Neurotrauma Management for the Severely Injured Polytrauma Patient

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Foreword

Competing Demands

We all deal with competing demands each and every day. You have a full clinic, and the CEO requests your presence at an "emergency" administrative meeting dealing with a safety issue. While slipping out of clinic for that meeting the ER pages you, and one of your patients is there having just had a seizure. Simultaneously, a nurse calls, and the family of one of your post-op patients has arrived and wants to talk with you. In the midst of this onslaught, your spouse calls and wants guidance on what the mechanic just relayed about the car. We each live versions of this scenario every day.

Being needed at multiple places at the same time with the expectation that we will give our full attention to important matters creates tremendous stress. Throughout our training and careers we learn to handle this challenge. We prioritize these competing demands, adapt to the situation, and successfully deal with the issues. We survive by developing supportive teams including administrative assistants, NP's, PA's, or residents to help us effectively manage the demands. The simplicity in managing our personal demands is that we alone are the subject matter expert and can independently make the decisions for which we must bear the consequences.

The polytrauma patient with a CNS injury has many unique needs that also create competing demands in a different context. In this situation the patient can't depend on himself or herself to manage these competing demands. The patient is totally dependent on the healthcare team to seamlessly work together to save his or her life and preserve their function. A therapy that optimizes treatment for an injured brain may be suboptimal for another non-cranial injury. The choice of treatment strategies and timing of interventions must take into account all of the patient's injuries and be prioritized appropriately. These complex decisions are required throughout the entire trauma system of care including in the prehospital environment, the ER or trauma bay, the OR, the ICU, the floor, the rehabilitation facility, and transitioning back to the home environment.

In medicine, our training and daily operations are too often organized in accordance with a silo mentality. Nurses have their reporting structure. Specialties such as General Surgery, Orthopedics, Critical Care Medicine, Neurosurgery, and Rehabilitation have their own independent physician departments and services. The Service Line concept and Trauma Services

development are efforts to mitigate the inefficiency that often results while working within the traditional silo structures. Leadership is critical to develop, inspire, and demand the teamwork crucial to success. All players involved in the care of a polytrauma patient must work within a context of competence, integrity, mutual respect, and clear communication. What is best for the patient must always trump any parochial or individual service interests. Our patients rely on continuity between the silos within our heathcare and trauma systems. Their lives and functional outcomes depend on us collaborating as highly functioning, effective, and efficient teams.

The purest environment I have ever witnessed for the care of the polytrauma patient has been during deployments to combat zones in Iraq and Afghanistan. In these highly structured environments, the multidisciplinary team works as a single unit without distractions of secondary administrative or strategic priorities. Everyone is completely focused on the patients 24 hours per day. Subspecialty barriers are broken down, and all members of this healthcare team live, work, play, and if necessary fight together. There is a discrete chain of command and defined responsibilities for decisions, but specialty expertise is respected and relied upon. All members are kept informed through regular formal and frequent informal communication processes.

This book is designed to provide a single reference that outlines the salient issues while highlighting the important contribution each specialty brings to the care of the polytrauma patient with CNS injury. The authors are all well respected experts in their fields, and have extensive experience working with other disciplines in a collaborative manner. I am confident this text will serve as an excellent reference, and be a useful addition to trauma and neurosurgical library collections, as we all continuously strive to improve our care for these very complex patients.

Jim Ecklund

Preface

When Jim Ecklund approached me to co-edit a text about the care of the polytrauma patient with CNS injury I knew it would be worth the effort. History has taught us that tremendous medical advances are made during periods of armed conflict. The severity of wounds, the volume of patients, the complexity of medical and surgical decision-making, and the teamwork inspired by wartime care bring professionals from many different disciplines together with an urgency and a sense of purpose that is sometimes difficult to achieve otherwise. Those lessons, and many others learned every day by our civilian friends and colleagues across many disciplines of medicine and surgery, are presented here. This multidisciplinary approach is not uncommon, but we have taken it a step further and asked our authors to specifically focus their chapters on the boundaries, the conflicts, and the solutions they have found when specialties intersect while caring for a critically ill neurotrauma patient.

Our goal is to leverage lessons learned by our military and civilian authors, apply them to the broader practice of complex trauma care, and help make them stick. The "stickiness" is the difficult part, because after each crisis we often fall back on our pre-crisis behaviors, and nowhere is this tendency more apparent than in military medicine. Nations throughout history have ramped up their medical systems during war, learned great lessons (from the ambulance systems of Napoleon to the flying ICUs of the current conflicts), and then disbanded their military healthcare system between wars—only to see the need to rebuild and relearn prior lessons for the inevitable next conflict.

We hope this book will add to the great works both completed and in preparation and inform the next generation of medical professionals who are entrusted with the lives of the world's most severely injured—military or civilian.

Jim and I have been privileged throughout our careers, to this very day, to work with some of the finest medical professionals around the world. Our patients have taken us on journeys requiring us to stretch the limits of our own skills, the teams we have led, and the organizations in which we have cared for those patients. In doing so it became ever more clear to us as we grew in our practice of neurosurgery that reaching across traditional boundaries and collaborating in a multidisciplinary fashion is not only good for patients but ultimately good for us. Our professional and personal lives

have been enriched immeasurably by our colleagues, so many of whom are contