bowel obstruction, and intussusception encountered in the rectum (25% reduction rate) (limited evidence) [4, 24, 25, 29, 30].

Which Imaging Studies Should Be Performed?

Summary of Evidence Ultrasound has higher accuracy in the diagnosis of intussusception than radiographs. Ultrasound also has higher diagnostic accuracy in identifying PLPs than radiographs or enema. The role of ultrasound findings in predicting success of reduction is not well known with available literature. Given current evidence, the diagnostic approach should include (a) abdominal radiographs if concern for other diagnoses such as constipation or for perforation; (b) sonography for diagnosis or exclusion of intussusception; (c) if positive, a surgical consult should be obtained prior to the enema reduction attempt; and (d) air enema reduction (or if no experience with the air technique, liquid enema) (moderate evidence).

Supporting Evidence

What Is the Diagnostic Performance of Abdominal Radiographs?

The presence of a curvilinear mass within the course of the colon (the crescent sign), particularly in the transverse colon just beyond the hepatic flexure, is a nearly pathognomonic sign of intussusception. The absence of bowel gas in the ascending colon is one of the most specific signs of intussusception on radiographs [31]. However, small bowel gas located in the right abdomen on radiographs may mimic ascending colon or cecal gas. Radiographs have low sensitivity and specificity, even when viewed by experienced pediatric radiologists (limited evidence) [31, 32]. Sargent and colleagues [30] reported 45% sensitivity in 60 children when evaluated prospectively by pediatric radiologists, using the enema as the reference standard (Table 36.1). Others report similar poor sensitivity in the detec-

Table 36.1 Summary of sensitivity and specificity of diagnostic imaging for intussusceptions

Test	Sensitivity (%)	Specificity (%)
Abdominal radiographs ^a	45	–
Ultrasound ^b	98–100	88–100
Enema ^c	100	100

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^aData from [4, 31]

^bData from [5, 35, 40, 41]

^cReference standard for ileocolic intussusception (does not include intussusception limited to small bowel); see [29]

tion of intussusception [4]. In a survey of the SPR 2004 attendees, Daneman found that 79% obtain radiographs, but this practice may not be under the control of radiologists [19]. Only 10% of pediatric radiologists in this survey preferred radiographs for the diagnosis.

What Is the Diagnostic Performance of Sonography?

Intussusception can be reliably diagnosed when a “donut,” “target,” or “pseudokidney” sign is seen using linear transducer sonography [33–36]. The optimal US technique in this population is well described [29–33]. There are no known contraindications or complications resulting from US for this purpose. US also plays a role in the evaluation of reducibility of the intussusception, the presence of a PLP mass, and the intussusception limited to small bowel, to diagnose or exclude residual intussusception after enema and to identify alternative diagnoses (limited evidence) [5, 35, 37, 38]. In a 2004 survey, 57% of North American pediatric radiologists reported the use of sonography to diagnose intussusception as compared to 93% of European pediatric radiologists in a 1999 survey [19, 39].

Sonography screening in children has been suggested to reduce cost, radiation exposure, and both patient and parental anxiety/discomfort with enema (limited evidence) [38]. Published series from single institutions suggest high accuracy,

approaching 100% in experienced hands, with sensitivity of 98–100% and specificity of 88–100% (limited evidence) (Table 36.1) [5, 35, 40, 41]. Eshed and colleagues found similar abilities in sonographic diagnosis of intussusception for staff radiologists as well as senior and junior radiology residents: sensitivity and specificity were 85 and 98% for staff radiologists, 75 and 96% for senior residents, and 83 and 97% for junior residents, respectively [42]. Given that the theoretical cost-effectiveness of sonography is dependent on the prevalence of intussusception, optimization of imaging will require stratification of subjects into different levels of probability of intussusception [43]. However, data are lacking for such stratification. Henrikson and colleagues noted a trend of decreased prevalence of intussusception (22%) in those children referred for enema and began sonographic screening (limited evidence). In their small series of 38 children, they were able to avoid 19 enemas in those with negative sonography, resulting in savings in both radiation exposure (an average of 8.2 mGy for negative enemas) and hospital charges [38]. Future cost-effectiveness modeling research will be needed to define the population that should undergo sonography.

What Are the Sonographic Predictors of Reducibility and Bowel Necrosis?

Del-Pozo and colleagues performed sonography in 145 children with intussusception and found that fluid seen inside the intussusception represented trapped peritoneal fluid and was associated with significantly fewer reductions on enema and with bowel ischemia at surgery (limited evidence) [44, 45].

Some US reports have noted that thicker bowel wall was associated with fewer enema reductions [35, 46], but others did not find this association [45]. Lack of color Doppler signal in the intussuscepted bowel wall suggested bowel ischemia in several small series (limited evidence) [47–49].

Free intraperitoneal fluid in small or moderate amounts is present in approximately half of children with intussusception and is not a contraindication for enema [36]. There are conflicting

reports that free peritoneal fluid is associated with fewer reductions [4, 25, 29, 37, 50]. Some descriptive studies report that the presence of lymph nodes trapped in the intussusception is associated with fewer reductions [37, 51]. For these US findings, due to the conflicting reports and/or small series, the evidence is inconclusive.

What Are the Pathologic Lead Points?

Approximately 2–6.3% of intussusceptions in children are caused by PLPs which are due to either focal masses or diffuse bowel wall abnormality. The most common focal PLPs are (in decreasing order of incidence) Meckel's diverticulum, duplication cyst, polyp, and lymphoma (moderate evidence) [1, 4, 52, 53]. Diffuse PLPs are most commonly associated with cystic fibrosis or HSP. Although the common teaching remains that focal PLPs are more common in older children, this is somewhat misleading. The relative prevalence of PLP with intussusception is higher in children over the age of 3 years, particularly for lymphoma. However, the absolute number of PLP in infants versus older children is approximately equal [1].

The detection of lead points by imaging remains problematic [54], although US is the noninvasive standard of reference. Air enema is less likely to identify a PLP as compared to liquid enema [53, 55]. In a systematic review of 27 air enema studies (4791 children) and 33 liquid enema studies (4665 children), air enema had 2% versus 6.2% at liquid enema [53]. In a large, single institution review, 66% of PLPs may be identified at US [56], and 40% of PLPs were diagnosed on liquid enema [4] and only 11% of PLPs at air enema 11% [55], so that some researchers suggest that US be used afterward to search for PLP (limited evidence) [4].

How Should Therapeutic Enema Be Performed?

Summary of Evidence The air enema is considered superior at reduction (moderate evidence), cleaner (based on appearance of peritoneal cavity at surgery when perforation occurs), safer, and

faster, with less radiation when compared to liquid enema (moderate evidence) [26, 57–61]. The recurrence rates for air versus liquid enema reductions do not differ (both are approximately 10%) (moderate evidence) [62]. The “rule of threes” used to guide liquid enema technique is supported by limited evidence. Barium is no longer the liquid contrast medium of choice due to the risk of barium peritonitis, infection, and adhesions when perforation occurs during the enema [26, 50, 58, 63]. Neither sedation nor medications increase the enema success rate (limited evidence). Direct comparison of reduction with fluoroscopy versus ultrasound has not been studied (insufficient evidence).

Supporting Evidence The role of imaging and the pediatric surgical consultation prior to the enema continues to vary across practices despite guidelines and pathways (ACR practice parameter for the performance of pediatric fluoroscopic contrast enema) [64]. In 2014, a regional survey of 30 pediatric surgeons in the Midwest revealed that only one-quarter required surgical consult prior to enema, and ultrasound was used to diagnose intussusception in only 55% of respondent sites [62, 65, 66].

A 2015 meta-analysis by Sadigh et al. summarized the therapeutic outcomes of enema reduction in 32,451 children with intussusception [53]. There were 102 included publications on reduction and/or perforation rates for enema, although most were retrospective. One hundred two published studies with at least 50 cases were largely Level-3 (limited evidence) investigations consisting of unselected but often consecutive case series. The average reduction rate for these 101 included studies was 83% for air (44 studies with over 16,000 children) versus 70% for liquid (52 studies with over 13,000 children) (Tables 36.2 and 36.3) [53]. One of the largest series was excluded from analysis as an outlier; using air enema in 6396 children, it reported reduction rates of 95% [54] (limited evidence). The analysis included a large international data set over four decades that limited conclusions due to heterogeneity of data yet suggested that air enema was a superior technique to liquid enema, regardless of

Table 36.2 Summary of published intussusception enema reduction rates and perforation rates and other outcomes. Air versus liquid enema reduction of intussusception, perforation rates, and rates of first recurrences and at 24 h (excluding direct comparison studies)

	Air				Liquid				P value
	No of studies	No of patients	Rate, % (95% CI)	Heterogeneity, I^2 (%); P value	No of studies	No of patients	Rate, % (95% CI)	Heterogeneity, I^2 (%); P value	
Success (reduction) rate	44	16,187	82.7 (79.9–85.6)	97; <0.001	52	13,081	69.6 (65–74.1)	98; <0.001	<0.001
Perforation rate	38	15,752	0.39 (0.23–0.55)	40; 0.04	30	9429	0.43 (0.24–0.62)	9; 0.87	0.73
First recurrence rate following enema reduction	26	10,494	6.0 (4.5–7.5)	89; <0.001	24	4004	7.3 (5.8–8.8)	71; <0.001	0.01
Recurrence rate within 48 h following enema reduction	9	1586	3.1 (1.1–5.1)	89; <0.001	11	1178	3.2 (1.9–4.5)	44; 0.03	0.93

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No number, *CI* confidence interval, I^2 inconsistency index, *N/A* not applicable

imaging guidance method. Another recent, yet smaller meta-analysis by Beres and Baird evaluated 19 studies that directly compared reduction rates of air versus liquid enema [66]. Although more than half of these studies had less than 50 cases per study arm, they did conclude that air was superior to liquid enema for intussusception reduction. However, while the air enema may be preferred in experienced hands, the liquid enema is also safe and effective. The air enema technique is well described in the literature [59, 61, 67]. Briefly, the enema tip should be placed within the child's rectum and taped in place with abundant tape. The child is placed in a prone position to allow the radiologist or assistant to squeeze the buttocks closed and prevent air from leaking. Air is rapidly insufflated into the colon under fluoroscopic observation. Once the intussusception is encountered, its reduction is followed fluoroscopically until it is completely reduced. Air should flow freely from the cecum into the distal small bowel loops to signify complete reduction. One critical safety issue is to keep air pressure below a maximum limit of 120 mmHg to avoid the risk of perforation [26, 50, 61].

Air Versus Liquid Enema

Two randomized trials comparing outcomes with air versus liquid enema technique exist, yet their conclusions differ, with one stating there is no difference and the other showing the air enema superior to liquid enema (moderate evidence) [68, 69]. Both trials were likely underpowered. In 1999, Hadidi and El Shah reported that air had a higher reduction rate than liquid enema ($p = 0.01$). Children were randomized with less than 48 h of symptoms to saline reduction under sonographic guidance ($n = 47$), air ($n = 50$), or barium ($n = 50$) under fluoroscopic guidance [58]. In 1993, Meyer and colleagues randomized 101 children to air ($n = 50$) or barium ($n = 51$) enema and found success rates of 76% for air and 63% for liquid enema [69]. The results were not statistically significant but suggested air was more effective. In addition, the trial used sedation and had lower reduction rates than those not using sedation [29]. The authors abandoned the use of sedation after this study. The use of sedation may reduce the intra-abdominal pressure children create by the Valsalva maneuver and is reported to improve reducibility at enema [50, 61]. More recent reports of air

Table 36.3 Summary of published intussusception enema reduction rates and perforation rates and other outcomes. Subgroup analysis of air versus liquid enema reduction success rates (excluding direct comparison studies)

	Air			Liquid			P value
	No of studies	No of patients	Rate, % (95% CI)	No of studies	No of patients	Rate, % (95% CI)	
Rate of lead points ^a	27	4791	2.0 (1.3–2.7)	33	4665	6.3 (4.2–8.3)	<0.001
Enema reduction guidance							
Fluoroscopy	23	6038	84 (82–86)	26	3534	68 (62–74)	<0.001
Ultrasound	4	454	89 (79–>99)	7	994	86 (81–91)	0.10
Year of publication							
1970s	0	0	N/A	3	584	73.3 (57.3–89.3)	N/A
1980s	6	9386	82.9 (74.4–91.05)	20	2897	61.1 (52.7–69.6)	<0.001
1990s	17	2961	76.4 (65.5–87.2)	15	1822	73.7 (67.8–79.5)	<0.001
2000s	14	2309	86.6 (83.6–89.6)	12	7052	77.9 (70.2–85.5)	<0.001
2010s	8	2181	77.2 (67.8–86.7)	2	726	65.9 (31.7–1.00)	<0.001
Country of publication							
USA	4	476	74.3 (56.7–92.0)	10	1092	61.3 (54.7–68.0)	<0.001
Non-USA	40	15,711	83.5 (80.7–86.3)	42	11,989	71.5 (66.2–76.7)	<0.001
Type of hospital							
Children's	26	12,666	83.1 (79.4–86.7)	19	2191	69.1 (63.5–74.6)	<0.001
Non-children's	18	3521	82.3 (77.7–87)	33	10,890	69.8 (63.3–76.2)	<0.001
Recruitment							
Consecutive	13	1774	80.7 (74.3–87.1)	9	1393	75.6 (66.8–84.3)	<0.001
Nonconsecutive	30	14,132	83.4 (80.1–86.7)	42	11,601	67.8 (62.6–73)	<0.001
Prospective	16	4674	83.6 (79.4–87.9)	8	809	79.9 (70.5–89.3)	0.01
Retrospective	28	11,513	82.1 (78.2–86)	44	12,272	67.7 (62.8–72.6)	<0.001

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No number, *CI* confidence interval, *I²* inconsistency index, *N/A* not applicable

^aThis rate is not limited to the patients who had unsuccessful enema reduction. Rather, this rate is among all the patients evaluated in each study; some of them underwent primary surgery and not enema reduction

reduction show better results than liquid enema reduction as discussed above [1, 53]. The superior air enema results may be due to the level of experience of those who use air reduction techniques as well as the presence of higher intraluminal pressure for air as compared to standard hydrostatic reduction [70, 71].

In a 1991 survey of American pediatric radiology chairs, Meyer found that only 24% were using air enema, but 64% used barium and 12% water-soluble contrast [20] as compared to 35% of international pediatric radiologists who used air enema [72]. More recently, in 2004, 65% of American pediatric radiologists reported using air enema, 33% used liquid enema (water-soluble contrast or barium), and 3% used liquid enema with sonographic guidance [19]. Some pediatric radiologists will use air for children older than 3 months, but for younger infants, especially neonates, they prefer liquid contrast due to the greater differential diagnosis in this group [29].

All children should have surgical consultation prior to enema (a) to assess for peritoneal signs precluding enema, (b) to identify children who cannot be reduced with enema or who are found to have perforation, and (c) for postreduction management. Prior to enema reduction, dehydration should be treated with intravenous fluid resuscitation. Children with evidence of peritonitis, shock, sepsis, or free air on abdominal radiographs are not candidates for enema. Radiologists should strive for enema reduction rates of 80%, but it will depend on their patient population (moderate evidence). Several reports estimate that the rate of spontaneous reduction based on sonographic and/or enema diagnosis prior to surgery is 10% (limited evidence) [1, 25, 46, 55].

Bratton and colleagues suggest that more experienced radiologists and caregivers at children's hospitals decrease the risk of surgical reduction, length of hospital stay, and cost of care (moderate evidence) [21]. Surgical management is performed when the patient is too unstable (shock, dehydration, or sepsis) for enema reduction, when the enema is unsuccessful, or when PLP is diagnosed.

The Rule of Threes

A general guideline to the liquid enema technique, often taught to radiology residents, is the "rule of threes": three attempts of 3-min duration, with the liquid enema bag at 3 ft. above the fluoroscopy table. There is little evidence to support this rule, particularly regarding the height of the enema bag [29, 73]. Many experienced pediatric radiologists alter this general guide in response to the clinical status of the patient and the movement of the intussusceptum mass achieved with the initial enema [25, 73]. For example, if the intussusception is partially reduced to where it most frequently hangs up, at the ileocecal valve, some radiologists will make further or longer attempts and/or raise the enema bag above 3 ft. The exam is tailored to the patient and performed in conjunction with the surgeon involved.

Radiation Dose

The dose deposited will depend on a number of factors, including the type of fluoroscopy equipment, the use of pulsed fluoroscopy, and the fluoroscopy time [1, 50]. A 1993 study reported a very low mean effective dose of 0.055 mSv for enema reduction of an intussusception [74]. Experienced pediatric radiologists using air enema averaged 95 s of fluoroscopy time to reduce an intussusception and 42 s to exclude one in a child without intussusception [61]. Air enema radiation doses average one-third to one-half less the dose for liquid enema [50].

Alternative Enema Approaches

A number of different approaches have been described to try to improve intussusception reduction on enema that include sedation, anesthesia, use of glucagon, manual palpation, and delayed repeat enema. In the past, sedation and sometimes anesthesia were commonly used to improve reduction rates, but case series showed no improvement (limited evidence) [1, 75, 76]. In a 1991 survey Meyer found that only 10% of respondents used sedation either always or almost always [20] as compared to 54% of international pediatric radiologists, and those using sedation reported lower reduction rates [68].

Therefore, few pediatric radiologists currently use sedation in the USA. Glucagon was shown not to improve enema reduction rates in one study [77] and is no longer used [20]. The use of manual palpation has been suggested to improve intussusception reduction at enema but has not been systematically studied [50, 78]. One study by Grasso et al. reported a reduction rate of 76% when manual palpation was used, less than the average of 80% in large series [78].

Fluoroscopy Versus Sonography Guidance

In the West (i.e., North America, parts of Europe, Australia), fluoroscopy is almost always used during enema reduction. There are increasing reports, primarily from Asia and Europe, on the use of sonography with either water [79–85] or air (77–79) [86–88] that show reduction rates as high as or higher than those using fluoroscopy. However, the experience level required for these techniques has not been studied nor has the ability of sonography to detect perforations (limited evidence).

Delayed Repeat Enema (DRE)

In the 15–30% of children who fail initial enema reduction, delayed repeat enema may avoid the need for surgical reduction. The use of delayed attempts at between 30 min and 19 h after initial attempt has shown promise in increasing the success of enema reductions (limited evidence) [89–93]. These four small series showed further reduction rates of 50–82% by waiting at least 30 min prior to further attempts at enema reduction. Further research to understand optimal timing and technique for delayed repeat enemas is needed. Daneman and Navarro, with the largest reported experience to date, suggest a delay of 2–4 h until further research yields more rigorous guidelines [29]. The child must remain clinically stable and be appropriately monitored during this time interval. Delayed enema should not be performed if the initial enema does not move the intussusception at all [29, 92]. A 2015 larger study, comparing DRE (502 children) with immediate surgery (1407 children) after failed enema, showed decreased need for surgical inter-

ventions, bowel resection, and length of hospital stay [94].

Where Should Patients Be Treated?

The meta-analysis by Sadigh et al. did not show a difference in air or liquid reduction rates or perforation rates by children's hospital or community hospital locations. There were, however, more publications using air enema techniques at children's hospitals compared to non-children's hospitals.

Bratton and colleagues performed a retrospective cohort analysis of all children hospitalized with intussusception in the state of Washington from 1987 through 1996 (moderate evidence) [21]. They investigated whether the rate of surgical management for these children varied by hospital pediatric caseload, measured by the annual number of pediatric hospital admissions. By reviewing the discharge data of all 507 children, they found an overall rate of surgical reduction of 53%, with 20% undergoing bowel resection. Rates of surgical reduction varied by pediatric caseload from 36% at hospitals with large pediatric caseloads to nearly double, 64%, at hospitals with low pediatric volumes. Children who underwent surgery versus enema reduction had similar gender and median age characteristics, but those who had bowel resection were more likely to have coexisting conditions. Median cost of hospital care for these children was \$5724 for surgical reduction and \$1184 for enema reduction.

What Are the Complications of Enema Therapy?

The most important potential complication of enema is bowel perforation. One hundred one published studies of this question were largely Level-3 (limited evidence) investigations consisting of unselected but often consecutive case series (Tables 36.2 and 36.3). For the 38 air enema publications, the combined perforation rate was 0.39%, 95% CI 0.23–0.55%, and for the 30 studies of children undergoing liquid enema, the combined perforation rate was 0.43% (95% CI 0.24–0.62%) [53]. There were no statistically significant differences between air and liquid enema perforation rates (Tables 36.2 and 36.3).

Ultimately, however, the risk of perforation depends on each radiologist's patient population and technique. Though determination of clinical predictors of perforation is complicated by lack of prospective studies, the one acknowledged key factor is symptom length greater than 48 h. Several reports in both pig models and children suggest that there may be preexisting focal perforation in the necrotic intussusciens or, less commonly, the intussusceptum that is rarely radiographically apparent as free air (moderate evidence) [24, 26, 29, 95–98]. The most common site is at or just proximal to the intussusception in the transverse colon [98]. Perforations with air tend to be smaller than those with liquid enema although the overall perforation rates are similar [26, 96].

In 1989, Campbell surveyed enema techniques and complications of North American pediatric radiologists [99]. Respondents' combined experience was 14,000 intussusception enemas. Although they did not report enema reduction rates, the combined perforation rate was 0.39% (55/14,000), with only one death. This study remains the basis for the risk of perforation that is explained to parents for consent prior to enema reduction (1 in 250 to 1 in 300) (limited evidence).

Barium is no longer the liquid contrast medium of choice for reduction of intussusception due to the risk of barium peritonitis, infection, and adhesions when perforation occurs during the enema (moderate evidence) [26, 50, 58, 63]. While iodinated contrast is now preferred and is considered a safer agent than barium, one should be aware that it may produce fluid and electrolyte shifts if perforation occurs, since contrast is absorbed from the peritoneum.

One complication unique to air enema is the tension pneumoperitoneum. In an early report, two deaths occurred from this complication, leading the proponents of air enema to advise having an 18-gauge needle readily available in the fluoroscopy room for emergent decompression [29, 50, 58]. Although theoretically possible, there have been no reports of air embolism.

What Are the Surgical Management and Complications?

Depending on the patient population, approximately 20–40% of children who undergo surgical reduction of their intussusception will require bowel resection [20% (17); 30–40%] [1]. If we estimate that 20% of children with intussusception will fail enema reduction and undergo surgical reduction, then only 4–8% of all children will require bowel resection. Ideally, only this population should need surgical intervention.

Short-term complications from laparotomy include infection and bowel perforation. The long-term risk of small bowel obstruction from adhesions is approximately 8% for neonates and 3–5% for those children older than 1 month [100].

Cost-Effectiveness Analysis

There are no known rigorous economic analyses on diagnosis and treatment strategies for intussusception, although one study evaluated the cost savings of more aggressive enema reduction compared to surgical reduction [23]. Stein and colleagues analyzed single institution billing records of 703 children with intussusception to compare government DRG reimbursements of hospital care in Australia (limited evidence). In 1993 Australian dollars, the government paid, on average, \$727 for enema reduction and \$4514 for surgical reduction in hospital care. With the broader indications for enema and the increased use of air, they noted decreased use of surgical reduction at their institution: in 1983, 65% children underwent surgical reduction decreasing to 25% in 1992 [23]. Ironically, the authors noted that hospital profit, however, is greater for surgical reductions.

What Is Appropriate Management in Recurrent Cases?

Summary of Evidence Overall intussusception recurrence rates average 12.7%, not significantly different for air versus liquid enema or sonographic versus fluoroscopic guidance techniques (moderate evidence) [62]. The recurrence rates

after surgical reduction are lower and range up to 5%, presumably due to the development of adhesions [101]. Repeat enema is both safe and effective in recurrent intussusception [1, 50, 53, 62, 101, 102] as long as the child remains clinically stable (limited evidence). There is insufficient evidence to support any particular approach beyond the performance of the enema and referral to a surgeon for shared decision-making with the patient.

Supporting Evidence In a meta-analysis of recurrences, Gray et al. summarized 16 studies for overall, 24 h, and 48 h recurrent intussusception rates after air, liquid, fluoroscopic, and sonographic-guided reduction methods. The goal was to understand the safety of outpatient management of this patient population. Recurrence rates at 24 h were 3.9%, 3.9%, and 2.4% for liquid enema, ultrasound-guided air enema, and fluoroscopic air enema, respectively. At 48 h, these rates were 5.4%, 6.6%, and 2.7%, respectively. In the meta-analysis by Sadigh, a secondary outcome evaluated recurrences (Tables 36.2 and 36.3). Nine of 44 air enema studies (20%) and 11 of 52 liquid enema studies (21%) reported recurrences within 48 h after enema. Among 1586 children from 9 air enema studies, the rate of intussusception recurrence within 48 h after enema reduction was 3.1%, while among 1178 children from 11 liquid enema studies, the rate of intussusception recurrence at 48 h was 3.2% (95% CI 1.9–4.5%). Like the Gray analysis, these combined early recurrence rates were not significantly different. Fifty percent of children who develop recurrent intussusception will present within 48 h, although recurrences have been reported up to 18 months later (limited evidence) [58]. No clear risk factors are known for why some children have recurrences although some have focal PLP. In those with PLP, children with diffuse bowel abnormality such as cystic fibrosis, HSP, or celiac disease may be treated with enema reduction more aggressively than those with focal PLPs.

The risk of PLP in children with recurrent intussusception is low. In one large series of 763 children, it was 8% (5/69) [58], only slightly

higher than the reported 5–6% incidence of PLP at first presentation of intussusception (insufficient evidence) [1]. No predictive clinical factors have been identified for PLP in these children with recurrent intussusception. Reduction with air enema was possible in 95% of recurrences in the largest reported experience (limited evidence) [1, 58].

When there is concern for PLP, sonography may play an important role and may detect 60% of PLPs (limited evidence) [1, 48, 101]. While US will not detect all PLPs, the risk of missing a PLP without other signs or symptoms to guide management is unlikely [52]. Ein reviewed 1200 intussusception cases covering 40 years' experience at 1 institution to analyze this risk. When the enema failed to detect lymphoma as a PLP, Ein noted the presence of clinical signs of illness of greater than 1 week, patient age greater than 3 years, weight loss, and palpable mass in all of these children (limited evidence).

In a randomized, double-blind trial comparing 144 children who received intramuscular corticosteroids versus 137 who received placebo before air enema reduction, Lin and colleagues reported significantly fewer intussusception recurrences at 6 months (moderate evidence) [3]. In both groups, the initial reduction rate was 85%. There were no recurrences in the children who received dexamethasone, compared to 5% in the placebo group. They hypothesized that steroids decreased the volume of mesenteric adenopathy and lymphoid hyperplasia in the terminal ileum and thus the risk of recurrence. However, further investigation of the risks and benefits of this intervention is needed.

Special Case: Intussusception Limited to the Small Bowel

With the increasing use of multi-detector CT scanners, radiologists are reporting more frequent presence of small, asymptomatic small bowel–small bowel intussusception [2, 93] (limited evidence) [2, 103]. These intussusceptions are typically transient, and, since the children are

asymptomatic, they are of no known clinical significance.

There is little evidence in the literature regarding the optimal diagnosis and treatment of symptomatic intussusception limited to the small bowel. Most authors agree, however, that the diagnosis is more difficult both clinically and radiologically [1, 25, 30]. Small bowel intussusceptions are unlikely to have associated abdominal mass or rectal bleeding. Treatment is virtually always surgical reduction. Special risk factors for small bowel intussusception include the early postoperative period after either intraperitoneal or retroperitoneal surgery, the presence of long enteric feeding tubes, diffuse PLP (cystic fibrosis or HSP), and small bowel polyps (limited evidence) [1, 30, 104].

Special Case: Intussusception with a Known Lead Point Mass

The optimal imaging approach to children with intussusception and known PLP is unknown. However, Daneman surveyed the SPR members at their 2004 annual meeting and found that 76% of respondents attempt reduction in these patients [19]. Some surgeons may request enema reduction in these children to partially reduce the intussusception and perhaps decrease the laparotomy incision size [91]. There is insufficient evidence to support any particular approach beyond referral to a surgeon for shared decision-making with the patient and, if requested, the performance of an enema [29, 68, 102].

Take-Home Tables

Table 36.1 summarizes the sensitivity and specificity of diagnostic imaging for intussusception. Table 36.2 summarizes the published intussusception enema reduction rates and perforation rates. Table 36.2 summarizes the comparison of air versus liquid contrast enema reduction and perforation rates; Table 36.3 summarizes the subgroup analysis of air versus liquid enema reduction success rates.

Imaging Case Study

Case 1

Figures 36.1 and 36.2 present the case of a 9-month-old boy who comes to the emergency department with a 1-day history of irritability, vomiting, and intermittent crying.

Suggested Imaging Protocol

Ultrasound for Clinically Suspected Intussusception

If there is a concern for alternative diagnoses such as constipation, 1–2 view abdominal radiographs (supine or prone and decubitus) (limited evidence) are often performed. The abdomen is scanned with a 5 MHz or higher linear transducer using the graded compression technique and a bowel or high-contrast application package. All four



Fig. 36.1 Linear sonography of the right mid-lower abdomen demonstrates the target sign of bowel intussusception. There is bowel within bowel and thickened walls of these loops due to edema. No primary lead point (PLP) is identified (Reprinted with the kind permission of Springer Science + Business Media from Applegate KE. Intussusception in children: diagnostic imaging and treatment. In Santiago LS, Blackmore CC (eds): *Evidence-based imaging: optimizing imaging in patient care*. New York: Springer Science + Business Media, 2006)

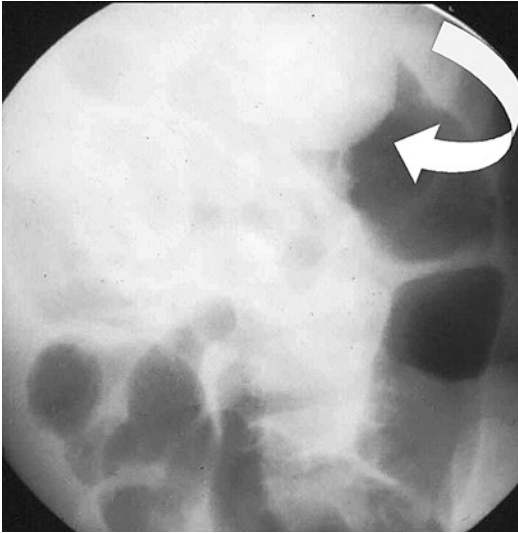


Fig. 36.2 The appearance of the intussusception at air enema reduction. The intussusception is encountered at the hepatic flexure, with the baby in a prone position (arrow). Air is insufflated into the rectum to push the intussusception retrograde until it is no longer seen on fluoroscopy, and there is air in multiple loops of small bowel (Reprinted with the kind permission of Springer Science + Business Media from Applegate KE. Intussusception in children: diagnostic imaging and treatment. In Santiago LS, Blackmore CC (eds): *Evidence-based imaging: optimizing imaging in patient care*. New York: Springer Science + Business Media, 2006)

quadrants of the abdomen must be scanned, typically in transverse planes, beginning with the right upper quadrant, to exclude an intussusception mass.

Air Enema for Reduction

Prior to performing the enema, consult the surgeon (moderate evidence). (If no experience with air or few cases seen per year, then perform liquid enema with water-soluble contrast using the guide of the “rule of threes” described previously.) The enema tip without a balloon should be placed within the child’s rectum and taped in place with abundant tape. With the child prone, the radiologist squeezes the buttocks closed to prevent air leak. Air is rapidly insufflated into the colon under fluoroscopic observation until the

intussusception is completely reduced, when air flows freely from the cecum into the distal small bowel loops. Air pressure must remain below a maximum limit of 120 mmHg to avoid the risk of perforation. Repeat enema for recurrences, including multiple recurrences (limited evidence).

Future Research Studies

- Investigate the optimal technique and timing of delayed, repeat enema reduction.
- Investigate the role of corticosteroids to decrease the rate of recurrence in a prospective controlled trial.
- Perform cost-effectiveness analyses of the role of US for the diagnosis of intussusception. This investigation would include the question: At what disease prevalence or individual case probability is US cost-effective prior to enema?

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Clinically Suspected Malrotation in Infants and Children: Evidence-Based Emergency Imaging

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Key Points

- Malrotation of the bowel is associated with risk of intestinal volvulus and can be fatal (strong evidence). Volvulus is a surgical emergency that is treated with the Ladd procedure (strong evidence).
- Infants and children diagnosed with symptomatic malrotation (without volvulus) should undergo Ladd procedure to fix the bowel and prevent future volvulus and intestinal obstruction from Ladd's bands (moderate evidence).
- Although consensus is lacking, asymptomatic children beyond infancy should undergo prophylactic Ladd procedure to avoid catastrophic midgut volvulus (limited evidence).
- The imaging test of choice is the upper gastrointestinal (UGI) series to diagnose or exclude malrotation (moderate evidence).
- 15–30% of UGI studies in children are indeterminate for malrotation versus normal variation due to the overlap of normal findings with malrotation, the

lack of consensus on UGI positive findings and technique, and the lack of consensus for when surgeons should perform prophylactic Ladd procedure (insufficient evidence).

Definition and Pathophysiology

Malrotation is a congenital, abnormal rotation of the bowel, usually both small and large bowels, within the peritoneal cavity. There is accompanying abnormal fixation by mesenteric bands, or there is absence of fixation of portions of the bowel, and this leads to an increased risk of acute or chronic volvulus, obstruction, and bowel necrosis. Malrotation has been diagnosed prenatally as well as incidentally at autopsy in the elderly [1, 2]. Intestinal malrotation covers the entire range of intestinal anomalies from readily apparent omphalocele in the newborn to asymptomatic “nonrotation” of the large and small bowels in an adult. While the large majority of individuals become clinically symptomatic as infants, an important minority occurs beyond infancy and without the typical clinical presentation of bilious vomiting [3–5].

The greatest concern in the patient with malrotation is volvulus. When there is malrotation,

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the mesenteric attachment of the midgut (the bowel from the ligament of Treitz to the distal transverse colon) is abnormally short or deficient. The gut can then twist clockwise around the SMA and lead either to intermittent abdominal distention and pain or acute bowel necrosis and perforation if the twist remains fixed [2, 6, 7]. Catastrophic volvulus results in ischemia of the entire midgut, and if the patient survives, they will need total parenteral nutrition until small bowel transplant.

Epidemiology

While pediatric healthcare workers are universally aware of the devastating potential complications from malrotation, it is not a common condition. The Centers for Disease Control and Prevention (CDC) survey registry of birth defects estimates that the prevalence of malrotation in infants under the age of 1 year is 3.9 per 10,000 live births [8]. Pediatric surgeons report that malrotation occurs more frequently, in approximately 1 in 500 live births in the United States, although this rate likely overestimates true incidence due to selection bias [9, 10]. There is a slight male predominance in malrotation incidence but no significant difference in incidence in Caucasian versus black infants in the United States.

Malrotation is a diagnosis usually made in the newborn and young infant; 60–75% of cases occur within the newborn period and up to 90% of cases occur within the first year of life [5, 10–13]. Malek and Burd used a national inpatient sample and excluded incidental Ladd procedures to estimate the incidence of urgent Ladd procedures in both infants and older children. They reported 5.3 per 1,000,000 or 362 annual cases of urgent Ladd procedures in American children older than 1 year, representing only 10% of all cases [5]. Therefore, there are approximately 3620 cases or 53 per 1,000,000 American children who undergo urgent Ladd procedure for malrotation each year.

Malrotation has a variable presentation and appearance, making it more difficult to have consensus on its clinical diagnosis and management

[14–17]. The classic presentation of malrotation associated with either duodenal obstructive bands or midgut volvulus in the newborn is bilious vomiting [7, 10, 18]. Volvulus is more common in infants and associated with a high rate of bowel necrosis and resection—44% and with high mortality—28% [19]. When there is midgut volvulus and small bowel necrosis, the baby may have short gut syndrome and dependence on total parenteral nutrition. Mortality in affected newborns was approximately 30% in the 1950s and 1960s [12, 19] but since then has markedly decreased to 3–5% today [19, 20].

The Ladd procedure is the standard surgery to treat malrotation with or without volvulus in infants and children. The surgeon detorses the volvulus (usually in a counterclockwise fashion), cuts the adhesive and, sometimes obstructing peritoneal bands, places the colon in the left abdomen and the small bowel in the right abdomen, and performs an incidental appendectomy. There is a small risk of recurrent volvulus with reports of 5% [21], 3.5% [22], and 1.8% [23].

Associated congenital anomalies are common, reported in up to 62% of cases, and usually involve the gastrointestinal tract (Table 37.1) [9, 13]. The most commonly reported anomalies not

Table 37.1 Syndromes associated with intestinal malrotation

Apple peel intestinal atresia
Brachmann-de Lange syndrome
Cantrell syndrome
Cat eye syndrome
Chromosomal abnormalities (13, 18, 21, etc.)
Coffin-Siris syndrome
Down's syndrome
Familial intestinal malrotation
FG syndrome
Heterotaxy syndrome (asplenia, polysplenia)
Marfan syndrome
Meckel syndrome
Mobile cecum syndrome
Prune belly syndrome

Adapted with permission from Taybi H, Lachman R. Radiology of syndromes, metabolic disorders, and skeletal dysplasias, 3rd ed. Chicago, IL: Yearbook Medical Publishers, 1990; 825–826

Table 37.2 Associated anomalies reported with malrotation

Absence of kidney and ureter
Biliary atresia
Congenital diaphragmatic hernia
Duodenal or small bowel stenosis or atresia
Duodenal web
Gastroschisis
Hirschsprung's disease
Imperforate anus
Intestinal pseudoobstruction
Intussusception
Malabsorption
Meckel's diverticulum
Omphalocele
Pyloric stenosis

Adapted with permission from Jamieson D, Stringer D. In Babyn PS (ed.). *Pediatric Gastrointestinal Imaging and Intervention* 2nd ed. Hamilton, ON: Decker, 2000; 311–332

only involve the duodenum (atresia and web), in 10% of cases, but also include Meckel's diverticulum, other intestinal stenoses or atresias, and Hirschsprung's disease [10, 13, 20]. There are a number of syndromes that have a higher risk of malrotation that include Down's syndrome and the heterotaxy syndrome (Table 37.2). Malrotation is obligate with omphalocele, gastroschisis, and left-sided congenital diaphragmatic hernia.

Overall Cost to Society

The cost of the imaging, evaluation, and care of patients with suspected malrotation in the United States is unknown. Since it is a rare condition with less than 400 urgent Ladd procedures per year, the cost of acute care is likely low. However, long-term costs and impact on quality of life for the minority with short gut syndrome and multivisceral transplants would be significant as well as readmissions both in the short term and in the long term for bowel obstruction caused by mesenteric adhesions [24]. Murphy and Spanon [24] report 26% of patients who underwent Ladd procedure at a tertiary hospital were readmitted

within 6 months after Ladd procedure, while 13% of patients required multiple readmissions and at least one surgery each to lyse adhesions. Neonates are more likely to develop adhesions compared to older children and adults.

Goals

In acutely symptomatic infants and children, the immediate goal of initial bowel imaging is to detect potentially life-threatening volvulus, enabling urgent surgical intervention and preventing bowel ischemia that may lead to either death or short gut syndrome in those who survive. Imaging to detect those infants and children with malrotation who are at risk of life-threatening volvulus is performed to allow non-urgent surgical treatment with the Ladd procedure. Additional imaging studies, such as repeat UGI series or enema to document the position of the cecum, may be performed to further characterize indeterminate results.

Methodology

A MEDLINE search was performed using PubMed (National Library of Medicine, Bethesda, Maryland) for original research publications discussing the diagnostic performance and effectiveness of imaging strategies in. Clinical predictors of malrotation with volvulus were also included in the literature search. The search covered the years 1966 to June 2015. The search strategy employed different combinations of the following key terms: (1) *malrotation*, (2) *volvulus*, (3) *radiography* or *imaging* or *gastrointestinal series*, (4) *sensitivity* and *specificity*, (5) *intestinal obstruction*, (6) *diagnosis*, and (7) *evidence based*. Additional articles were identified by citation indices and review of the reference lists of relevant papers. This review was limited to human studies and the English language literature. The author performed an initial review of the titles and abstracts of the identified articles followed by review of the full text in articles that were relevant.

Discussion of Issues

What Are the Clinical Predictors of Malrotation and Volvulus?

Summary of Evidence Neonates will present with vomiting that is either bilious or will progress to bilious in 95% of cases [13, 20, 25]. Most neonates have volvulus at surgery (moderate evidence). Most children older than 1 year have abdominal pain as the major presenting symptom. However, the presentation of malrotation in older children is much more varied and non-specific, and this leads to long delays in diagnosis (moderate evidence). There are no clinical or imaging predictors for volvulus in patients with malrotation, although some subtypes of malrotation have higher risk of volvulus than others (moderate evidence).

Supporting Evidence The hallmark of malrotation presenting in the neonate is bilious emesis [20, 25]. When malrotation presents with bilious emesis, there is likely volvulus or bowel obstruction from adhesive bands. Bilious emesis suggests obstruction below the insertion of the common bile duct and in the newborn should be attributed to bowel obstruction until proven otherwise. It can be seen in any cause of bowel obstruction from the duodenum to the rectum (e.g., Hirschsprung's disease) as well as ileus [26, 27]. However, in two series of neonates with bilious emesis, only 20% [26, 27] and 38% [27, 28] of them had intestinal obstruction that required surgery.

Approximately 10% of symptomatic malrotation will occur beyond infancy. Catastrophic volvulus of the midgut (with bowel ischemia), while less common than that in infants, occurs in both children and adults [28–32]. In children older than 1 year, the clinical presentation is quite variable and leads to long delays in diagnosis—with reports up to 5 years [33–36]. Most children older than 1 year have abdominal pain as the major presenting symptom which is non-specific. Abdominal physical exam is unremarkable in 85% of these children at initial presentation [25].

The absence of abdominal distension, presence of diarrhea, or a normal abdominal radiograph do not exclude malrotation. The range of reported presentations of malrotation with or without volvulus include chronic intermittent pain, vomiting, failure to thrive, chylous ascites, diarrhea, malabsorption, internal hernia, malnutrition, mesenteric lymphocele, pneumonia, and pneumatosis [11–14, 36–38]. Malrotation is also reported incidentally in asymptomatic adults [13, 32, 39].

Who Should Undergo Imaging and What Is the Diagnostic Performance of Imaging in the Diagnosis or Exclusion of Malrotation?

Summary of Evidence All infants and children with clinical suspicion of malrotation should undergo UGI series if they are clinically stable. The upper gastrointestinal (GI) series examination is the gold standard for radiographic diagnosis of malrotation and volvulus, and it is often the only imaging test performed (moderate evidence) [11–14, 20, 40]. The technique and interpretation must be meticulous to diagnose or exclude malrotation because of the variation of normal that overlaps malrotation. There is a lack of consensus in the radiology community on which images and views are necessary although the American College of Radiology has a pediatric UGI guideline [41]. Published case series from single institutions report false-positive rates of approximately 15% and false-negative rates of 3–7% for the diagnosis of malrotation on UGI (Table 37.3) [10, 15, 42, 45, 46, 54].

Supportive Evidence When an infant presents with signs and symptoms that strongly suggest malrotation with volvulus, surgeons will not use imaging and take the infant directly to the operating room. If the clinical presentation is less acute, they may request an abdominal radiograph and UGI series.

Abdominal Radiographs

While commonly performed in infants and children with vomiting, plain radiographs are neither sensitive nor specific for the diagnosis of malrotation with volvulus. Radiographs of patients with malrotation and volvulus range from normal to distal bowel obstruction [11–13, 18, 55]. When volvulus or obstruction is present, the most common appearance is of gas in the stomach and a paucity or total lack of other bowel gas.

UGI Series

The UGI series is a fluoroscopic study with barium (or in very ill patients, sometimes iodinated contrast is used) to visualize the anatomy and peristalsis of the stomach and duodenum. It is an inexpensive, easy to perform, and widely available test. The UGI series remains the imaging gold standard for the diagnosis of malrotation with or without volvulus. Yet, when compared to surgical findings, there are known false-positive and false-negative results (Table 37.3). Long et al. reported a 15% false-positive rate in a series of 81 infants and children undergoing a Ladd procedure after UGI study reported malrotation (limited evidence). They also stated that the most common reason for false-positive UGIs was the failure to recognize normal variations that mimic malrotation. These variations include a “wandering” duodenum, a mobile duodenum, and “duodenum inversum” [45, 46]. The inferior displacement of the normal duodenal–jejunal junction (DJJ) is often seen in infants and children from dilated adjacent stomach, small and large bowels, the presence of a feeding tube, as well as from enlargement of the spleen or liver [3]. Finally, the UGI study has known false-negative results reported 2–7% of the time (Table 37.3). Long notes that in those 2% of the malrotated cases with a normal position of the DJJ, the cecal position was not normal [45, 46].

Contrast Enema

The contrast or barium enema was the primary imaging test to diagnose or exclude malrotation in the mid-twentieth century until research showed the UGI to be more accurate [6, 7, 40,

Table 37.3 Diagnostic performance of imaging for malrotation (based on single institution case series with references in parentheses); Oxford evidence levels ranging up to 2b

Test	Sensitivity (%)	Specificity (%)
UGI series (range)	93–98	79–93
	93 [42, 43] 95 [10] 96 [44] 97 [15] 98 [45, 46] 98 [47]	79 [44] 85 [15] 85 [45, 46] 93 [48]
Barium enema (abnormal cecal position) (range)	60–87	
	87 [44] 84 [45, 46] 80 [49] 69 [42] 68 [50] 60 [43]	87 [15]
Ultrasound of SMA–SMV relationship (on axial view)	67 [51, 52] 67 [53] 98 ^a [47]	79 [47]

^aDoes not include those patients where the SMA/SMV were not visible due to overlying bowel gas

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56]. The enema is performed to show the position of the entire colon but in particular to show whether the cecum is normally positioned in the right lower quadrant of the abdomen. Problems with this approach include (a) the presence of a variant of normal, the mobile cecum in 15% of all age groups, (b) the laxity of peritoneal ligaments in infants and young children may allow the cecum to be displaced by dilated bowel, a cause of false positive, and finally, (c) normal cecal position in 13–40% of malrotated patients (Table 37.3). Compare this false-negative rate for the enema of 13–40% to that of the UGI false-negative rate of 2–7%. The false-positive rate of enema (13%) [15] is similar to that for UGI

(15%). While the enema is not the preferred imaging test for malrotation, it is useful in uncertain cases at UGI to document cecal position.

Cross-Sectional Imaging (US, CT, and MR)

Yousefzadeh et al. have suggested that sonography may be equivalent to the UGI series diagnosis or exclude malrotation [57]. They describe the importance of documenting the third portion of the duodenum as it passes between the SMA and aorta. Confirmation of this result has not been published. Diagnostic performance of the relative positions of the SMA and SMV on US (and cross-sectional) imaging is lower than that of the UGI but can reveal malrotation in children with non-specific abdominal symptoms. The SMV is normally located anteriorly and to the patient's right of the SMA. When the SMV is to the left, this relationship is the reverse of normal or if the SMV is directly anterior to the SMA, it raises the possibility of malrotation [51, 53, 58, 59]. When the SMV is directly anterior to the SMV, Dufour et al. reported that 28% of these cases had malrotation [53]. False positives occur and include patients with scoliosis. Further, up to one-third of cases of malrotation have a normal SMA–SMV relationship [51, 53]. Finally, the technical feasibility of visualizing the SMA/SMV relationship depends on the ability of the sonographer, the cooperation of the child, and the amount of overlying bowel gas that may obscure it. A US study of over 300 children showed that in 26% it could not depict the SMA/SMV relationship [58]. Therefore, ultrasound is inadequate for this diagnosis (limited to moderate evidence).

Similar to US, the SMA/SMV anatomic relationship has been reported in normal and malrotated patients using CT and MR [52, 60–62]. In one CT study of 166 patients, 89% of normal patients had a normal SMA/SMV relationship [52].

Volvulus: Diagnostic Performance of UGI, Sonography, and CT

Volvulus can be an intermittent phenomenon, and therefore its imaging detection does not always

correlate with the surgical findings in several series. The UGI study has a sensitivity of 54% [49] to 79% [44]. On UGI, a corkscrew appearance with proximal duodenal obstruction is the typical finding indicating volvulus. The “Z” shape of the duodenum can mimic volvulus but represents malrotation and duodenal obstruction from Ladd's bands [63].

Imaging is specific for the finding of a swirling pattern of small bowel and mesentery around the SMA and has been reported with sonography and CT in addition to UGI. Several reports describe the “whirlpool” sign first on US [64, 65] and then on CT of midgut volvulus confirmed at surgery [66].

There are several additional sonographic signs of midgut volvulus that have been measured by Chao et al. [Oxford evidence level 2b] [67]. They performed a prospective 3-year study of 31 neonates with suspected malrotation that demonstrated a sensitivity and specificity of duodenal dilation with tapering configuration for detecting volvulus were 89% and 92%, respectively; of fixed midline bowel, 89% and 92%; and of dilation of distal superior mesenteric vein, 56% and 73%. The whirlpool sign had sensitivity and specificity of 89% and 92%;

How Should the UGI Series Be Performed?

Summary of Evidence The UGI series must be performed with careful attention to anatomic detail that includes the patient positioning and the limited use of barium. It is critical to be familiar with the variation of normal and the subtle signs of malrotation (limited evidence) [44–46, 68].

Supporting Evidence The critical anatomy that the UGI documents is the position of the duodenal–jejunal junction (DJJ) which is located to the left of the left vertebral body pedicle at the L1 or L2 level and posterior on the lateral view. There is overlap of the UGI appearance of subtle malrotation with that of normal variations, and some

estimate that 15% [3] to 30% [13] of UGI studies may be indeterminate. Long noted that the most common reason for false-positive UGIs was the failure to recognize normal variations that mimic malrotation. These variations include a “wandering” duodenum, a mobile duodenum, and “duodenum inversum” [13, 18, 45, 46, 68]. One of the most common reasons for false-positive UGI is the inferior displacement of the DJJ [44–46]. The inferior displacement of the normal duodenal–jejunal junction (DJJ) is often seen in infants and children from dilated adjacent stomach, small and large bowels, as well as from enlargement of the spleen or liver. Sizemore also noted that inferior displacement of the DJJ causes false positives but also found that the jejunal position results in both false positives and negatives [44]. When the jejunum is located in the right upper abdomen, the radiologist was more likely to report malrotation even if the DJJ is normally positioned. Equally, when the jejunum is located normally in the left upper abdomen, the radiologist was more likely to report a normal UGI study even with abnormal DJJ position.

Katz and colleagues described seven signs of malrotation on UGI series in infants and young children [68]. The presence of one of these signs may not be abnormal, but the presence of more than one should raise suspicion of malrotation and perhaps further imaging. One finding of interest was the ability of the radiologist to manually displace the normal DJJ position because of normal laxity of the peritoneal ligaments in children under the age of 4 years. It should not be surprising then that extrinsic “masses” such as gastric distention, small bowel distention, and splenomegaly will displace the normal duodenum and lead to false positives in the unaware [3, 69, 70]. Feeding tubes may also displace the normal DJJ [3].

A number of different approaches have been described in the literature to decrease the false-positive and false-negative results on UGI [3, 13, 18]. The goal is to document normal mesenteric attachments for the midgut by inferring the position of the ligament of Treitz. No imaging currently shows this ligament, and therefore we use

the position of the visualized DJJ instead. The second, third, and fourth portions of the duodenum are retroperitoneal and therefore posterior in the abdomen on lateral view. On frontal view, the DJJ is normally located to the left of the left vertebral body pedicle at L1 or L2 level. It is important to document this position on both the frontal and lateral views. On the lateral view, the distal duodenum should remain posterior to the stomach. When the third portion of the duodenum courses anteriorly, it suggests malrotation. Koplewitz and Daneman reported that 70% of proven malrotation cases had this finding [71].

There are a number of reasons that the DJJ may be displaced, particularly inferiorly displaced, on the frontal projection. This displacement is not uncommon in normal infants and young children who have lax peritoneal ligaments that allow mobility of the small bowel. Premature infants are more likely to have a horizontal position of their stomach that orients the duodenal bulb more superiorly than the DJJ. An overdistended stomach from too much barium or air from a crying baby will inferiorly displace the DJJ. Small bowel obstruction, splenomegaly, and scoliosis may displace the DJJ on UGI. Other suggested techniques to optimize the diagnostic performance of the UGI include to (a) document the first pass of barium through the duodenum under fluoroscopic observation; (b) avoid overfilling the stomach with barium; (c) when in doubt, review other imaging studies; and (d) perform delayed abdominal radiographs to document the position of the cecum.

What Imaging Is Appropriate in Indeterminate UGI Cases?

Up to 30% of UGI studies may be indeterminate in young infants [3, 13]. Either the imaging is not clearly normal or abnormal *or* the clinical presentation does not match the UGI study findings. When uncertainty exists about whether the DJJ position is a normal variant or malrotation, either repeat UGI examination or evaluation of the cecal position may be helpful in indeterminate cases. The simplest solution is to continue the UGI series by following the barium course

through the small bowel to document cecal position. In young infants it can be difficult to distinguish small from large bowel so that either an enema (if urgent) or a repeat UGI is recommended. In hospitalized infants, repeat UGI examination (often possible the following day) can be performed via nasogastric tube which allows control of the amount of barium needed and limits fluoroscopy time. Alternatively, an enema can be performed on the same day to document the cecal position. The recommended action will depend on the urgency of definitive diagnosis and the degree of clinical suspicion for malrotation. The imaging choice should be performed in conjunction with the referring clinician.

Special Situation: The Older Child (at Low Risk?)

Summary of Evidence The risk of symptomatic volvulus, either acute or chronic, from malrotation in an older child (beyond infancy) or adult is real but low. Unfortunately, there are no clinical or imaging predictors for volvulus in those patients with malrotation, although some subtypes of malrotation have higher risk of volvulus than others (moderate evidence). Given the reports of catastrophic acute volvulus in older children, and one decision analytic model, prophylactic Ladd procedure is recommended in both symptomatic and asymptomatic children (limited evidence).

Supporting Evidence Approximately 10% of urgent Ladd procedures in the United States are performed in children beyond infancy and in adults [5]. Older children and adults with symptomatic malrotation are a heterogeneous and poorly defined group, with many clinical presentations. Some may present with catastrophic volvulus, while others will have years of abdominal complaints. There is no argument that those with acute volvulus undergo Ladd procedure. There is less consensus to perform a Ladd procedure pro-

phylactically in those children (and adults) with less acute or no symptoms.

Small case series of malrotation with acute midgut volvulus are reported in both older children and adults by many surgeons [11, 12, 28–31, 33, 34, 43, 54, 72, 73]. The clinical manifestations in older patients are often much less straightforward than are those in neonates and encompass a wide variety of signs and symptoms [15, 28–32]. This situation has led to controversy and confusion in the literature about whether older children and adults need surgical intervention [18, 54]. Most published case series recommend prophylactic Ladd procedure in both symptomatic [11, 12, 28, 33, 72] and incidentally detected malrotation [33, 34, 43, 54, 72, 73] in children, but others recommend a watch and wait approach [38].

At present, there is no method for predicting which patients will develop volvulus as a result of malrotation. Given this situation and the often confusing manifestations in older children, it is important that subtle abnormalities in the upper GI series be documented and discussed with the referring clinician and patient. Long average delays of 1.7 years [34], 2.3 years [33], and up to 5 years [35] in the diagnosis of malrotation in symptomatic children after infancy document the challenges of diagnosing the condition in older patients. Symptoms of malrotation in older children and adults range from acute abdominal pain and vomiting to mild intermittent pain and malabsorption [11–13, 17, 32, 69, 74, 75]. Other reported manifestations and complications of malrotation include short gut syndrome, feeding difficulties, diarrhea, small bowel obstruction, adhesive bands, internal hernia, malnutrition, failure to thrive, chylous ascites, mesenteric lymphocele, pneumatosis, and pneumonia [11–14, 18, 36, 37]. Malrotation also may be an incidental imaging finding, especially in adults [15, 32, 39].

Malek and Burd used Markov decision analysis to understand treatment options for children (beyond infancy) with asymptomatic malrotation. They used a national sample and data on mortality from volvulus and elective surgery to

compare quality-adjusted life expectancy for children who undergo Ladd procedure and those who do not. They showed gains in quality-adjusted life expectancy that were the highest if asymptomatic malrotation was treated at the age of 1 year rather than observation. These gains persisted but decreased when the Ladd procedure was performed in older children, up to age 20 years. In adults, the model showed the preferred treatment strategy to be no surgery [4].

Special Situation: The Infant or Child with Heterotaxy Syndrome

Summary of Evidence Infants with heterotaxy syndrome typically have complex congenital heart disease that results in high morbidity and mortality. Most of these infants also have malrotation. Current evidence on asymptomatic case management is lacking. However, a 2015 American Pediatric Surgical Association evidence summary states to screen for malrotation with the UGI series, but there is no consensus on whether these infants should undergo elective Ladd procedure given their higher risk of postoperative complications from their complex heart disease and other medical problems [76].

Supportive Evidence Heterotaxy syndrome (also termed asplenia and polysplenia or situs ambiguous) is defined as visceral malposition and dysmorphism that is associated with indeterminate cardiac atrial arrangement. Most infants and children diagnosed with heterotaxy syndrome (HS) will have congenital heart disease, and many will have severe complex lesions [77, 78]. Mortality for the asplenia type of heterotaxy is as high as 80% in the first year of life [77, 78]. Therefore, controversy exists regarding the role of UGI series screening and prophylactic Ladd procedure not only in these infants with malrotation but also in those who have complex heart disease and other medical conditions. Small case series show that most (sometimes all) children with heterotaxy will have malrotation and some develop acute midgut volvulus that requires urgent Ladd procedure [79–82].

Table 37.4 Diagnostic performance of imaging for midgut volvulus (reference in parentheses)

	Sensitivity (%)	Specificity (%)
UGI	54–79 [44, 49]	98 [70]
Whirlpool sign ^a on US	83–92 [64, 65]	92–100 [65, 67]

^aDefined as the swirling appearance, usually in a clockwise direction, of the small bowel, mesentery, and vessels indicating volvulus

Used with permission from Springer Science from Applegate KE. Imaging of Clinically Suspected Malrotation in Children in Medine LS, et al., eds: Evidence-Based Imaging in Pediatrics: Improving the Quality of Imaging in Patient Care. New York: Springer Science; 2010

Small case series show a risk of midgut volvulus in heterotaxy syndrome infants with known malrotation. These authors also conclude that screening UGI studies should be performed in all heterotaxy infants (insufficient evidence) [79–81, 83]. The UGI will not only diagnose malrotation but also detect duodenal obstructions from either Ladd’s bands or associated duodenal stenoses. Some authors also recommend prophylactic Ladd procedure in a select group of these infants that are stable from the cardiac disease [81, 83]. There is insufficient evidence to suggest that all heterotaxy infants should undergo Ladd procedure given the severe congenital heart disease in many that results in either early mortality or high risk of postoperative complications and mortality from this elective procedure. A 2013 survey of North American pediatric surgeons and cardiologists showed 84% believe HS infants should be screened with UGI, yet 55% would be comfortable with conservative management (non-prophylactic Ladd procedure) [84].

Take Home Tables and Figure

Tables 37.1, 37.2, 37.3, and 37.4 present, respectively, syndromes associated with malrotation, anomalies reported with malrotations, diagnostic performance of imaging for malrotation, and diagnostic performance of imaging for volvulus. Figure 37.1a, b presents a normal UGI series in an infant.

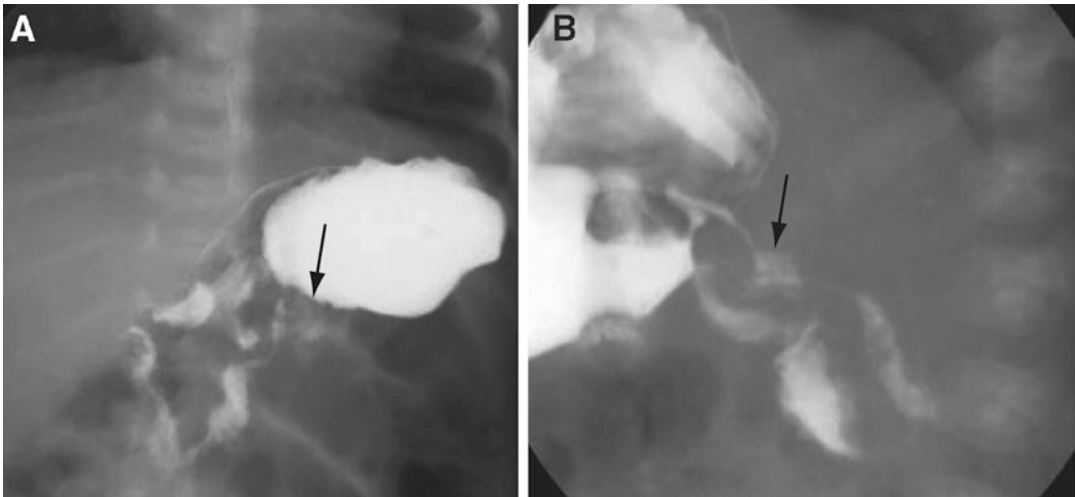


Fig. 37.1 Normal UGI series in an infant with the *arrows* showing the position of the normal duodenal–jejunal junction (DJJ) on both anteroposterior (**a**) and lateral views (**b**). The ligament of Treitz position is inferred by the DJJ position. UGI criteria for normal DJJ position are to be located left of the left vertebral body pedicle at the level of the inferior aspect of the duodenal bulb on frontal projection. On the lateral view, the second through fourth

portions of the duodenum are retroperitoneal and located posteriorly with the DJJ at the level of the duodenal bulb. (Reprinted with permission of The Radiological Society of North America from Applegate from Applegate KE, Anderson JM, Klatte EC Intestinal malrotation in children: a problem-solving approach to the upper gastrointestinal series. *Radiographics* 2006;26:1485–1500)

Imaging Case Studies

Case 1

Figure 37.1a, b presents normal UGI series in an infant, showing normal duodenal–jejunal junction.

Case 2

Figure 37.2a–c presents malrotation in two different children: a 3-month-old female with gagging and coughing with feeding and an older child who had bilious vomiting.

Suggested Imaging Protocols

- UGI series is the preferred single imaging test. Should include true frontal and lateral views

to document the position of the entire duodenum and the duodenal–jejunal junction.

- If UGI series is indeterminate, (a) repeat the UGI on a subsequent day or (b) either perform a contrast enema or continue the UGI series with small bowel follow-through to document the position of the cecum.

Future Research

- Consensus on standard technique and explicit criteria for the diagnosis or exclusion of malrotation on UGI series
- Consensus on explicit criteria for the diagnosis or exclusion of malrotation at laparotomy
- Decision analysis and consensus on the role of Ladd procedure for (a) children beyond infancy who present with asymptomatic or atypical symptoms for malrotation and (b) infants with heterotaxy syndrome.

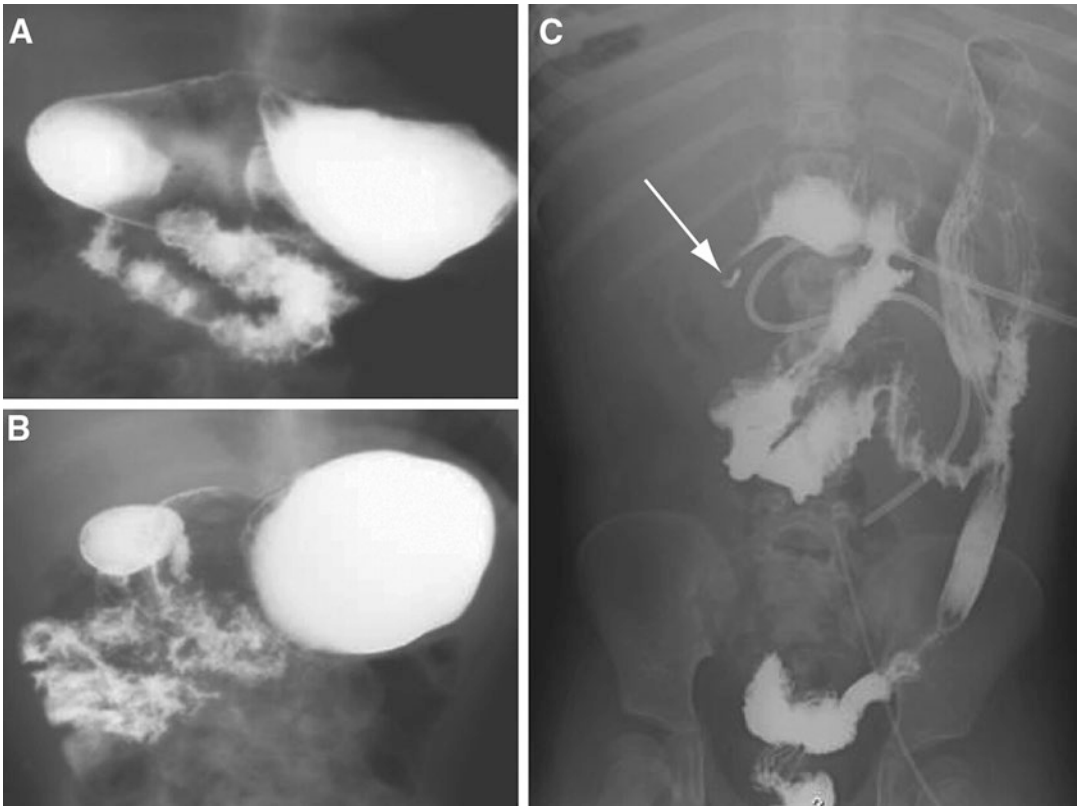


Fig. 37.2 Malrotation in two different children. (a) and (b) are a UGI series of a 3-month-old female with gagging and coughing with feeding. UGI/SBFT demonstrated the DJJ over the left pedicle inferior to the level of the pylorus (a). This appearance raised the question of malrotation. Delayed images demonstrated the small bowel to lay in the right abdomen (b) and the cecum to lie in the left upper quadrant, confirming the presence of malrotation. At surgery, this infant was malrotated and underwent a Ladd procedure with appendectomy. (c) An older child

who had bilious vomiting underwent a delayed film (c) after gastric tube injection that demonstrates the cecum in the epigastric regions and therefore the inferred short small bowel mesentery due to its close proximity to the duodenum (*arrow* showing barium-filled appendix). (Reprinted with permission of The Radiological Society of North America from Applegate from Applegate KE, Anderson JM, Klatte EC Intestinal malrotation in children: a problem-solving approach to the upper gastrointestinal series. *Radiographics* 2006;26:1485–1500)

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Non-traumatic Hip Pain in Infants and Children: Evidence-Based Emergency Imaging

38

Martin H. Reed and G. Brian Black

Key Points

- Radiographs of the hips in neutral and frog leg lateral positions are the standard diagnostic imaging studies in the initial investigation of a child with hip pain (insufficient evidence).
- Ultrasound is the standard imaging modality to diagnose a hip effusion in the initial investigation of a child with hip pain (insufficient evidence).
- The use of magnetic resonance imaging may be an alternative option in case of inconclusive findings after radiography and ultrasound (insufficient evidence).

Definitions and Pathophysiology

A child presenting with hip pain may in fact have pain from pathology in other regions such as the spine, elsewhere in the pelvis, or the knee [1]. This discussion will focus on non-traumatic hip pain resulting from hip pathology. Imaging of traumatic hip injuries in children is dealt with in another chapter of this book (Chap. 31 on lower extremity injuries). The most common causes of pain in the hip in a child are primary bone diseases such as Legg-Calvé-Perthes (LCP) disease or slipped capital femoral epiphysis and distention of the joint capsule by a joint effusion [2].

Epidemiology

Non-traumatic hip pain represents less than 1% of pediatric emergency department (ED) admissions [2, 3]. Transient synovitis is by far the most common cause of hip pain in children [2, 3]. It is most prevalent in children between the ages of 3 and 8 years and is approximately twice as common in males as in females [4]. The three other important causes of hip pain in children, all of which are far less common than transient synovitis, are septic arthritis, Legg-Calvé-Perthes disease, and slipped capital femoral epiphysis [2, 3]. The hip is the second most common site of septic arthritis in children, and most patients present below the age

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of 10 years with a median age of 1.5 years [5]. Legg-Calvé-Perthes disease has a peak age of onset in white children at 5 years of age, but it can affect children from 2 to 14 years of age, and it is at least twice as common in boys as it is in girls [6]. Slipped capital femoral epiphysis has an average age at diagnosis of 12 years and is seen predominately in children between 10 and 16 years; it has a slight male predominance [7]. Obesity is a significant predisposing factor [8].

Overall Cost to Society

There is no information available in the literature on the cost to society of non-traumatic hip pain in children in general or of the four common causes discussed in this chapter.

Goals of Imaging

Transient synovitis is a self-limiting disease, and if it can be diagnosed with confidence clinically, no imaging should be required [4]. The goal of imaging, therefore, is to diagnose the three other common causes of hip pain in children, septic arthritis, LCP disease, and slipped capital femoral epiphysis.

Methodology

Two primary PubMed searches were carried out. The first was a search linking septic arthritis, LCP disease, and slipped capital femoral epiphysis with diagnostic imaging and accuracy. These searches produced no results. A second series of searches was undertaken linking diagnosis with septic arthritis, transient synovitis, LCP disease, and slipped capital femoral epiphysis with the limits publication dates 10 years, humans, language English, and child: birth to 18 years. Relevant articles were searched for their references and appropriate references were examined.

Discussion of Issues

What Is the Role of Radiography in the Initial Diagnostic Imaging of a Child with Hip Pain?

Summary of Evidence Radiography is the recommended initial imaging tool in children presenting with hip pain. However, the diagnostic accuracy of radiography in non-traumatic causes of pediatric hip pain has not been well studied (insufficient evidence).

Supporting Evidence Radiographs of the hips in neutral and frog leg lateral positions are usually recommended as the initial imaging examination for a child with a painful hip [1, 9]. A radiograph in neutral position ideally should include the whole pelvis without gonadal shielding to increase the likelihood of identifying pathology elsewhere in the region which may be causing the hip pain [1, 9]. Radiographs are not a reliable modality for identifying hip effusions. Rosenberg and Mortensson studied 47 children with ultrasonography and radiography of whom 40 had unilateral transient synovitis with a hip effusion diagnosed by ultrasound. Joint width on the radiograph did not correlate with the presence of a hip effusion, and, although soft tissue abnormalities around the hip did occur more frequently in the presence of a joint effusion, the findings were not frequent enough to be reliable for diagnosis [10].

Although the diagnostic accuracy in radiographs in LCP disease has not been determined, the radiologic abnormalities are well known. In the early stages, the proximal femoral epiphysis appears flattened and sclerotic, and there is sometimes a subcortical linear lucency. These abnormalities are better seen on the frog leg lateral view. Later in the stage of the disease, the proximal femoral epiphysis becomes fragmented, and the femoral head widens [11].

Radiography is also recommended as the initial imaging examination to diagnose slipped capital epiphysis. The standard neutral and frog

leg lateral views of the hips should usually be obtained, and as in LCP disease, the abnormalities are best seen on the frog leg lateral view. However, if there is clinical concern about an acute slip, only the neutral view should be requested because the frog leg lateral view may make the slip worse [12]. Klein has described a line that can be drawn along the lateral side of the femoral neck to cross the epiphysis. He noted that with slipped capital femoral epiphysis, the line does not cross the edge of the proximal femoral epiphysis [13]. However, it has been shown that this is not always reliable [14], and Green et al. have suggested that the distance between the Klein line and the edge of the epiphysis should be measured on both sides and a 2 mm difference is also diagnostic of slipped capital femoral epiphysis [15]. Blurring and widening of the proximal femoral growth plate is another sign of slipped capital femoral epiphysis on the neutral view, and there may be a crescentic region of increased density in the metaphyseal region caused by the underlying posteriorly slipped epiphysis [16]. The accuracy of none of these signs has been adequately assessed.

For both LCP disease and slipped capital femoral epiphysis, the frog leg lateral views usually best demonstrate the abnormalities. Therefore, Bomer et al. have recommended that only lateral views need to be obtained in the assessment of pediatric hip pain. They carried out a retrospective study of 524 children examined because of hip pain. Twenty of these had slipped capital femoral epiphysis, and 22 had LCP disease. The abnormalities were seen on all frog leg lateral views, but in two of the cases of LCP disease, the abnormality could not be seen on the neutral view [17].

What Is the Role of Ultrasound in the Initial Investigation of a Child with Hip Pain?

Summary of Evidence To evaluate for a possible hip joint effusion in a child, ultrasound is recommended, though it may not be useful in

establishing a correct diagnosis (insufficient evidence).

Supporting Evidence Ultrasound is considered to be the standard imaging modality to assess the possibility of a hip joint effusion in a child [18]. The accuracy of ultrasound in assessing hip joint effusions has not been rigorously assessed. It has also been shown that ultrasound cannot distinguish between septic arthritis and transient synovitis [19]. Septic arthritis of the hip does require urgent treatment, but the decision as to whether to tap a hip effusion for diagnostic purposes and to relieve pressure must be made on clinical grounds [20].

Is There a Role for Magnetic Resonance Imaging (MRI) in the Initial Investigation of a Child with Hip Pain?

Summary of Evidence MRI could be an option to establish the correct diagnosis in a child with non-traumatic hip pain in case of inconclusive findings after radiography and ultrasound (insufficient evidence).

Supporting Evidence In a prospective study of 50 children presenting with hip pain to their ED, White et al. found that the sensitivity and specificity for MRI in making a diagnosis were 0.79 and 1.00, respectively, while for standard imaging, which included ultrasound and x-rays, it was 0.70 and 0.57, respectively. They therefore recommend MRI as the initial imaging modality for assessment for hip pain in children [21].

Take-Home Points

- Neutral and frog leg lateral views of the hips are a reasonable initial diagnostic imaging examination to assess a child with hip pain.
- Ultrasound should be considered as the initial imaging modality in a child under 10 years of

age where the most likely diagnosis is transient synovitis or septic arthritis.

Imaging Case Studies

Case 1

Figure 38.1a, b shows Legg-Calvé-Perthes disease of the right hip in an 8-year-old boy.

Case 2

Figure 38.2a–c shows slipped capital femoral epiphysis in an 11-year-old girl.

Case 3

Figure 38.3a, b shows a transient synovitis right hip in a 5-year-old boy.

Suggested Imaging Protocol

Neutral and frog leg lateral radiographs of the hips are generally considered to be the standard initial imaging modality in the evaluation of a child with hip pain. However, if a diagnosis of transient synovitis can be made clinically with reasonable confidence, no imaging may be required. If the onset of the hip pain is reasonably acute, suggesting a diagnosis of transient synovitis or septic arthritis rather than LCP disease or slipped capital femoral epiphysis, particularly in children under the age of 10 years when slipped capital femoral epiphysis is rare, ultrasound could reasonably be considered as the initial imaging modality.

Future Research

- Development and validation of a clinical decision rule [22] to guide physicians in determining whether a child with hip pain is more

Fig. 38.1 An 8-year-old boy: Legg-Calvé-Perthes disease of the right hip. (a) Neutral view of the hips showing slight compression and increased density of the proximal right femoral epiphysis. (b) Frog leg lateral view showing a subcortical linear lucency (arrow)

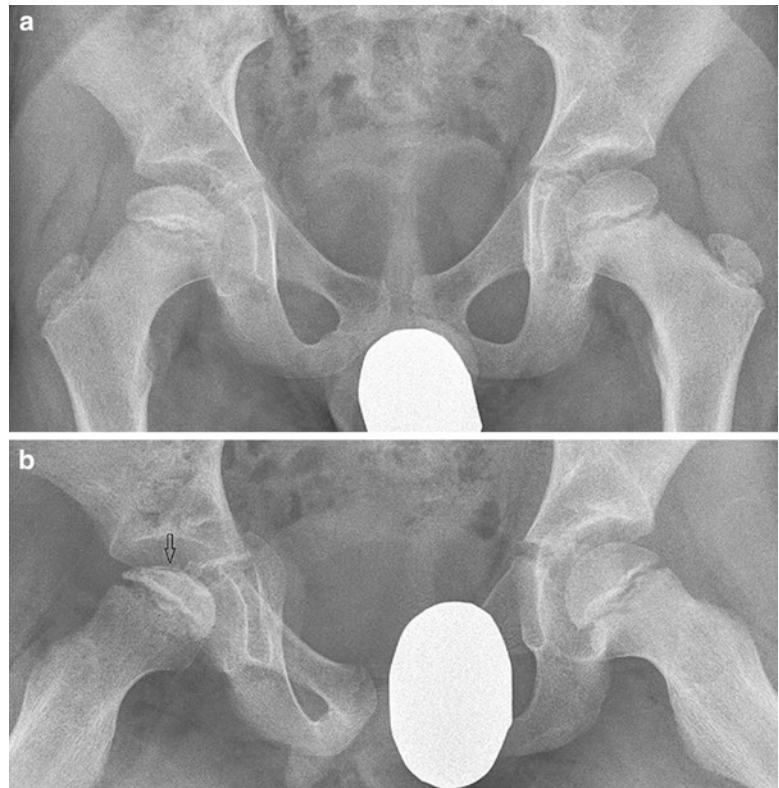


Fig. 38.2 An 11-year-old girl: slipped capital femoral epiphysis on the left. **(a)** Neutral view of the hips showing irregular widening of the growth plate of the proximal left femur and an area of increased density in the metaphysis medially caused by the underlying slipped epiphysis. **(b)** The Klein line intersects the epiphysis of the femur on the right but not on the left. **(c)** The frog leg lateral view shows the posterior displacement of the slipped epiphysis

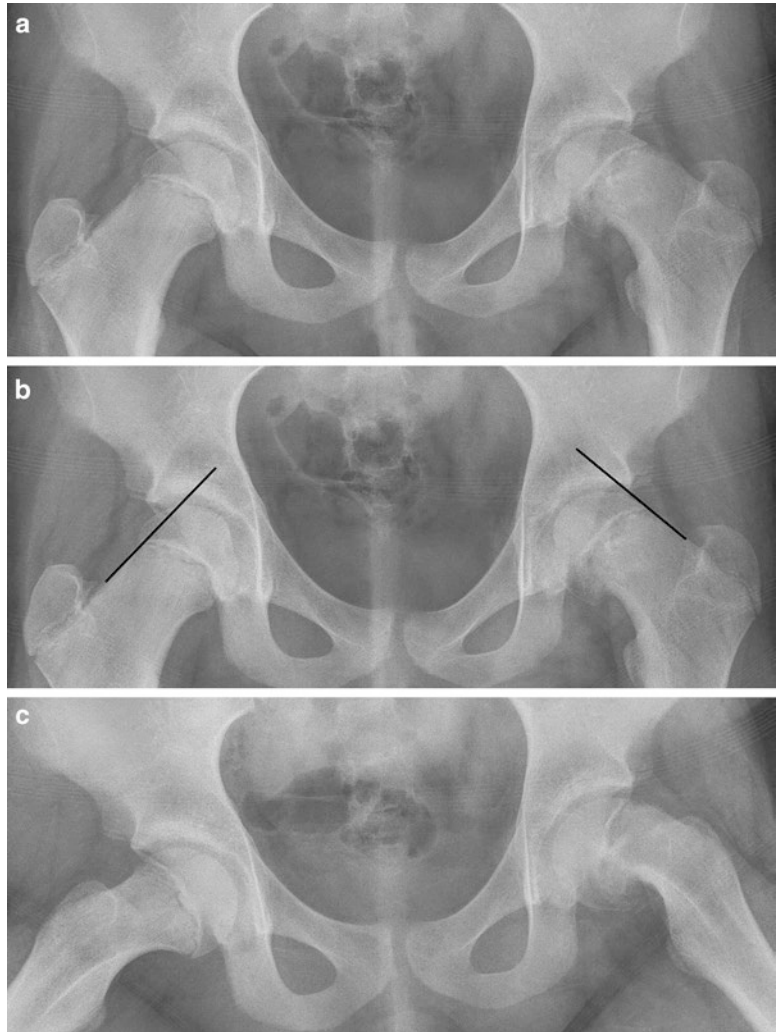
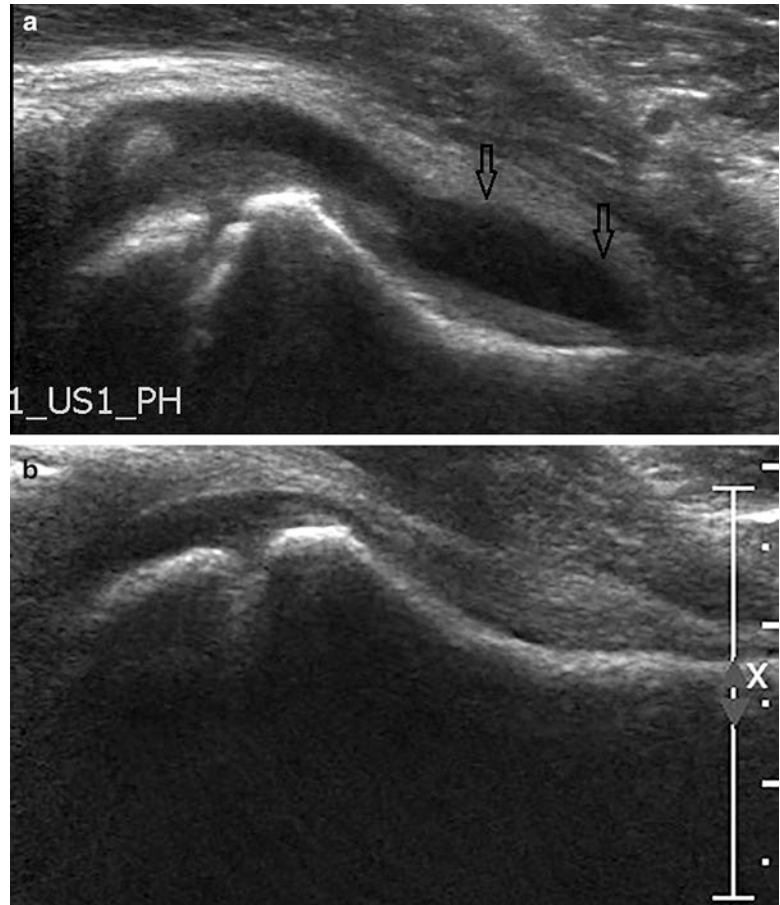


Fig. 38.3 A 5-year-old boy: transient synovitis right hip. (a) Ultrasound of the right hip showing fluid distending the joint capsule (*arrows*). (b) Normal left hip for comparison



likely to have transient synovitis or septic arthritis than LCP disease or slipped capital femoral epiphysis.

- Development and validation of a reliable clinical decision rule to distinguish between transient synovitis and septic arthritis.
- Determination of whether a single frog leg lateral x-ray would be adequate to diagnose LCP disease and slipped capital femoral epiphysis.
- Determination of whether MRI should be the initial imaging modality for assessing children with hip pain. Consideration of cost and availability would have to be included in this decision.
- The accuracy of none of these imaging modalities for these conditions has been rigorously determined. However, because there are no good reference standards, determining the true

accuracy of imaging for diagnosing these conditions would be very difficult to do.

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Foreign Body Aspiration in Children: Evidence-Based Emergency Imaging

39

Joost van Schuppen and Rick R. van Rijn

Key Points

- Most of the aspirated foreign bodies in children are radiolucent; therefore chest radiographs are useful to detect the effects of aspiration, such as hyperinflation or volume loss (moderate evidence).
- Up to 37% of the chest radiographs obtained in the acute phase may not show abnormalities in foreign body aspiration (moderate evidence).
- In children with normal chest radiographs who have a high clinical suspicion of aspiration, chest CT could be performed to exclude or detect a foreign body (moderate to limited evidence).
- CT of the chest does not only detect foreign bodies but is also helpful to locate the foreign body and guide bronchoscopy (moderate to limited evidence).

Definitions and Pathophysiology

Aspiration of a foreign body in a child and its subsequently becoming lodged in the larynx, trachea, or bronchi is a potential life-threatening situation, which requires rapid diagnosis and intervention by rigid bronchoscopy under general anesthesia. Morbidity and mortality are higher in younger children compared with older children. Delayed diagnosis increases the incidence of complications, ranging from 64% after 7 days to 95% at 30 days [1].

Orji and Metrangelo described the most sensitive clinical symptom for aspiration as a history of choking crisis followed by a period of paroxysmal or persistent coughing. The most specific symptom is witnessed aspiration [1, 2].

Aspiration is more common in younger children (<3 years) and in boys (> 60%) [3–9] with a peak incidence between 1 and 2 years of age [10]. Most aspirations (73–86%) in children are observed by parents/caregivers or relatives [3, 8, 11, 12]. When aspiration occurs in unsupervised children, the clinical history can be challenging. Depending on the level where the foreign body lodges, the clinical symptoms and physical exam may differ. When a foreign body gets trapped at the level of the trachea or larynx, the primary symptom will be stridor and respiratory distress. Paroxysmal or persistent coughing, decreased breath sounds, and wheezing are also frequent clinical features [3, 7–9, 12, 13]. When the foreign

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body gets lodged at the level of the bronchi, symptoms may be less obvious. Airway obstruction can cause air trapping, with hyperinflation, or the opposite, with post obstructive atelectasis. With unsupervised aspirations, young patients most often present acutely with recurrent or persistent symptoms, such as coughing or later with recurrent pneumonia, fever, or asthma, usually diagnosed by pediatricians [12].

Most (70–96%) aspirated foreign bodies are radiolucent, with roughly 60–95% composed of organic material. Twenty-five percent of aspirations are located in the lower trachea, with 75% in the bronchi, and 52–67% reported on the right side [1, 3, 5, 7, 9, 11, 13–15]. The gold standard for the diagnosis of foreign body aspiration is rigid bronchoscopy.

Epidemiology

The highest incidence of aspirations is seen in children under 3 years of age. One hypothesis is that this is the result of their propensity to put foreign objects into their mouths and the absence of molars, leading to an insufficient chewing function.

In 2001 in the USA, according to the CDC, an estimated 17,537 (95% CI 12,319–22,755) children aged <14 years were treated in EDs for choking-related episodes yielding an estimated incidence of aspirations of 29.9 per 100,000 with 160 reported deaths in this cohort [15]. In 2005 in the USA, 90 children under 14 years died of ingestion and aspiration [16]. In Europe, the estimated annual incidence in children aged 0–14 is about 50,000, 10% of which are fatal [6].

Overall Cost to Society

There is little literature on the overall cost to society. A recent publication by Kim et al. based on a nationwide inpatient assessment between 2009 and 2011 comprising a total of 1908 ± 273 children estimated the costs in the USA to be approximately \$12.8 million per year [17].

Goals of Imaging

The goal of imaging in foreign body aspiration is to confirm or exclude aspiration of a foreign body, hereby preventing unnecessary bronchoscopy. Imaging can also be used to determine the position of a foreign body to guide intervention and to detect complications of the aspirated foreign body.

Methodology

A PubMed search was performed using a combination of the following MeSH terms: *radiology*, *radiography*, *aspiration*, *foreign*, *bodies*, and *foreign bodies*. Based on the reference lists of the included articles, several additional articles were considered. The search was limited to English language, pediatric, and human studies. Publication status was not limited. Abstracts were reviewed and selected on relevance, as well as review articles and guidelines.

Discussion of Issues

What Is the Imaging Modality of Choice in Suspected Foreign Body Aspiration in Children?

Summary of Evidence The first modality of choice to exclude aspiration of foreign body in children is inspiratory chest radiography (moderate evidence). An image in forced expiration or the lateral decubitus position can be considered. Most foreign bodies are radiolucent, so the imaging strategy is aimed at demonstrating the consequences of aspiration, such as air trapping/hyperinflation or atelectasis. Airway fluoroscopy has, in experienced hands, a higher sensitivity and specificity compared to radiography. However, given the current decreased expertise in fluoroscopy and the widespread availability of CT, it is easier to perform a CT which can be used to guide bronchoscopy [18].

With normal chest radiographs and persistent clinical suspicion of aspiration, chest CT can be

performed to exclude or confirm aspiration. Some studies have suggested omitting the chest radiograph in the diagnostic work-up and performing a low-dose CT with a suggestive history and physical exam [19]. But no evidence was found to justify this strategy.

CT has a high sensitivity of up to 100% and a specificity between 66.7 and 100% for foreign body aspiration (limited evidence) [18]. It is quick and does not demand sedation. Although CT still uses a higher radiation dose than chest radiography, low-dose protocols can be used safely to rule out foreign bodies (limited evidence) [20, 21]. Therefore, bronchoscopy can be obviated. CT can also be used to guide bronchoscopy.

There is not enough data available regarding the use of MRI with suspected aspiration of foreign body (insufficient evidence).

Supporting Evidence

Chest Radiography

Chest radiographs are usually performed PA in inspiration. Forced expiration and lateral decubitus views may be added to detect air trapping distal to the obstructed foreign body.

Since most foreign bodies are radiolucent (74–96%) [1, 3, 9, 18], the purpose of imaging is to demonstrate indirect signs of bronchial obstruction. Up to 84% of studies are abnormal [3, 22], but sensitivity and specificity of radiographs are low to intermediate [3, 12, 21], and in 14–49% chest radiographs can be normal in foreign body aspiration [1, 3, 9, 13, 14, 18, 21–23]. Specificity for a radiopaque foreign body is high (96–100%) with low sensitivity, which is 20–30% [1, 22]. The most commonly reported radiographic signs of obstruction are obstructive emphysema and air trapping. Retrospective studies and literature reviews show these signs to be present in 17–69% of cases [3, 12, 18, 22]. These, in combination with a visible foreign body, are the most specific signs on chest radiographs with a specificity of up to 94% reported but low sensitivity [22].

According to a literature review, the sensitivity of chest radiographs in the acute phase is

lower than that of radiography obtained 24 hours after aspiration [18]. Later, still lobar consolidation can be seen on radiographs.

Fluoroscopy

Fluoroscopy can be helpful in small children when expiratory images are too difficult to obtain. Fluoroscopy increases the accuracy for diagnosis of aspiration [14]. A prospective study including 37 pediatric patients with a clear history of aspiration of foreign body reported a sensitivity of 63% and a specificity of 50%, with a positive predictive value of 95% and a negative predictive value of 8.3% [19]. In a retrospective study of 136 children undergoing bronchoscopy for aspiration, 43.7% of the fluoroscopy studies were reported as normal [22]. A small prospective study including 19 infants and children reported the sensitivity of digital subtraction (DSA) to detect a foreign body in the trachea or main bronchi as 100% [24]. In DSA the foreign body creates an interruption in the lumen of the bronchus or trachea. In the same study, the reported specificity was low, at 17%.

The technique is operator dependent and less often used for this indication, since CT nowadays is readily available, easier, and quicker [18]. Another problem is that radiology residents receive less fluoroscopy training nowadays because of the preferred use of CT, leading to a limited number of radiologists having sufficient experience with this technique.

Chest CT

Different studies report a high sensitivity of nearly 100% and specificities between 66.7 and 100%, as well as positive predictive values of 93–97% and a negative predictive value of 100% for chest CT [18–20, 25, 26]. Computed tomography can depict the foreign body and determine its position, shape, and possible complications (Fig. 39.3a, b), hereby guiding bronchoscopy and lowering its operating time and adverse effects. The presence of pus or mucus can make the diagnosis of a radiolucent foreign body more challenging and can cause false-negative results. Artifacts may also lead to false-positive results, and small foreign bodies (<3 mm) can be hard to

detect. Air trapping, emphysema, atelectasis, pneumothorax, and bronchiectasis can be demonstrated more reliably than with radiography. Adding 3D virtual bronchoscopy increases sensitivity and specificity of foreign body detection by CT [11, 19, 21, 25, 27, 28].

Prospective studies, although relatively small, showed that with negative chest radiography in patients with a high clinical suspicion, a chest CT with or without virtual bronchoscopy should be performed to exclude a foreign body and to avoid unnecessary rigid bronchoscopy. In a study with 40 patients, including 20 with normal chest radiographs, all patients underwent rigid bronchoscopy. The 20 patients with normal radiographs also had CT virtual bronchoscopy performed, revealing 12 foreign bodies, one false negative and one false positive, and could have avoided 6 rigid bronchoscopies [28]. Based on their findings, the authors concluded that in patients with a positive clinical diagnosis and a negative chest radiograph, CT virtual bronchoscopy should be considered. In another prospective study with 37 patients, 16 of those who had a foreign body aspiration, proven by bronchoscopy, 8 had normal chest radiographs, but all were detected on CT [21].

MRI

Some case reports describe the added value of determining the location of aspirated peanuts by MRI [29, 30]. However, no larger studies were found on the use of MRI in diagnosis of foreign body aspiration in children. Since MRI is a time-consuming and costly procedure that might require sedation, its role seems limited.

Are Added Radiographs in Forced Expiration, Lateral Decubitus, or Fluoroscopy to the Radiograph in Inspiration Helpful for the Diagnosis of Foreign Body Aspiration?

Summary of Evidence Lateral decubitus and forced expiratory films, which may be helpful to delineate hyperinflation, air trapping, and mediastinal shift, are often advised when foreign body is suspected. Nevertheless, these films do not

seem to be of added value in terms of sensitivity and specificity (limited evidence). A lateral film of the c-spine may be helpful to determine the exact position of radiopaque foreign bodies and detect them in larynx and high up in the trachea (limited evidence).

Supporting Evidence In case of suspicion of foreign body aspiration, an added forced expiratory radiograph (Fig. 39.5a, b) may be helpful to demonstrate air trapping and mediastinal shift. In young children, a lateral decubitus view can simulate an expiratory film. However, retrospective studies suggest that the added value of decubitus films was very limited, especially when performed routinely. The reported sensitivity for decubitus views was 27%, while it was 55% for an AP chest radiograph, while specificity was somewhat higher, 67% compared to 50% on AP views [31]. Brown et al. compared standard frontal views to standard frontal views with added decubitus views in one group and standard views with forced expiration views in another group. The first group showed a sensitivity of 56% and a specificity of 79% for the standard view only. A sensitivity of 56% and a specificity of 64% were seen when a decubitus view was added. In the second group, a standard view only showed a sensitivity of 33% and a specificity of 70%. When a forced expiratory view was added, sensitivity was 62% and specificity 72% [32].

There is no evidence to support the routine addition of these additional views. A lateral radiography of the c-spine is useful when a foreign body is trapped in the larynx or upper trachea. It also can help in differentiating between a location in esophagus or trachea.

Which Radiological Findings Are Important to Detect in Foreign Body Aspiration?

Summary of Evidence Chest radiographs may be completely normal but may also show pathology. None of the radiological findings are pathognomonic for foreign body aspiration [1, 3, 18, 22] (moderate evidence). The foreign body is most often radiolucent, consisting of organic material/

food. Most abnormalities on a chest radiograph are a result of air trapping or obstruction of airways. The most common sign on radiography is hyperinflation/air trapping. This may be associated with mediastinal shift. Pneumothorax and pneumomediastinum can complicate air trapping. Other consequences of obstruction include atelectasis or consolidation/pneumonia (moderate evidence).

Supporting Evidence

Hyperinflation

The most common signs of obstruction are obstructive emphysema and air trapping (Fig. 39.2a, b), which are present in 17–70% of cases [3, 8, 12, 13, 18, 33]. According to a retrospective study, air trapping is the most specific sign of obstruction with a specificity of 93.8% [22]. This high specificity was confirmed for localized air trapping by another retrospective study, with a reported sensitivity of 51%, a PPV of 74%, and a NPV of 70% [33]. Air trapping is the result of partial obstruction of bronchi, creating a ball valve effect. By comparing inspiratory and expiratory images, emphysema and air trapping may be demonstrated more easily. Mediastinal shift can be also seen. In young children, obtaining an expiratory film might be impossible, and here a lateral decubitus film may prove helpful.

During fluoroscopy, respiratory movement can be analyzed. Mediastinal shift or decreased movement may be demonstrated at the site of aspiration due to air trapping. This was reported in 56% of cases in a small retrospective study, with a specificity of 74.3% and a sensitivity of 67.5% [22]. CT can detect hyperinflation and mediastinal shift with higher specificity and sensitivity than radiography (Fig. 39.3a, b).

Atelectasis

Atelectasis occurs with complete bronchial obstruction, causing distal collapse of the lung (Fig. 39.4). Retrospective studies show atelectasis to be present in 12–41% of cases [3, 12, 18]. A prospective study including 142 patients describes atelectasis in 7% of patients with aspiration and 4% in patients without aspiration; values for sensitivity and specificity could not be calculated [33]. CT depicts atelectasis and medi-

astinal shift with higher specificity and sensitivity compared with radiographs.

Consolidation/Pneumonia

Consolidation is also described as a frequent sign in foreign body aspiration [13, 22], namely, in up to 47% of cases, with specificities ranging between 18.8 and 100% and sensitivities of 5.5–40.5%. A prospective study including 142 patients described consolidation in 15% of the cases with aspiration but also in 21% of patients without aspiration [33]. In cases with recurrent pneumonia or bronchiectasis, a foreign body should also be kept in mind. CT can depict consolidation and mediastinal shift with high sensitivity and specificity.

Pneumothorax and Pneumomediastinum

Pneumothorax and pneumomediastinum are rare complications of foreign body aspiration. They occur due to rupture of bronchus by foreign body or alveolar rupture [11]. CT has a very high sensitivity to detecting small pneumothoraces and pneumomediastinum.

Miscellaneous

Decreased vascular markings were seen in 14% of cases of foreign body aspiration in a retrospective study including 280 small children [3]. Aspiration of a disk battery, although very rare, should be kept in mind in case of a coin-shaped foreign body (Fig. 39.6a, b). Delayed diagnosis and extraction of batteries can cause major complications with poor outcome [34].

Take-Home Tables and Figures

See Tables 39.1 and 39.2 that highlight and summarize specificity and sensitivity of modalities. Figure 39.1 provides a helpful flowchart.

Imaging Case Studies

Case 1

Figure 39.2a, b shows chest radiographs of a 1-year-old girl with witnessed foreign body aspiration.

Table 39.1 Sensitivity and specificity values to detect foreign body aspiration by modality

	Clinical history (%)	Physical exam (%)	Chest radiograph (%)	Chest fluoroscopy (%)	CT (%)
Sensitivity	75–92	56–86	33–96	63.3	100
Specificity	0–92	26–72	63–96	50	66–100
PPV	50–86.2	n/a	n/a	95	97.1
NPV	0–84	n/a	n/a	8.3	100

Data from references [18, 19, 31–33]. *n/a* not available (or not applicable)

Table 39.2 Sensitivity and specificity of radiological abnormality on chest radiograph to detect aspirated foreign body

	Sensitivity (%)	Specificity (%)	PPV (%)	NPPV (%)
Normal chest radiograph	20.0	66.7	78.6	12.0
Abnormal chest radiograph	80–83.2	33–52.9	88.0	21.4
Foreign body	22–26	93.8–100	100	15.3
Hyperinflation	6–51	66.7–93	(74 ^a) 88.9	(70 ^a) 16.2
Mediastinal shift	(67.5 ^b) 25.5	(74.3 ^b) 66.7	82.4	12.8
Atelectasis	12.7–40	75–77.8	91.7	17.5
Consolidation	5.5–40.5	18.8–100	100	14.8
Pneumothorax	NR	NR		
Pneumomediastinum	NR	NR		

NR not reported

^aFor obstruction

^bOn fluoroscopy

Different studies were used, some of which had very small numbers. So some data have a high level of variability

Data from references [1, 2, 12, 13, 21, 22, 33]

Case 2

Figure 39.3a, b shows coronal reformats and minimal intensity projection of a CT in an 18-month-old boy with a history of choking during feeding.

Case 3

Figure 39.4 shows a chest radiograph of a 6-month-old girl with a choking accident during eating.

Case 4

Figure 39.5a, b shows radiographs of a 1-year-old boy with suspicion of foreign body aspiration.

Case 5

Figure 39.6a, b shows radiographs of an 18-month-old boy with a suspicion of aspiration/ingestion of disk battery.

Future Research

Future research should investigate:

- The added value of expiration and lateral decubitus
- Sensitivity and specificity of ultralow-dose CT
- Whether there is still a role for the chest radiograph or whether an ultralow-dose CT should be the first diagnostic imaging test performed in patients with a suggestive history of foreign body aspiration

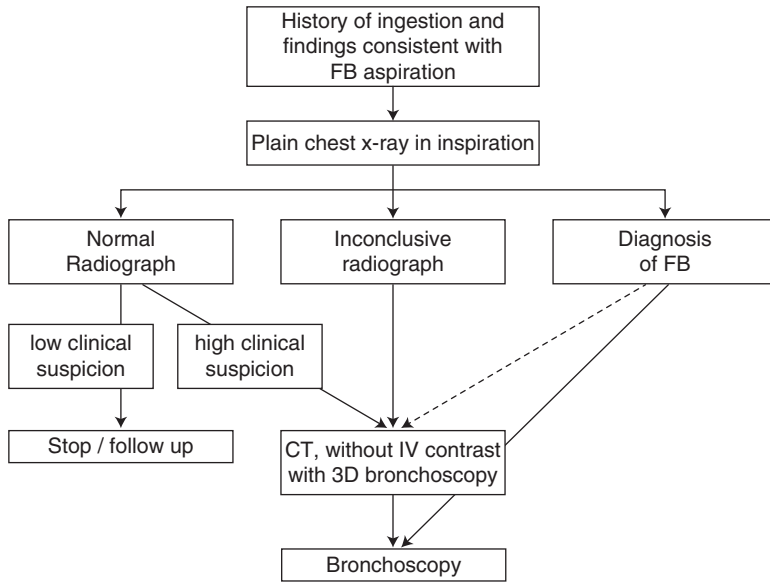


Fig. 39.1 Flowchart for diagnosis of foreign body aspiration

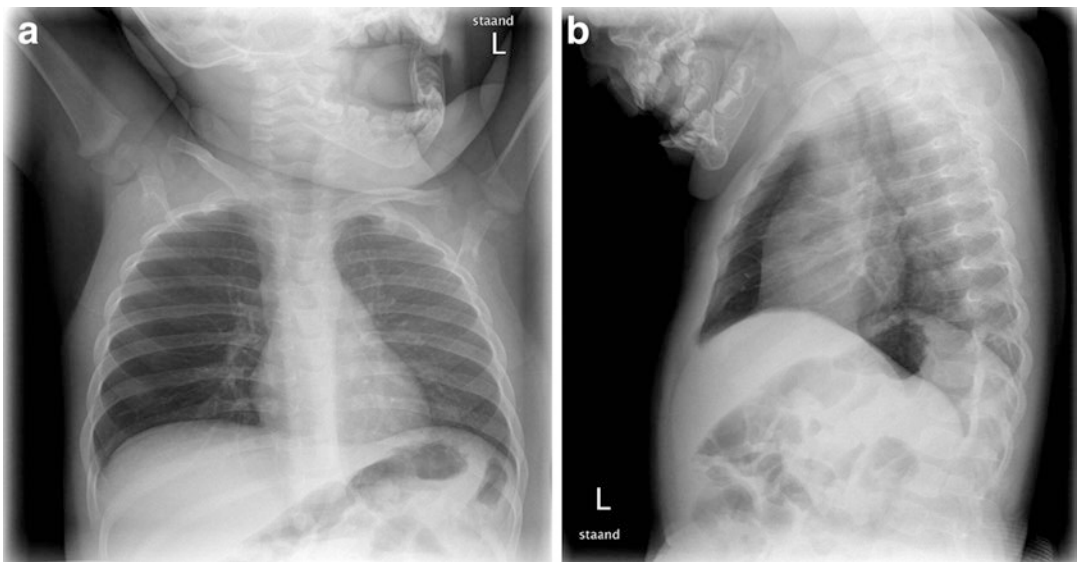


Fig. 39.2 AP (a) and lateral (b) chest radiograph of a 1-year-old girl with witnessed foreign body aspiration. There are hyperinflation and lucency of the right lung with

shift of heart and mediastinal structures to the left. No radiopaque foreign body is seen. A peanut was removed with bronchoscopy from the right main bronchus

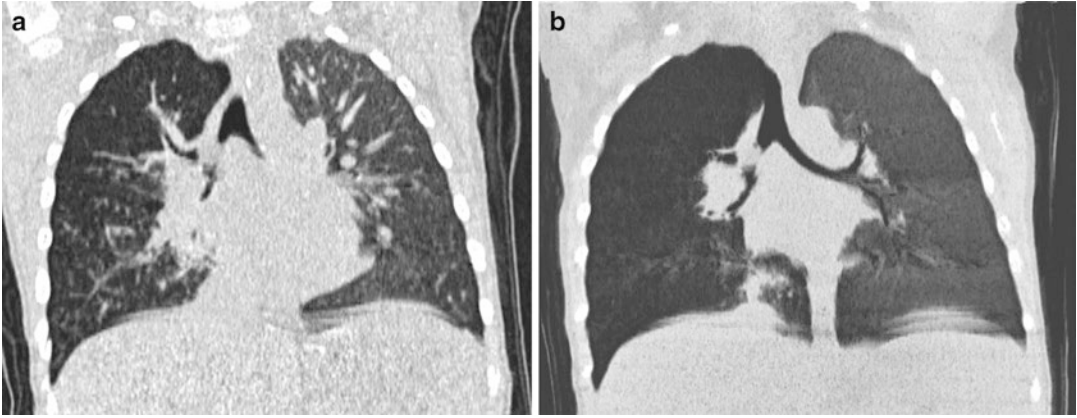


Fig. 39.3 Coronal reformats (a) and minimal intensity projection (b) of a CT in an 18-month-old boy with a history of choking during feeding. CT revealed a radiolucent foreign body in the right main bronchus, with hyperinflation of the right lung. Organic material was removed at bronchoscopy

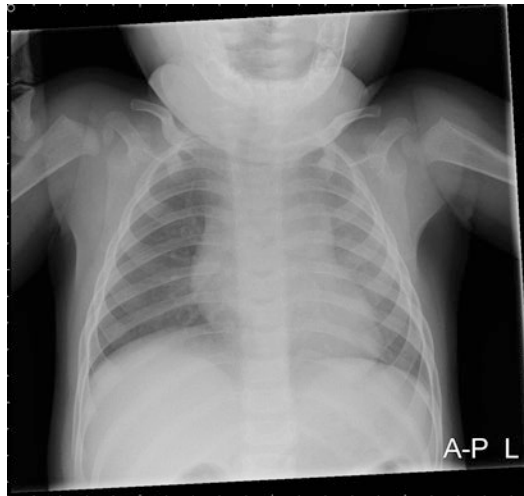


Fig. 39.4 AP chest radiograph in a 6-month-old girl with a choking accident during eating. There is a clear volume loss of the left lung. Bronchoscopy revealed a piece of bread in the left main bronchus

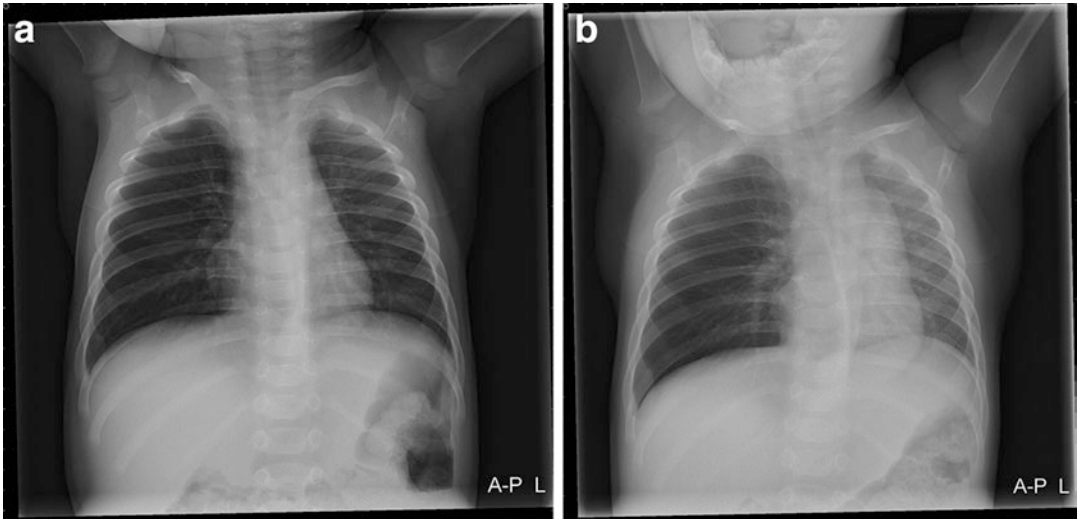


Fig. 39.5 AP chest (a) and forced expiratory (b) radiographs of a 1-year-old boy with suspicion of foreign body aspiration. There are lucency and hyperinflation of the right lung. No radiopaque foreign body was shown. The forced expiratory

view (b) shows collapse of the left lung in expiration and marked air trapping in the right lung, with shift of the heart and mediastinal structures toward the left. Bronchoscopy revealed a piece of apple in the right main bronchus

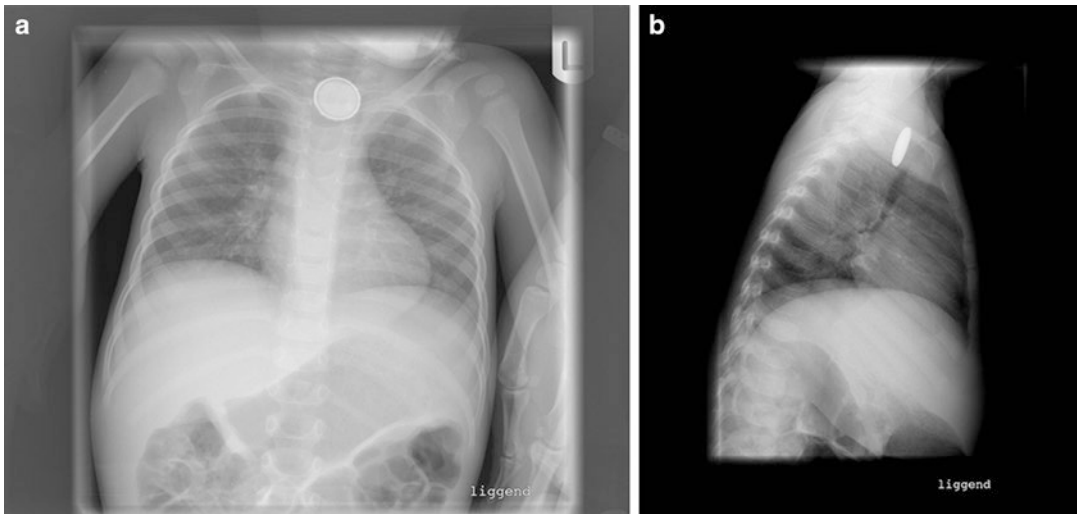


Fig. 39.6 AP chest radiograph (a) and lateral view (b) of an 18-month-old boy with a suspicion of aspiration/ingestion of disk battery. The radiographs show the typical appearance of a disk with a surrounding radiopaque ring,

located in the upper trachea. No signs of obstruction were seen. Direct bronchoscopy was performed and the battery removed

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Acute Urinary Tract Infection in Infants and Children: Evidence-Based Emergency Imaging

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Key Points

- Contradictory study outcomes provide us with limited conclusions about the long-term outcomes of children with UTI.
- The presence of UTI should be considered in any child 2 months to 2 years of age with unexplained fever (strong evidence).
- The presence of fever, in the presence of a positive urine culture from an appropriately collected urine sample, reasonably distinguishes between cystitis (lower tract) and pyelonephritis (upper tract) infections (moderate evidence).
- Routine imaging during an acute episode of UTI is not necessary to make the diagnosis (moderate evidence).
- Pyelonephritis, and hence renal scarring, can occur with or without the exist-

tence of vesicoureteral reflux (VUR) (strong evidence).

- The 2011 American Academy of Pediatrics (AAP) guideline does not recommend prophylactic antibiotic therapy in patients of 2 months to 2 years of age with VUR (strong evidence).
- The new 2011 AAP guideline recommends a renal/bladder ultrasound (RBUS)

(continued)

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examination after a first febrile UTI in all children aged 2 months to 2 years to detect possible upper urinary tract abnormalities, obstruction in particular, and “watchful waiting for a second UTI” before further imaging (strong evidence).

- RBUS performed after the first febrile UTI will have abnormalities in up to 15% of patients (2–3% false positive); of these, 1–2% will lead to actionable management (surgery or referral).
- The new 2011 AAP guideline recommends voiding cystourethrography (VCUG) to be performed in both boys and girls only after the second episode of UTI or in the presence of findings suggesting high-grade VUR or obstructive uropathy in RBUS (strong evidence).
- The American College of Radiology has developed appropriateness criteria ranking evidence for imaging in four pediatric scenarios and provided the estimated radiation exposures after first urinary tract infection.
- Ultrasound evaluation of the kidneys and bladder is a readily available, safe modality but is insensitive for the diagnosis of acute pyelonephritis (moderate evidence).
- Ultrasound has poor sensitivity and specificity for the identification of VUR (moderate evidence).
- If evidence of VUR is detected by US then VCUG is indicated (strong evidence).
- Currently, only the DMSA test can adequately predict the later development of renal scar (moderate evidence).
- Neonates that had moderate to severe prenatal hydronephrosis should undergo RBUS (limited evidence).

Definitions and Pathophysiology

Cystitis is defined as inflammation or infection of the bladder and most commonly occurs from retrograde ascent of perineal bacteria up the ure-

thra into the bladder. After infancy, girls, with much shorter urethras than boys, have an eight-fold higher incidence. The vast majority of infections in infants and children are caused by *Escherichia coli*. Non-*E. coli* infections tend to occur with greater frequency in boys and in association with underlying genitourinary abnormalities such as urinary tract obstruction or vesicoureteric reflux. Infections with enterobacteria and enterococci also occur in young girls, *Staphylococcus aureus* in adolescent girls, and *Proteus* in young boys [1–3]. Appendages such as pili facilitate pathogen adherence to the uroepithelium and are important in pathogenesis of uropathogens [4]. The diagnosis of a febrile urinary tract infection is made when a urine culture produces growth of greater than 100,000 colony-forming units per cubic centimeter of a single pathogen, from an adequately obtained urine specimen in the setting of a fever of ≥ 38 °C. As for infants and children of 2–24 months old, the American Academy of Pediatrics (AAP) suggests that a diagnosis requires evidence of infection from both abnormal urinalysis results (pyuria and/or bacteriuria) and positive urine culture results (more than 50,000 colony-forming units (CFUs) per mL of a uropathogen cultured from a urine specimen obtained through catheterization or suprapubic aspiration) [5]. The presence of fever increases the probability of kidney involvement as in pyelonephritis.

Pyelonephritis can result from blood-borne infection, particularly in the newborn period. However, some infants and children with pyelonephritis acquire the renal infection by ascent of bacteria from the bladder [6–8], perhaps as a result of reflux of infected urine from the bladder. Studies estimate that 30% of children and up to 70% of infants with a UTI have VUR [9]. Vesicoureteral reflux is a congenital condition characterized by the retrograde flow of urine from the bladder to the kidneys. Vesicoureteral reflux is more common in girls and is usually detected before the age of 2 years. Family history and Caucasian race are risk factors for VUR [10]. It is graded on a one to five scale: grade I is reflux from the bladder into the distal ureter but not into the renal col-

lecting system; grade II reflux extends into the renal collecting system; grade III reflux causes distention of the ureter and renal collecting system; grade IV reflux results in tortuosity of the dilated ureter; and grade V reflux shows marked dilation and tortuosity of the ureter and renal collecting system with marked calyceal blunting.

Prevention of renal scarring has long been the goal of therapy for pediatric UTI. Risk factors for renal scar formation after UTI include young age, female sex, VUR, recurrent infection, WBC and C-reactive protein level, bacterial virulence, and genetic susceptibility [11–15]. However, histologic examination of scarred kidneys that were surgically removed, in particular from young, refluxing males, shows focal renal dysplasia alongside of segmental scarring. This raises the question that some observed renal abnormalities may be congenital in nature, rather than acquired from infection [16].

Epidemiology

Urinary tract infection is one of the most common infections in children with approximately 19 episodes per 1000 children annually. During the first 6 years of life, 8% of all girls and 2% of all boys will have a symptomatic urinary tract infection [17]. In febrile infants and children, somewhere between 1 and 17% will prove to have a urinary tract infection [1, 17–19].

Results of DMSA scans performed soon after a first UTI in children 2 years of age and younger suggest that 75% of these children with coexisting fever and bacteriuria will prove to have pyelonephritis [20]. Caucasian girls with fever are more likely to have a UTI than African American girls or boys of any ethnicity [21, 22]. Uncircumcised male infants also have an increased risk of UTI in the first few months of life [23–26]. In a multicenter, prospective on 1025 febrile infants ≤ 60 days of age, Zorc et al. showed that uncircumcised male infants had a higher rate of UTI (21.3%) compared with female (5.0%) and circumcised male (2.3%) infants [26].

The overall prevalence of VUR is uncertain as most of cases involving children are asymptomatic. Also large-scale population screening using voiding cystourethrography VCUG has not been done and cannot be justified. Most review articles suggest a frequency of around 1% in well children [27–30]. During the first year of life, boys may have a higher rate and grade of VUR than girls [31–33]. There are studies which provide good evidence for heritability of VUR. Kaefer et al. demonstrated an 80% concordance in monozygotic and 35% concordance in dizygotic twins [34]. The overall incidence of VUR in siblings of infants and children with VUR was found to be about 37% in one study of 482 siblings, with decreasing incidence in older siblings as follows: 46% for siblings under 2 years, 33% for 2–6 years, and only 7% when older than 6 years of age [35]. There is no known correlation between index patient reflux grade, sex, and cortical scars with the likelihood of sibling reflux [36].

Even in children with no identifiable urinary tract abnormality, recurrent febrile UTIs may cause significant morbidity. In one study of 850 children, 45% of girls and 14% of boys had recurrent UTI. In those with a negative imaging workup (renal US and VCUG) after febrile UTI, 28% of girls and 4% of boys developed a recurrent febrile UTI [37].

Overall Cost to Society

In the United States, UTIs account for more than 1 million outpatient visits among children younger than 18 years and about 25,000 visits to urologists for evaluation and treatment of VUR annually [38]. Monetary costs of hospitalization, antibiotic therapy, loss of work for caregivers, imaging evaluation, and complications of infections and therapy have not been scientifically studied in the United States, though there has been some attempt to do so in other countries such as Britain, Australia, and Israel [39–41]. It is clear that the approach to

treatment and subsequent imaging, despite professional society guidelines, varies greatly from region to region throughout the United States [5, 42–47].

Goals of Imaging

There are two immediate goals of imaging in the setting of urinary tract infection (1): to identify urinary tract obstruction and resultant urinary stasis that may warrant surgical intervention to lessen the risk of sepsis, recurrent infection, and preserve renal function and (2) to prevent the formation and/or minimize the progression of renal scars by identifying patients at increased risk of progressive scar formation. The long-term goal is to prevent the complications of chronic renal scars, namely, hypertension, chronic renal failure (CRF), and complications of pregnancy in women. Renal scars may form as a result of pyelonephritis both with and without accompanying VUR, Table 40.1 [16].

Methodology

A Medline search was performed by an experienced, trained medical librarian using PubMed (National Library of Medicine, Bethesda, Maryland) for original research and review articles, including clinical trials and meta-analyses, targeted at discussing the diagnosis, treatment, and imaging of urinary tract infection in infants and children. Both English language and non-English language searches were performed, though the non-English literature was only included if an English translation of the abstract was available and the content deemed vital and worthy of further investigation. Animal studies were included as well. The search covered the years 1966 through September 2015. After review of available abstracts, the entire text of relevant articles were obtained and read in detail by the first author.

Discussion of Issues

What Is Known About the Natural History of Urinary Tract Infections in Infants and Children?

Summary of Evidence Few studies provide us with the long-term outcomes of children with UTI [65], despite the very large, often poor quality, and sometimes conflicting amount of literature since the earliest UTI study in children and young adults by Bright in the early nineteenth century [66]. The modern study of urinary tract infections began in the mid-twentieth century when children were evaluated with the evolving radiologic tools of voiding cystourethrography (VCUG) and intravenous urography (IVU), a test only rarely used today [67].

Supporting Evidence Table 40.1 summarizes the complex and at times conflicting literature that addresses the relationship between urinary tract infection, VUR, and renal cortical scarring in various cohorts, beginning in 1964. One important point to keep in mind is that 90% of infants and children with febrile UTI will not have recurrence [68].

Because acute symptoms of most UTIs seem to resolve uneventfully, even without treatment, the main emphasis on diagnosis and treatment of UTIs rests on the belief that doing so will reduce the risk of renal scarring and associated sequelae specially in does with underlying VUR [69, 70]. Higher grades of VUR have been associated with a greater frequency of renal scar formation after UTI by many studies [12, 64, 71]. In a study by Lee et al., 48 children with unilateral VUR were followed for 6 months to evaluate the risk of scar in refluxing versus non-refluxing kidneys. Out of 48 refluxing renal units, 23 (47.9%) had renal scar on DMSA scan. Renal scars were also seen in 7 (14.6%) of 48 non-refluxing renal units [60]. Other studies of renal units report similar results [72]. By studying patients with unilateral VUR and comparing the risk of scar formation in refluxing vs. non-refluxing renal units, these studies could minimize possible effects of factors

Table 40.1 Summary data on the role of imaging in children with UTI

First author	Specialty of first author	Study design	Year of publication	Number of patients	Number of kidneys	Population studied	Overall <i>N</i> with reflux (%)	Overall <i>N</i> with scars (%)	Scars in the population with VUR (%)	Scars in the population without VUR (%)	Period of follow-up
Kunin [1]	Preventive medicine	R	1964	107	NA	School-age children with UTI	19%	13% (IVU)	NA	NA	NA
Smellie [22]	Pediatrics	R	1964	200	NA	3 days–12 years	34%	17% (IVU)	NA	NA	NA
Rolleston [48]	Radiology	P	1970	175	350	3 days–12 months UTI without obstruction	49%	NA	22% (IVU)	NA	5 years
Pylkkänen [49]	NA	P	1981	252	NA	Infants and children with UTI	8%	3% (IVU)	40%	0%	2 years
Bourchier [50]	NA	R	1984	100	NA	Infants with UTI	36%	10% (IVU)	NA	NA	NA
Jakobsson [51]	Pediatrics	P	1992	106	NA	0–15.9 years with symptomatic UTI	25%	52% (DMSA)	88%	40%	2 months
Ditchfield [52]	Radiology	P	1994	150	300	>5 years	33%	NA	NA	NA	NA
Benador [8]	Pediatrics	P	1997	107	NA	0–16 years	36%	60%	63%	63%	2+ months
Jakobsson [51]	Pediatrics	P	1997	185	NA	UTI in child <10 years	37%	36%	51%	27%	2 years
Wennerstrom [53]	Pediatrics	P	1998	688	NA	0–15 years with first symptomatic UTI	33%	11% (IVU)	26%	3%	NA
Gelfand [54]	Radiology	P	2000	919	NA	Birth→1 year UTI, separated by age 0–1 year, 10 years	29% 46% 18%	NA	NA	NA	NA
Honkinen [2]	Pediatrics	R	2000	134	NA	UTI with bacteriuria from birth to 15 years 1 week–3 months 3–11 months 12 months to 15 years	33% 41% 56%	NA	NA	NA	NA
Smellie [55]	Pediatrics	P	2001	228 149	NA	Infants and children with UTI who were found to have reflux with follow-up at 5 and 10 years	100%	43% 42%	43% 42% (DMSA)	NA	5 years 10 years

(continued)

Table 40.1 (continued)

First author	Specialty of first author	Study design	Year of publication	Number of patients	Number of kidneys	Population studied	Overall <i>N</i> with reflux (%)	Overall <i>N</i> with scars (%)	Scars in the population with VUR (%)	Scars in the population without VUR (%)	Period of follow-up
Ilyas [56]	Nephrology	R	2002	208	NA	>2 years 2–8 years >8 years	51% 47% 28%	NA	NA	NA	NA
Moorthy [57]	Radiology	R	2005	108	216	<1 year with UTI	12% of kidneys	4% (DMSA)	16%	2%	NA
Gonzalez [58]	Pediatrics	P	2005	161	322	0–1.2 years with defects on DMSA during UTI	28%	32%	(varies with > 60% reflux grade)	47%	
Garin [59]	Pediatrics	P	2006	218	NA	3 months–18 years with defects on DMSA during UTI (excludes reflux)	52%	24%	NA	NA	1 year
Lee [60]	Pediatrics	P	2006	48	96	<1 year with known unilateral VUR	100%	31%	48%	15%	6 month
Tseng [61]	Pediatrics	R	2007	142	NA	<2 years	30%	1.4%			1 month
Montini [62]	Pediatrics	P	2007	502		1 month–7 years with diagnosis of acute pyelonephritis	20%	13.7–17.7% at 12 months post treatment			12 months
Sheu [63]	Pediatrics		2009	79		1–120 months with febrile UTI	40%				
Zaffanello [64]	Pediatrics	P	2009	65		<2 years with the first UTI and normal prenatal ultrasound	55%	19%			
Lee [11]	Pediatrics	P	2012	213		<1 year with pyelonephritis		17.4% (DMSA)	39%	8%	

Summary of investigations to identify the frequency with which urinary tract infections (UTI), vesicoureteric reflux (VUR), and renal cortical scars coexist. In the early years, the presence of scars tended to be evaluated with intravenous urography (IVU), the best available tool at the time. More recently, scars have been more sensitively identified with 99mTc-labeled dimercaptosuccinic acid (DMSA), enhanced further with the use of single photon emission computed tomography (SPECT). Each requires an intravenous puncture and ionizing radiation, but placement of a bladder catheter is rarely required

Abbreviations: *R* retrospective, *P* prospective, *IVU* intravenous urogram or pyelogram (Adapted with kind permission of Springer Science+Business Media from Barnewolt CE, Connolly LP, Estrada CR, Applegate KE. Urinary Tract Infection in Infants and Children. In Medina LS, Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science+Business Media, 2010)

such as genetic susceptibility and bacterial virulence. A meta-analysis of by Shaikh et al. including 1280 patients younger than 18 years indicated that the greatest risk factor for renal scarring is the presence of grade IV or V vesicoureteral reflux. However, such degree of reflux was only present in 4.1% of the patients [73].

Acute pyelonephritis is not always associated with VUR [2, 7, 8, 22, 48–54, 56–59]; renal cortical scars occur in children with a history of UTI but no VUR [7, 8, 11, 51, 53, 58, 59]. Moreover, evidence show that many cases of VUR might be in fact a part of other congenital abnormalities of the kidney and therefore the increased risk of scar formation in such patients can't be attributed to VUR alone [74, 75].

The prevalence of VUR markedly and spontaneously diminishes in the first few years of life, Table 40.1 [1–3, 6–8, 22, 48–59]. The likelihood of resolution of VUR increases with decreased grade and with unilateral VUR. Some data suggest that neither gender nor the presence or absence of renal cortical scars affect the rate of VUR resolution, while others suggest that resolution of VUR occurs more quickly in boys and in the absence of renal cortical scars [53, 55, 76, 77].

In 1812, Bell described the anatomy of the ureterovesical junction, explaining the configuration that prevents regurgitation of the urine into the ducts of the kidney, emphasizing the importance of the ureteral obliquity [78]. Assuming that reflux of infected urine leads to a high incidence of pyelonephritis and resultant scars, prevention of such reflux should decrease the incidence of scarring, thus improving long-term outcomes. However, studies comparing outcomes of patients treated with prophylactic antibiotic (medical treatment) and antireflux procedures (surgical treatment) have not shown a distinct difference between the two groups [59, 79–98].

Large studies suggest that prophylactic antibiotic therapy does not prevent recurrent UTI and therefore may not prevent progression of renal compromise. Further, surgical or endoscopic correction of VUR may not improve long-term outcome in these children. Nagler and colleagues performed a meta-analysis of randomized con-

trolled trials to evaluate the benefits and harms of different treatment options for primary VUR. They identified eight studies, including 1039 children comparing long-term antibiotic therapy with surveillance or placebo and ten trials including 1141 children evaluating the value added by long-term antibiotics to surgical or endoscopic correction of VUR. They concluded that compared with no treatment, the use of long-term, low-dose antibiotics did not significantly reduce the number of repeat symptomatic and febrile UTIs in children with VUR. Antibiotic prophylaxis did reduced the risk of future renal parenchymal damage, but the number needed to treat was large at 33, and since treatment is usually needed over a prolonged period, they stated that the long-term benefits of this effect are uncertain and this needs to be balanced against a number of measurable and unmeasurable costs and risks [99, 100].

The incidence of new cases of end-stage renal disease (ESRD) in Australia and New Zealand did not diminish with the use of prophylactic antibiotics and surgical treatment of VUR [39]. Salo et al. found no patients among the 1576 reviewed cases for whom childhood UTIs were the main cause of subsequent CKD [101]. Active treatment of VUR doesn't seem to reduce the occurrence of CKD, and prospective follow-up studies show well-preserved renal function in patients with VUR [102]. Updated from new summary evidence since the 1999 guideline, the 2011 American Academy of Pediatrics (AAP) guideline does not recommend prophylactic antibiotic therapy in infants and young children of 2 months to 2 years of age with VUR [5].

What Can Imaging Reveal in the Setting of UTI?

Summary of Evidence Routine imaging during an acute episode of UTI is not necessary to make the diagnosis (moderate evidence). In nonroutine cases that require imaging, the gold standard imaging test to diagnose pyelonephritis is technetium-99m dimercaptosuccinic acid (Tc-99m DMSA) (moderate evidence), although

ultrasound (particularly with the use of Doppler), computed tomography (CT), and magnetic resonance imaging (MRI) are used with lower sensitivity and specificity [103].

Table 40.2 provides information about the diagnostic performance of tests for UTI, pyelonephritis, VUR, and renal scarring. Currently, only the DMSA test can adequately predict the later development of renal scar (moderate evidence).

If the patient is not responding to usual medical therapy, a complication, such as abscess formation, may be suspected. Renal abscesses can be detected with cross-sectional imaging; the choice of US versus CT or MR depends on the size of the child and the availability and experience of the imager. The American College of Radiology has developed appropriateness criteria and provided the estimated radiation exposures for imaging subgroups of children after first urinary tract infection [115]. The diagnostic test performance for the detection of renal scar and VUR in infants and children is shown in Table 40.2.

Supporting Evidence

Abdominal Radiographs

Abdominal radiographs have essentially no role in the evaluation of suspected UTI in infants and children, unless other diagnoses are under consideration. Radiographs can suggest the alternate diagnoses of the gastrointestinal tract, large abdominal masses, and abnormal abdominal/retroperitoneal calcifications.

Sonography

Ultrasound evaluation of the kidneys and bladder is a readily available, safe modality but is insensitive for the diagnosis of acute pyelonephritis (moderate evidence) and even for the diagnosis of renal abscess. Acute pyelonephritis is suspected with focal swelling, loss of corticomedullary differentiation, and/or a decrease in relative vascularity. Doppler US only marginally improves sensitivity and specificity. It is a useful modality for the qualitative evaluation of urinary tract obstruction at the level of the ureteropelvic junction, ureterovesicular junction, and sometimes for bladder outlet obstruction with the

observation of bladder wall thickening. Quantitative grading systems exist for the systematic description of hydronephrosis, though they are not universally adopted [116]. Ultrasound provides no direct, quantifiable measure of renal function.

Ultrasound has poor sensitivity and specificity for the identification of VUR (moderate evidence) [117–127]. Specifically, the observation of hydronephrosis does not indicate the presence of VUR, and the absence of hydronephrosis does not exclude the diagnosis of VUR, even high-grade VUR, as VUR is an intermittent phenomenon. These limitations may be improved with documentation of changes in collecting system caliber [117]. Changes in renal pelvic diameter (>4 mm) have been associated with high-grade VUR and renal damage.

Intravenous Pyelogram (IVP)

Prior to the era of cross-sectional imaging, IVP was the mainstay of urologic imaging. It has the advantages of availability and assessment of renal function, obstruction, and overall anatomy. It has the disadvantages of venipuncture, risk of iodinated contrast reaction, and exposure to ionizing radiation. It is insensitive, when compared to Tc-99m DMSA, for detection of both acute infection and cortical scars. It has no role in the diagnosis or exclusion of VUR. Therefore, its role is limited to patients with complex ureteral anatomy or postoperative ureteral obstructions.

Computed Tomography (CT) and Magnetic Resonance Imaging (MRI)/MR Urography (MRU)

Contrast-enhanced CT and MR do not play a role in routine UTI, although they may detect pyelonephritis during emergent imaging of a child with abdominal pain. CT and MR have lower sensitivity and specificity, on average, compared to DMSA for the detection of pyelonephritis and renal scar. Both provide moderate sensitivity and specificity for pyelonephritis, cortical scarring, abscess formation, urinary tract obstruction, and anatomic variants such as subtle duplex systems [104, 128–131]. In the

Table 40.2 Reference standard test and diagnostic test performance for the detection of UTI, pyelonephritis, renal scar, and VUR in infants and children

Test	Sensitivity (%)	Specificity (%)	Reference standard	References
UTI			Urine culture	
Cloudy appearing urine	90	72–82		
Urine dipstick ^a	96	99		
Urine culture (clean catch)	75–100	57–100		
<i>Pyelonephritis</i>			DMSA	
Fever >38.1 °C	47	56		
Fever ≥39 °C for 2 days (age <2 years)	95	31		
Ultrasound (with power Doppler)	57	82		[104]
DMSA	50–91			[6]
CT or MRI	87–92	88–94		[104]
Renal or bladder congenital anomalies, obstruction			US	
<i>VUR</i>			VCUG	
RNC (radionuclidecystogram)	50–87	88		[105]
US	18	88		[106]
	50	77		[107]
MR-VCUG	76–100	68–96		[108–110]
Renal scarring			DMSA	
DMSA nuclear scintigraphy	94	100		[111]
Ultrasound				[112]
Diffuse scarring	47	92		
Focal scarring	5	98		
MRI ^b	77	87		[113]

^aPositive for protein, leukocyte esterase, and nitrate

^bMRI without gadolinium compared to DMSA as the gold standard [113]

Data from Whiting et al. [114] unless otherwise stated

(Adapted with kind permission of Springer Science+Business Media from Barnewolt CE, Connolly LP, Estrada CR, Applegate KE. Urinary Tract Infection in Infants and Children. In Medina LS, Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science+Business Media, 2010)

case of CT and MR contrast agents, adverse reactions have been reported. Gadolinium administration with MRU is accompanied by risk of nephrogenic systemic fibrosis if the child has renal dysfunction [132].

Takazakura et al. found that magnetic resonance voiding cystourethrography (MRVCUG) is 90% sensitive with a specificity of 96% for detecting VUR, suggesting it is a safe diagnostic test of reflux nephropathy which is performed without radiation [133, 134]. Other studies on this modality have also shown acceptable sensitivity and specificity [108–110, 135]. However, all these studies used limited sample size.

Nuclear Medicine

Tc-99m dimercaptosuccinic acid (Tc-99m DMSA) is the gold standard for detection of both acute pyelonephritis, with the observation of flare-shaped regions of decreased radioactivity, and renal scars, as indicated by focal loss of cortical bulk [136]. It is far more sensitive and specific in general than ultrasound and CT or MR. It has the disadvantages of the need for venipuncture to administer the radiopharmaceutical and exposure to radiation. However, the radiation dose per study is relatively low (1 mSv).

Tc-99m mercaptoacetyltriglycine (Tc-99m MAG3) and Tc-99m diethylenetriamine pentaacetic acid (Tc-99m DTPA) each provide quanti-

fiable data to diagnose and exclude urinary tract obstruction, often using intravenous furosemide challenge. Tc-99m MAG3 provides little other anatomic details. Tc-99m DTPA can be used to assess physiologic parameters such as differential renal function, renal plasma flow, and glomerular filtration. Both also require venipuncture to administer the radiopharmaceutical and exposure to radiation.

Evaluation for Vesicoureteric Reflux

The only reliable way to diagnose or exclude VUR is with a voiding cystogram, either VCUG using iodinated contrast agents and fluoroscopy or radionuclide cystogram (RNC) using the radiotracer Tc-99m pertechnetate, instilled along with saline into the urinary bladder, with continuous observation with a gamma camera during the filling and voiding phases. The rate of VUR in children with documented febrile UTI is 24% or lower [5]. The prevalence of VUR in normal infants and children is unknown. There are also the contrast-enhanced urosonography test that uses sonographic contrast agents [137] and the MRI-VCUG that avoids ionizing radiation exposure. Sonographic contrast is approved outside of North America and both tests will be discussed below [137]. Both the VCUG and RNC require placement of a urethral catheter, which can be an uncomfortable procedure, particularly in inexperienced hands. While briefly uncomfortable, the examination is generally not associated with complications [138]. Both tests use small amounts of ionizing radiation. Though the development of pulsed fluoroscopy equipment has lessened the discrepancy in dose between the two studies, RNC continues to have lower exposures than does VCUG [128–130, 139]. However, RNC is less available in general and community hospitals, and, therefore, fluoroscopic VCUG is more commonly performed. The RNC is generally used for girls because the visualization of the urethra is not essential unless there are symptoms of voiding dysfunction without UTI; the fluoroscopic VCUG is required in this subset of girls and in all boys to demonstrate the anatomy of the male urethra, an important source of obstruction in boys with febrile UTI.

What Are the Recent Updates to the Diagnosis and Management of the Initial Febrile Urinary Tract Infection in Infants and Children 2–24 Months?

Summary of Evidence The diagnosis of UTI is now made on the basis of the presence of both pyuria and at least 50,000 colonies per mL of a single uropathogenic organism in an appropriately collected specimen of urine [5] (strong evidence). Infants and young children should receive 7–14 days of antimicrobial treatment and should then receive close clinical follow-up monitoring to permit prompt diagnosis and treatment of recurrent infections [5] (strong evidence). Renal and bladder ultrasound (RBUS) should be performed to evaluate for anatomic abnormalities [5] (moderate evidence).

Synthesis of the current evidence does not support the prophylactic use of antimicrobial to prevent febrile recurrent UTI in infants without vesicoureteral reflux (VUR) or with grade I to IV VUR [5] (strong evidence). As a result of this, the latest clinical practice guideline from the American Academy of Pediatrics (AAP) does not recommend routine assessment with voiding cystourethrography (VCUG) after the first febrile UTI. However, VCUG is indicated if renal and bladder ultrasonography reveals hydronephrosis and scarring or if other findings suggest either high-grade VUR or obstructive uropathy and in other atypical or complex clinical circumstances [5]. Also, VCUG should be performed if there is a recurrence of febrile UTI (moderate evidence).

Supporting Evidence In 2011, the AAP updated its clinical practice guideline for the diagnosis and management of the initial urinary tract infection in febrile infants and children 2–24 months. This is based on new evidence since the 1999 practice guideline (changes are highlighted in **bold** below). The main recommendations are as follows.

In a febrile infant or young child with no obvious source for the fever, 5% of cases will have UTI [140, 141]. In those that require immediate antimicrobial therapy, the clinician should ensure

that a urine specimen is obtained for both culture and urinalysis before antimicrobial therapy is administered. The urine specimen should be obtained through catheterization or suprapubic aspiration (SPA). This is because the diagnosis of UTI cannot be established reliably from urine collected in a bag (strong evidence) [5].

In a febrile infant or young child with no apparent source for the fever that does not require immediate antimicrobial therapy, the clinician should assess the likelihood of UTI. If the likelihood of UTI is low, then clinical follow-up monitoring without testing is sufficient (strong evidence) [5]. If the likelihood of UTI is not low, the clinician should either obtain a urine specimen through catheterization or SPA for culture and urinalysis or obtain a urine specimen through the most convenient means to perform a urinalysis. If the urinalysis results suggest a UTI, then a urine specimen should be obtained through catheterization or SPA and cultured. If the urinalysis result does not suggest a UTI, then monitoring the clinical course without initiating antimicrobial therapy is reasonable [5].

The AAP guideline recommends that to diagnose UTI requires both pyuria and at least 50,000 colonies per mL of a single uropathogenic organism in a specimen of urine obtained through catheterization or SPA (moderate evidence) [5]. Antimicrobial therapy is equally efficacious used as orally or parenterally. Treatment should be based on local antimicrobial sensitivity patterns (strong evidence). Antimicrobial therapy should be of 7–14 days duration (strong evidence) [5].

Diagnostic Imaging

Febrile infants with UTIs should undergo renal and bladder ultrasonography (RBUS) (moderate evidence) [5]. The purpose of RBUS is to detect anatomic abnormalities that require further evaluation with either additional imaging or urologic consultation. In addition, RBUS can evaluate the renal parenchyma and assess renal size which can be used to monitor renal growth. Overall, the yield of actionable findings is relatively low [5]. RBUS in this population will yield abnormal results in ~15% of cases, and 1–2% will have significant abnormalities that would lead to action

(e.g., additional evaluation, referral, or surgery). Between 2 and 3% will be false-positive results, leading to unnecessary and invasive evaluations.

The most significant change in the practice guideline that affects imaging is that VUCG should not be performed routinely after the first febrile UTI [5]. Voiding cystourethrography is only indicated if RBUS reveals abnormalities such as hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy or other atypical or complex clinical circumstances (strong evidence) [5]. For the past 40 years, after an initial UTI, children have been assessed to detect the presence of childhood genitourinary abnormalities of which VUR is the most common. This is based on the strategy of protecting the kidneys from further damage after an initial UTI. Voiding cystourethrography is often used to detect VUR. Management of VUR included continuous/prophylactic antimicrobial therapy, and surgical intervention if VUR was persistent, or recurrences of infection were not prevented with antimicrobial prophylaxis. However, the proportion of infants with high-grade VUR among all infants with febrile UTIs is small, and there are a significant number of infants who develop pyelonephritis without VUR [5]. Also, the effectiveness of antimicrobial prophylaxis has been in question for the last decade for patients who have VUR. **The current evidence does not support the use of antimicrobial prophylaxis to prevent febrile recurrent UTI in infants without vesicoureteral reflux (VUR) or with grade I to V VUR [5].**

For these reasons, VUCG is no longer routinely recommended by the AAP. Further evaluation with VUCG can be conducted if there is a recurrence of febrile UTI [5].

The last recommendation is that once a febrile UTI is confirmed, parents or guardians should be instructed to seek prompt medical evaluation for future febrile illnesses, to ensure that recurrent infections can be detected and treated promptly (moderate evidence). This may be of greater importance regardless of whether VUR is present or the child is receiving antimicrobial prophylaxis [5]. Table 40.3 summarizes the best current

Table 40.3 Summary take-home points based on the best current evidence

The prevalence of UTI in febrile infants and young children remains about 5%
Among children who do not receive immediate antimicrobial therapy, UTI can be ruled out on the basis of completely negative urinalysis results
Given the significant risk of renal scarring among children with febrile UTI, and some evidence suggests that early antimicrobial treatment mitigates that risk, prompt diagnosis and treatment of UTI are recommended
There is no significant difference in rates of recurrence of pyelonephritis/febrile UTI for children of all ages without VUR who received antimicrobial prophylaxis and those who do not
There is no significant difference in rates of recurrence of pyelonephritis/febrile UTI for children of all ages with grades I–V VUR
There is no significant difference in rates of recurrence of pyelonephritis/febrile UTI for children 2–24 months of age with VUR of any grade who received antimicrobial prophylaxis and those who do not
There is no significant difference in rates of recurrence of pyelonephritis/febrile UTI for children 2–24 months of age without VUR who received antimicrobial prophylaxis and those who do not
There is no significant difference in rates of recurrence of pyelonephritis/febrile UTI among children 2–24 months of age with grades I–V VUR who received antimicrobial therapy and those who do not
There is a statistically significant difference in rates of recurrence of any type of UTI for children of all ages with VUR who received antimicrobial prophylaxis and those who do not. However, most of this effect is attributable to reductions in rates of cystitis or asymptomatic bacteriuria and no pyelonephritis/febrile UTI, which would not be expected to lead to ongoing renal damage
There is no significant difference in rates of recurrence of any type of UTI for children of all ages without VUR who received antimicrobial prophylaxis and those who do not
Therefore, the current evidence does not support antimicrobial prophylaxis to prevent UTI when VUR is diagnosed by VCUG. The lack of difference in outcomes between those treated with antimicrobial prophylaxis and those not treated calls into question the use of VCUG to diagnosis VUR. Especially, as VCUG is one of the most uncomfortable radiologic procedures performed with children

(continued)

Table 40.3 (continued)

The current evidence (using number to treat analysis) suggests that approximately 100 children would need to undergo VCUG to prevent one UTI in the first year. The current literature also indicates that the evidence benefit is the same or better for children without VUR. This further calls into question the benefit of VCUG

From a cost-effective perspective, these data argue against VCUG after the first UTI

VCUG after a second or third UTI should have a higher yield for higher grades of reflux. However, the optimal care for infants with higher-grade reflux is still unclear

Ultrasonography of the kidneys, ureters, and bladder after the first UTI has poor sensitivity. However, the procedure is less invasive and less uncomfortable than VCUG and is without radiation

Data from Finnell et al. [142]

evidence including the latest clinical practice guidelines for the diagnosis and management of initial urinary tract infections in febrile infants and young children from the American Academy of Pediatrics.

What Are Reasonable Imaging Strategies When Caring for a Male Infant or Child with a History of a Febrile Urinary Tract Infection?

Summary of Evidence In boys, the incidence of infection, beyond the newborn period, is lower than in girls, and the grade of VUR tends to be higher in neonatal boys than in girls [33, 143]. Some boys presenting with their first UTI will have posterior urethral valves, a correctable, mechanical obstruction to urinary flow. Therefore, most current guidelines recommend imaging to identify upper urinary obstruction and/or posterior urethral valves. The American Academy of Pediatrics guideline recommends a renal/bladder ultrasound examination after a first febrile UTI in all children aged 2 months to 2 years to detect possible upper urinary tract abnormalities, obstruction in particular [5].

The purpose of renal and bladder ultrasound (RBUS) is to detect anatomical abnormalities, particularly obstruction, which warrants further evaluation. Unlike the 1999 version, the new AAP guideline recommends VCUG to be performed in both boys and girls only after second episode of febrile UTI or when there are findings suggesting high-grade VUR, obstructive uropathy, or abnormalities on RBUS. However, even then, the AAP guideline suggests that the preference of parents should be taken into consideration as VCUG is an uncomfortable procedure and involves a low dose of ionizing radiation.

Two important imaging strategies that differ for boys versus girls include the importance of defining the anatomy of the male urethra at VCUG (typically not needed in girls) and the importance of understanding higher UTI risk in uncircumcised male infants less than 6 months old.

The guideline of the UK's National Institute for Health and Clinical Excellence (NICE) doesn't recommend routine imaging to diagnose VUR either. NICE guideline reserves ultrasonography only for children of all age groups with atypical UTI and infants younger than 6 months. Atypical UTI is defined as septicemia or ill-looking child, poor urine flow, abdominal or bladder mass, elevated creatinine, failure to respond to treatment with suitable antibiotics within 48 hours, or infection with non-*Escherichia coli* organism [144].

Supporting Evidence Ultrasound is well tolerated, is readily available, requires no sedation, does not use ionizing radiation, and can identify higher grades of obstruction; however, it does not identify VUR reliably [145]. The widespread use of fetal ultrasonography, which frequently identifies children with obstructive lesions of the urinary tract in utero, has further decreased the clinical value of performing US after the first UTI. Hoberman et al. recommend that in children who have a normal prenatal ultrasonography performed in an experienced center after 30–32 weeks of gestation, sonography is not indicated after their first UTI [20]. However, not all fetuses are screened, the quality of screening varies widely between geographic areas, and variation in maternal body habitus can affect the sensitivity of this tool [68, 146].

Therefore, most guidelines support ultrasound to be included as a first-line screen [5, 144].

Some believe that low sensitivity and specificity of US in diagnosis of VUR make it an unreliable first-line screening modality, and a practice of performing VCUG only in the presence of abnormal US findings leaves a considerable number of patients with undiagnosed VUR [127]. In a study by Kimata et al., which included 306 patients of 4–72 month of age, they found that VUR was reported significantly less frequently when VCUG is performed only in the presence of abnormal US (stratified approach) compared to the group in whom VCUG was performed after the first UTI regardless of US results (non-stratified approach) [125].

Finnell et al., using the data from technical report of the AAP guideline, argue that watchful waiting after the first UTI can serve as a diagnostic test in itself [142]. Recurrent UTI has a positive predictive value of 55% for VUR of grade III or higher, and no recurrence of UTI has a negative predictive value of 81% for not having VUR. Downs et al. state that because renal scarring among children who have VUR occurs with UTI, those children who do not have subsequent UTIs would not be expected to suffer, further, preventable renal damage (that would be identified with imaging). So even if therapy for VUR was known to improve long-term outcomes, the benefit of finding VUR in children who do not have a recurrent UTI is doubtful [147]. Moreover, sensitivity and specificity of US increase when studying higher grades of VUR [148].

In a commentary by Wan et al. on behalf of the urology section of the AAP, they questioned the design of the studies cited in the AAP guideline as well as validity of the results drawn from a meta-analytic combination of the data in these studies [149]. The American Urological Association guideline also recommends both US and VCUG to be performed in all children aged 2 months to 2 years after the first febrile UTI. Prophylactic antibiotic therapy is also recommended for children less than 1 year of age with VUR with a history of a febrile urinary tract infection, children with VUR grades III–V, or children with bladder/bowel dysfunction [150].

Renal cortical scintigraphy with Tc-99m DMSA is more sensitive for scars than ultrasound but is reserved for patients found to have high-grade reflux [103, 136, 151–154]. The intention is to use the presence or absence of scars, reliably identified, as a guide to clinical management [155]. Magnetic resonance imaging is an appealing alternative because of its lack of use of ionizing radiation, but it tends to be less widely available, is expensive, and requires sedation of the infant or young child [104, 131]. Since only a minority of infants and children with proven pyelonephritis will develop scars, Tc-99m DMSA is not recommended for all cases [20, 156–158].

Finally, a quantitative assessment of obstruction is recommended if ultrasound reveals the presence of moderate to severe hydronephrosis. By definition, this includes kidneys shown to have gross calyceal dilatation, not just pelviectasis, in the absence of VUR. This can be performed with either Tc-99m MAG3, Tc-99m DTPA, or MRU. Magnetic resonance urography has the advantage of lack of use of ionizing radiation but tends to be less widely available and requires sedation of the infant or young child.

What Are Reasonable Imaging Strategies When Caring for a Female Infant or Child with a History of a Febrile Urinary Tract Infection?

Summary of Evidence Girls have a much higher incidence of UTI than boys. Similar to the recommendations for boys, most current guidelines state that renal US is recommended to identify upper urinary obstruction and VUR after the first febrile UTI.

Supporting Evidence Ultrasound evaluation of both kidneys and the bladder is used to detect congenital anomalies and obstruction. The reasoning is similar to the situation for boys, with one additional motive: the possible identification of an obstructing ureterocele, usually as part of the upper moiety of a duplex collecting system. While ureteroceles can occur in boys, the incidence is four to seven times more common in girls (Fig. 40.5a–j) [159, 160]. An ecto-

pic ureter in a duplex system may insert below the bladder sphincter in girls but *never* in boys, making girls wet every day and every night. Evaluation of this potential anatomy requires at least VCUG and may need MRI/MRU or direct cystoscopy to detect.

Special Case: Postnatal Management of Fetal Hydronephrosis

Summary of Evidence Fetal sonography detects hydronephrosis (pelvicaleiectasis or dilated ureters) in 1–5% of all pregnancies [161]. Currently, there are growing attempts to standardize fetal genitourinary system ultrasound technique, timing, and subsequent postnatal evaluation [162, 163]. The postnatal imaging with (a) resolution of hydronephrosis and (b) persistent hydronephrosis varies widely based on a lack of consensus. The most common current recommendation is to perform renal and bladder US in neonates that had moderate to severe prenatal hydronephrosis (limited evidence).

Supporting Evidence A meta-analysis was recently performed to determine whether the degree of antenatal hydronephrosis and related antenatal ultrasound findings are associated with postnatal outcome. Although the risk of VUR was similar for all degrees of fetal hydronephrosis, the risk of any postnatal pathology versus the degree of antenatal hydronephrosis was 12% for mild, 45% for moderate, and 88% for severe fetal hydronephrosis. Overall, children with any degree of antenatal hydronephrosis were at greater risk of postnatal pathology as compared with the normal population. Moderate and severe antenatal hydronephrosis has a significant risk of postnatal pathology, indicating that comprehensive postnatal diagnostic management should be performed. Mild antenatal hydronephrosis may carry a risk for postnatal pathology, but additional prospective studies are needed to determine the optimal management of these children [161].

Infants with a history of mild hydronephrosis may not require postnatal evaluation. Distinction between these two groups assumes that the fetal

ultrasound examination attempts to characterize the degree of dilatation, does so correctly, and consistently and accurately conveys this information to the postnatal caregivers. This may not be the case [146].

A recent systematic study, evaluating a group of nearly 500 newborns with thorough prenatal and postnatal evaluation, found a VUR incidence of 9%. This study reports that approximately 75% of those with VUR have low-grade reflux that resolves rapidly (grades I–III), but about one-quarters have a high-grade reflux. In the group with high-grade VUR, spontaneous resolution by 2 years of age was rare. Encouragingly, persistent reflux was rarely associated with impaired renal function [164–166]. A study of over 1500 infants with persistent postnatal grade II hydronephrosis (using the Society for Fetal Urography grading system) showed that screening for VUR and treatment with prophylactic antibiotic decreased the risk of febrile UTI when compared with the group who were not screened [167]. In a meta-analysis of 34 studies reporting VUR incidence among 4756 infants, VUR was detected in an average of 16% of infants who had prenatal hydronephrosis (PNH). Despite high rate of VUR in infants with history of PNH compared to general population (16 vs 1%) according to the American Urological Association, postnatal screening cystography in such infants remains an “option” rather than a “recommendation.” The reason is lack of prospective study demonstrating benefit of reflux detection in asymptomatic neonates [45].

An increasingly popular approach to the postnatal evaluation of infants with fetal hydronephrosis is to (a) perform the initial RBUS at 7–10 days after birth [168] and (b) use postnatal ultrasound as a tool to determine whether or not further imaging is recommended [164]. If hydronephrosis, scarring, or renal dysplasia are discovered by careful postnatal ultrasound, further evaluation with a follow-up RBUS, or if significant, a reflux study, either RNC or VCUG, is suggested. However, some infants with high-grade VUR will not be discovered by this technique. The challenge is to determine how much pelviectasis/hydronephrosis is required to warrant VCUG (Figs. 40.7a–i and 40.8a, b).

It is important to realize that, throughout this analysis of imaging of UTI, we have been operating under the assumption that sterile VUR does not cause impairment in renal function. Some evidence shows that renal cortical defects are related to the presence of high-grade, sterile VUR [169–171].

Take-Home Tables and Figures

Table 40.1 summarizes the literature on the role imaging of UTI in children. Table 40.2 provides information about the diagnostic performance of tests for UTI, pyelonephritis, VUR, and renal scarring. Table 40.3 summarizes the best current evidence including the latest clinical practice guidelines for the diagnosis and management of initial urinary tract infections in febrile infants and young children from the American Academy of Pediatrics.

Figures 40.1 and 40.2 show flowcharts that provide a strategy for the imaging evaluation of male and female infants and children; Figures 40.1 and 40.2 assume that prophylactic antibiotics will not be used.

Imaging Case Studies

Case 1

Figure 40.3a–g shows the case of an adolescent boy who first presented at 14 years of age with a febrile UTI and hematuria.

Case 2

Figure 40.4a–e shows the case of a boy who first presented at 2 years of age for evaluation after second febrile UTI.

Case 3

Figure 40.5a–j shows a case of a 2-month-old female infant who presented with a febrile UTI.

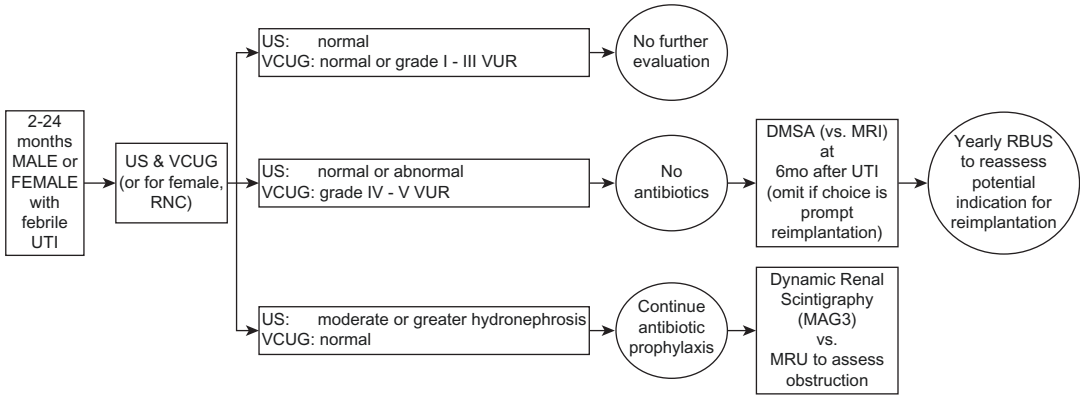


Fig. 40.1 This flowchart provides a suggested strategy for the imaging evaluation of male and female infants and young children aged 2–24 months with initial febrile UTI. It is based on the 2011 American Academy of Pediatrics guideline (this may be revised if new evidence emerges) and assumes that the use of prophylactic antibiotic is of no

demonstrable benefit in improving overall outcomes but remains commonly used (*US* ultrasound, *VCUG* voiding cystourethrogram, *DMSA* 99mTc-labeled dimercaptosuccinic acid, *MRI* magnetic resonance imaging, *MAG3* 99mTc-labeled mercaptoacetyltriglycine, *MRU* magnetic resonance urography, *RNC* radionuclide cystogram)

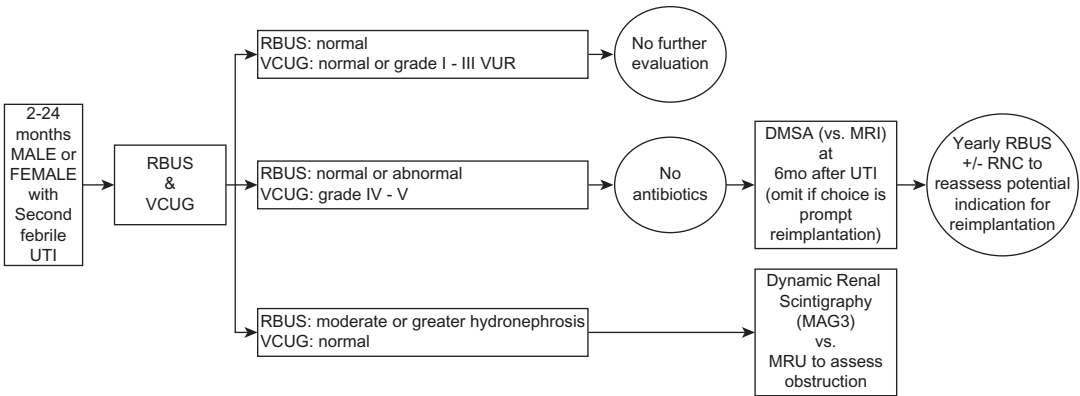


Fig. 40.2 This flowchart is a modified version of Fig. 40.1. The suggested strategy is for recurrent febrile UTI, and it is again based on the AAP 2011 guideline for infants and young children, aged 2–24 months (*US* ultrasound, *VCUG* voiding cystourethrogram, *DMSA* 99mTc-

labeled dimercaptosuccinic acid, *MRI* magnetic resonance imaging, *MAG3* 99mTc-labeled mercaptoacetyltriglycine, *MRU* magnetic resonance urography, *RNC* radionuclide cystogram)

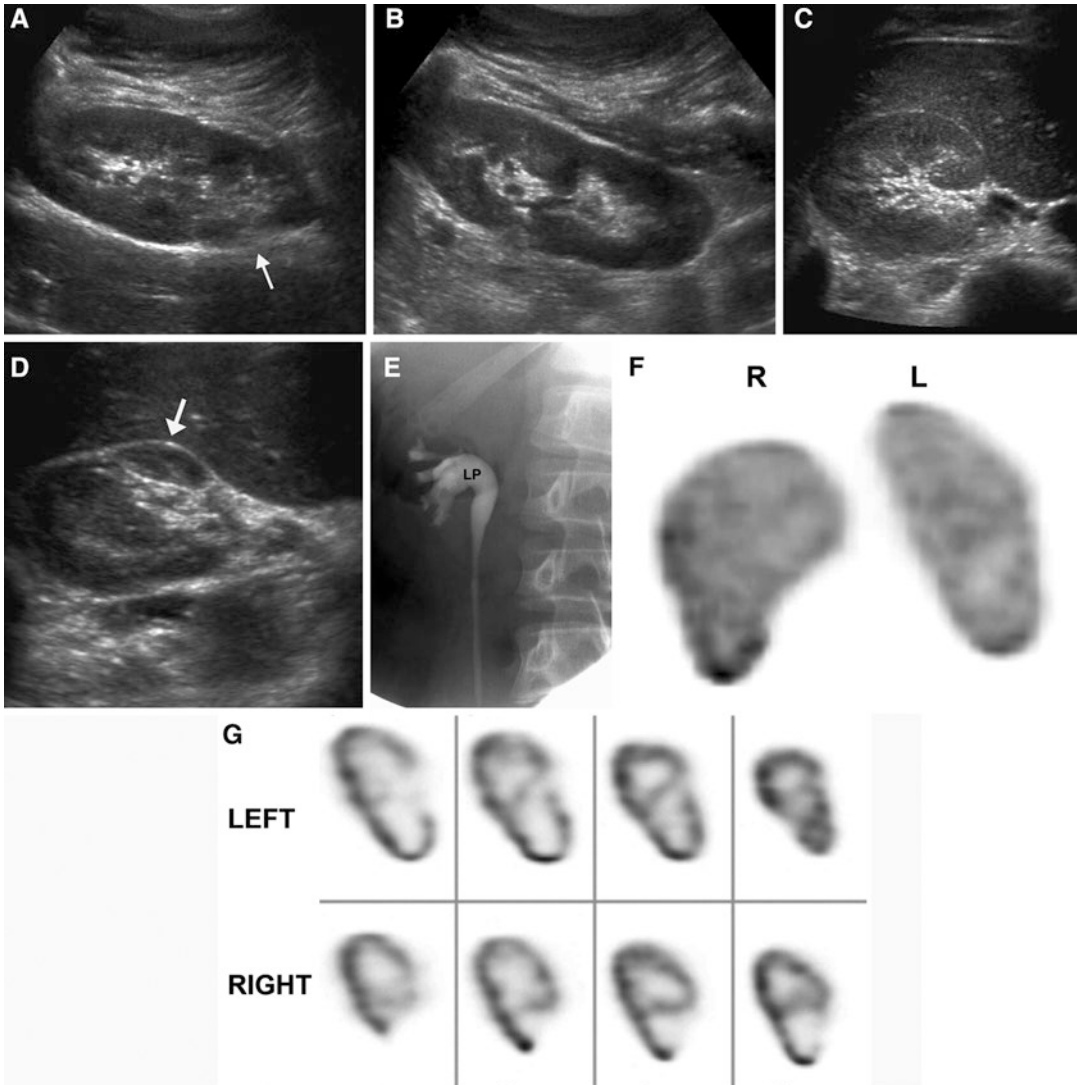


Fig. 40.3 These series of images were performed over a period of 3 months for evaluation of an adolescent boy who first presented at 14 years of age with a UTI and hematuria. Evaluation began with ultrasound, where it was suspected that the right kidney contained a duplex collecting system and there was evidence for associated right lower pole scarring (**a**), prone sagittal view of the right kidney; *arrow* indicates site of focal cortical thinning; (**b**), prone sagittal view of normal appearing left kidney; (**c**), normal transverse view of the upper pole of the right kidney; (**d**), transverse view of the scarred right lower pole; *arrow* indicates site of anterior cortical thin-

ning, raising the question of VUR into the lower moiety, which was subsequently proved by VCUG (**e**) (LP lower pole). Tc-99m DMSA confirmed the suspicion of right lower pole scarring on reconstructed (**f**) and source SPECT views (**g**). (Reprinted with kind permission of Springer Science+Business Media from Barnewolt CE, Connolly LP, Estrada CR, Applegate KE. Urinary Tract Infection in Infants and Children. In Medina LS, Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science+Business Media, 2010)

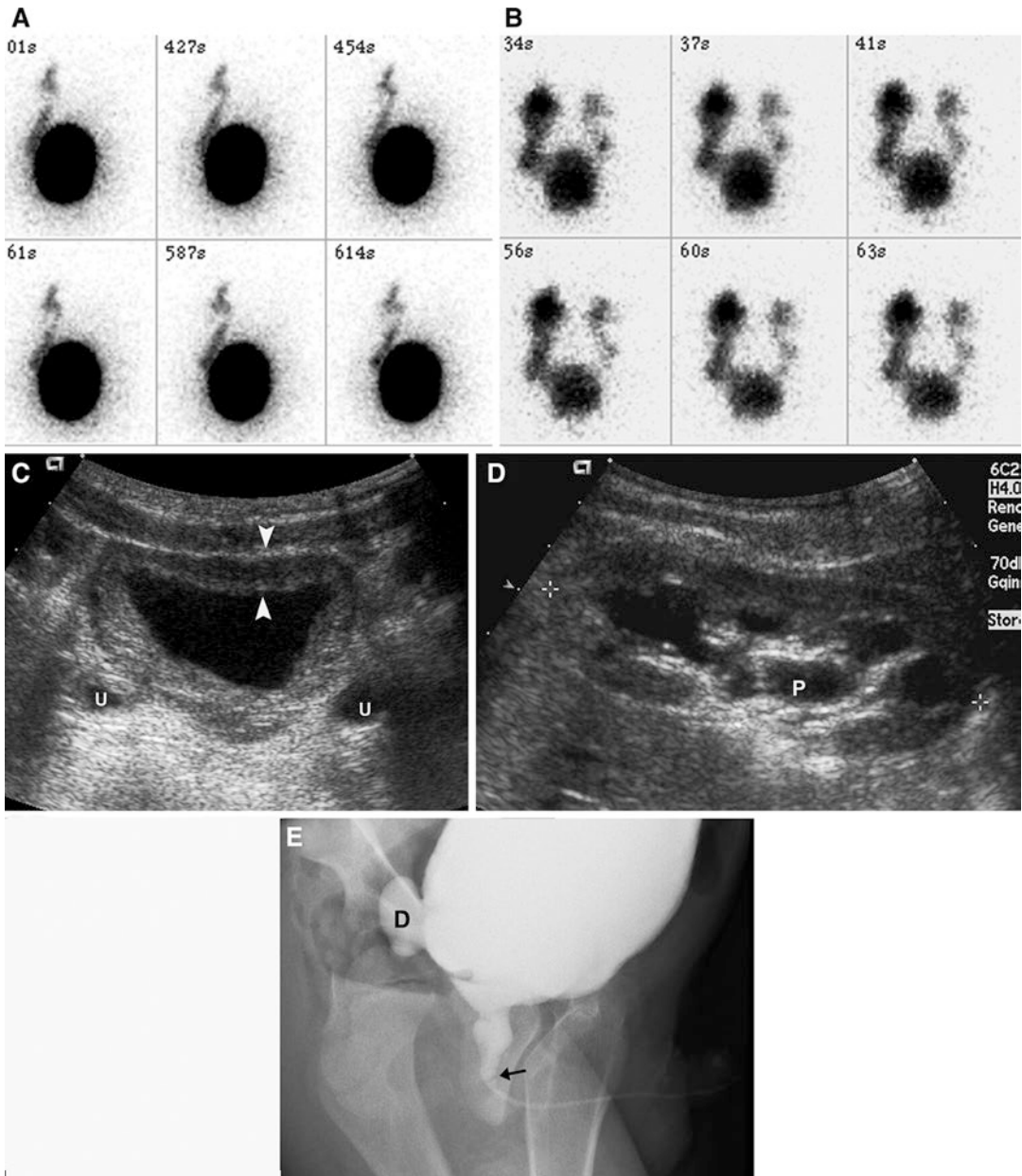


Fig. 40.4 This example is a lesson in the importance of careful evaluation of urethral anatomy in boys. Interestingly, this little boy first presented at 2 years of age for evaluation after recurrent UTI. Radionuclide cystogram demonstrated left grade 2 VUR on prone views (a), which had become bilateral and increased in grade 1 year later (b). Subsequent reimplantation was performed, and a postoperative ultrasound revealed bilateral, distal hydroureter, bladder wall thickening, and persistent hydronephrosis (c) transverse view of the urinary bladder; u, distal hydroureter; arrowheads indicate a thickened bladder wall; (d), prone, sagittal view of the moderately hydronephrotic right kidney; p, dilated renal pelvis. Subsequent VCUG (e) revealed the presence of

previously unrecognized posterior urethral valves (arrow) and a moderate-sized bladder diverticulum (D diverticulum). Theoretically, progression of VUR and subsequent ureteral reimplantation may have been avoided had the presence of posterior urethral valves been initially recognized and addressed (by performing VCUG rather than RNC) (Reprinted with kind permission of Springer Science+Business Media from Barnewolt CE, Connolly LP, Estrada CR, Applegate KE. Urinary Tract Infection in Infants and Children. In Medina LS, Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science+Business Media, 2010)

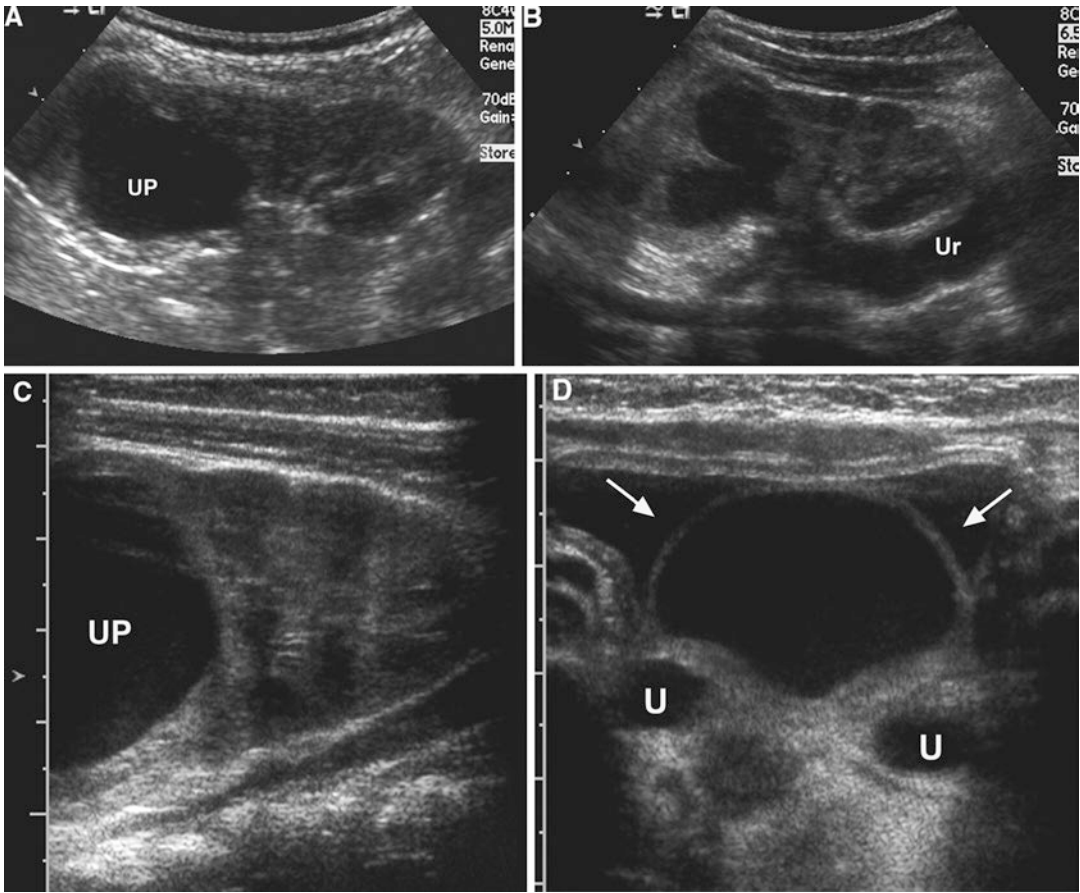


Fig. 40.5 This 2-month-old female infant presented with a febrile UTI, where her initial ultrasound demonstrated the presence of a duplex left kidney, with upper pole hydronephrosis (a–c), (sagittal views of the left kidney demonstrating a dilated upper pole pelvis (UP) and dilated upper pole ureter (Ur)), associated with a moderately large ureterocele and bilateral, distal hydronephrosis (d), (transverse view of the bladder demonstrating dilated distal ureters (u) and a ureterocele (arrows)). Therefore, a VCUG was performed on the same day, revealing a filling defect within the urinary bladder on early-fill views of the bladder (e), (arrowheads outline left ureterocele) and on an oblique view of the right side (f), (arrowhead, left ureterocele; arrow, refluxing right ureter), with the additional observation of high-grade VUR on the right (g). (B bladder, RU dilated, refluxing right ureter). With voiding, the ureterocele prolapsed into the urethra (h), (arrowheads, ureterocele prolapsing into the urethra). Subsequent

Tc-99m DMSA, both routine (i) and pinhole views (j), revealed a photopenic defect in the left upper pole. Without the ultrasound and VCUG findings, this may have been difficult to differentiate from a large focal scar. With the identification of a complex anatomic anomaly by ultrasound, it was important to redirect from RNC to VCUG to demonstrate the finer points of urinary tract anatomy that could not have been fully discerned by RNC. This is one of only a few situations where VCUG, rather than RNC, is preferable in girls and can be determined based on screening RBUS (Reprinted with kind permission of Springer Science+Business Media from Barnewolt CE, Connolly LP, Estrada CR, Applegate KE. Urinary Tract Infection in Infants and Children. In Medina LS, Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science+Business Media, 2010)

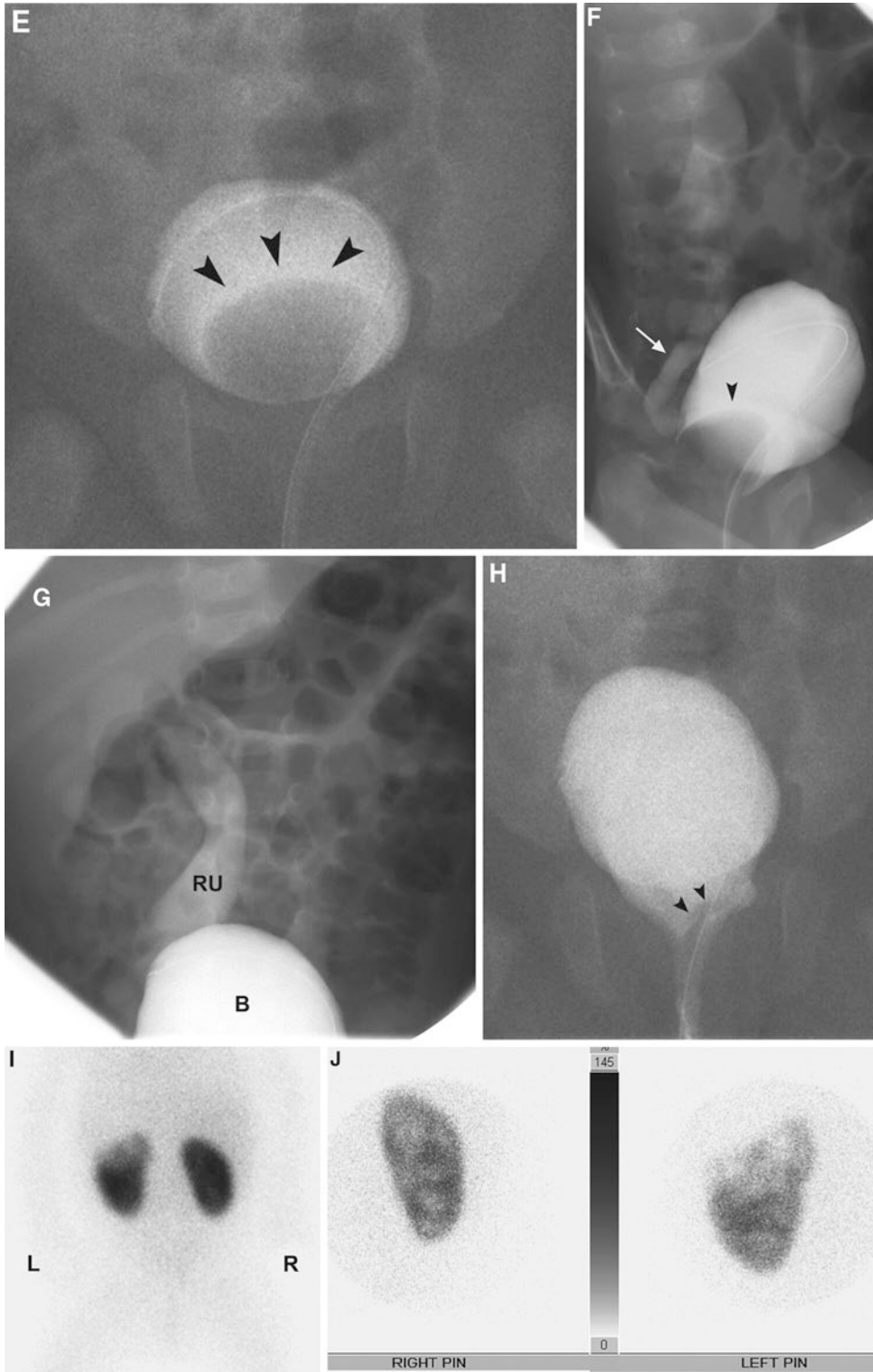


Fig. 40.5 (continued)

Case 4

Figure 40.6a–c shows a case of a 2-year-old little girl who presented with a febrile UTI and was found to have VUR.

Case 5

Figure 40.7a–i shows the case of a male fetus who was revealed to have bilateral hydronephrosis that was followed periodically throughout pregnancy and was last imaged prior to delivery at 35 weeks gestation. Figure 40.8a, b shows postnatal ultrasound views of the kidney obtained at 2 weeks of age, after the fetal diagnosis of hydronephrosis.

Suggested Imaging Protocols for Urinary Tract Infections in Infants and Children

See Figures 40.1 and 40.2.

Future Research

- Large, multicenter, prospective, controlled studies of infants and children less than and greater than age 2 years with carefully diagnosed febrile UTI, assessing the controversies of (a) appropriate use of imaging (RBUS and VCUG) and up to what age?, (b) the genetic factors more associated with renal scar and with VUR, and (c) which children benefit from surgical or endoscopic management of VUR to improve long-term renal function and decreased recurrent UTI
- Development of nonimaging predictors of risk of recurrent febrile UTI and/or progression of renal impairment after febrile UTI
- Standardization of prenatal and postnatal evaluation of hydronephrosis to predict outcome
- Optimization of a short and standardized automated protocol for MRU in infants and children

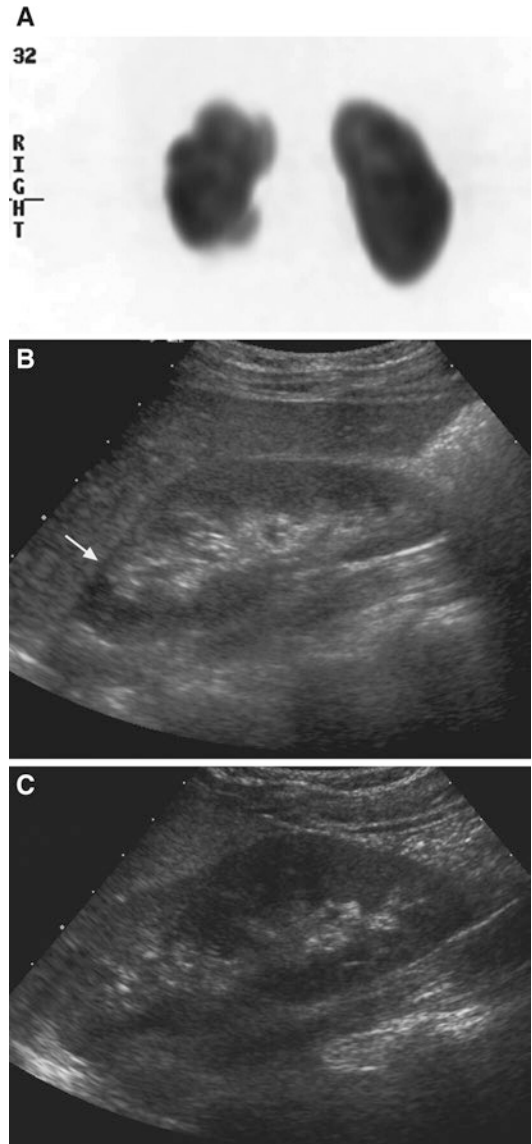


Fig. 40.6 This 2-year-old little girl presented with a recurrent febrile UTI and was found to have VUR. Tc-99m DMSA revealed evidence of scarring of both the upper and lower poles of the right kidney but no scars on the left (a). These scars were only faintly discernible on ultrasound and perhaps only with knowledge of the Tc-99m DMSA findings (b) (sagittal view of the right kidney; arrow, subtle, focal area of cortical thinning; (c), sagittal view of the normal left kidney) (Reprinted with kind permission of Springer Science+Business Media from Barnewolt CE, Connolly LP, Estrada CR, Applegate KE. Urinary Tract Infection in Infants and Children. In Medina LS, Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science+Business Media, 2010)

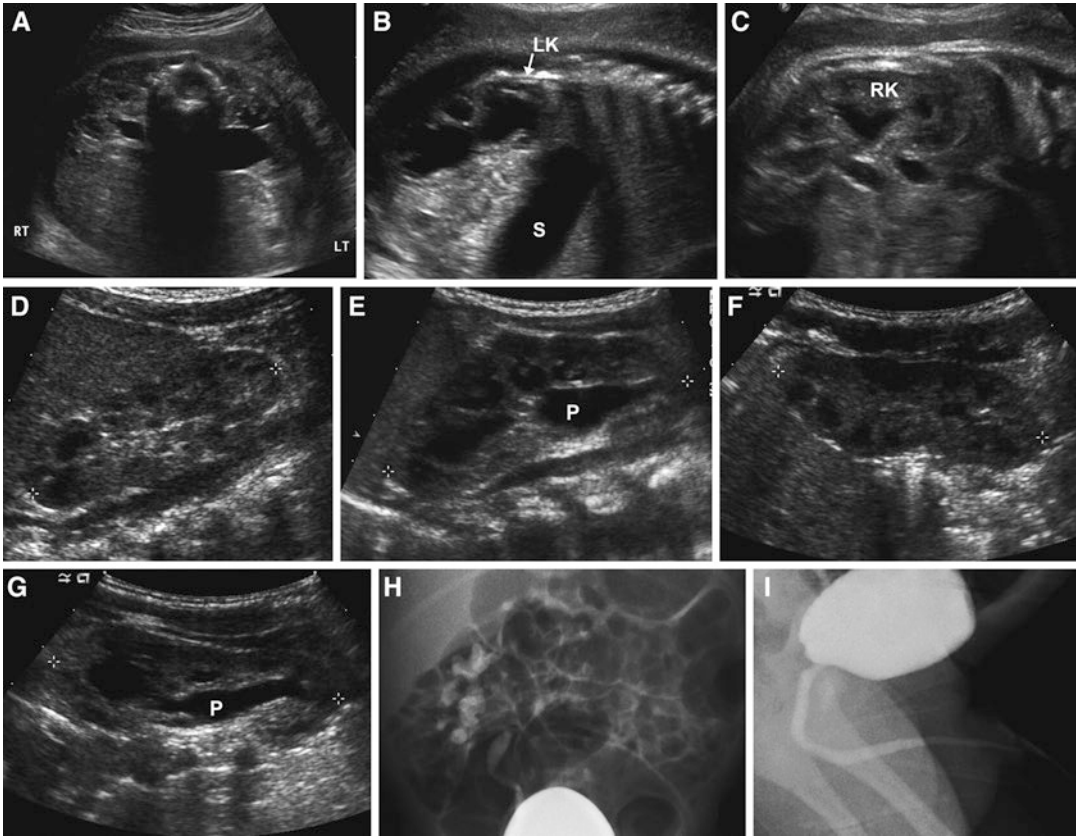


Fig. 40.7 Routine prenatal ultrasound screening of this male fetus revealed bilateral hydronephrosis that was followed periodically throughout pregnancy and was last imaged prior to delivery at 35 weeks gestation (**a**), (transverse view showing mild right and moderate left hydronephrosis; **b**), sagittal view of the moderately hydronephrotic left fetal kidney, *S* stomach, *LK* left kidney; **c**), sagittal view of the mildly hydronephrotic right fetal kidney, *RK* right kidney). After delivery, at 10 days of life, postnatal renal ultrasound revealed a normal appearing right kidney and mild to moderate left hydronephrosis (**d**), (supine view of normal right kidney; **e**), supine view of moderately hydronephrotic left kidney (**f**), prone view of normal right kidney; **g**), prone view of moderately hydronephrotic left kidney). VCUG on the same day as the ultra-

sound revealed grade III VUR on the right (the side where the postnatal ultrasound had been normal) (**h**) and no VUR on the left (implying the presence of some degree of obstruction at the level of the left ureteropelvic junction). The urethra was normal (**i**). This example illustrates the great challenge in predicting or excluding the presence of VUR on ultrasound alone (Reprinted with kind permission of Springer Science+Business Media from Barnewolt CE, Connolly LP, Estrada CR, Applegate KE. Urinary Tract Infection in Infants and Children. In Medina LS, Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science+Business Media, 2010)

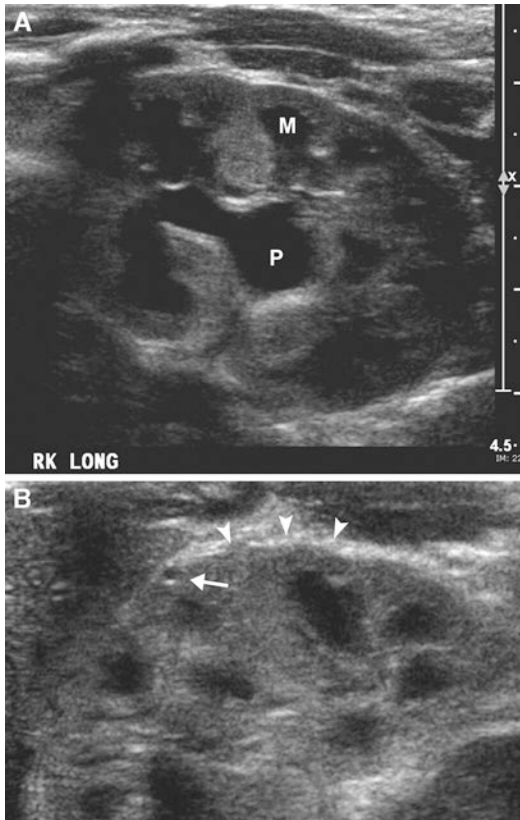


Fig. 40.8 These postnatal ultrasound views of the kidney were obtained at 2 weeks of age, after the fetal diagnosis of hydronephrosis. At worst, one might describe this as mild to moderate hydronephrosis (**a**) (*p* renal pelvis, *m* medullary pyramid). Nonetheless, high detail views reveal several very tiny cortical cysts along the renal cortical surface (**b**), (*arrow*, tiny cyst; *arrowheads*, cortical surface of kidney). These subtle findings suggest the possibility of renal dysplasia and probably warrant formal evaluation for VUR, with VCUG in males, to exclude the possibility of posterior urethral valves, and RNC in girls, minimizing radiation exposure (Reprinted with kind permission of Springer Science+Business Media from Barnewolt CE, Connolly LP, Estrada CR, Applegate KE. Urinary Tract Infection in Infants and Children. In Medina LS, Applegate KE, Blackmore CC (eds): *Evidence-Based Imaging in Pediatrics: Optimizing Imaging in Pediatric Patient Care*. New York: Springer Science+Business Media, 2010)

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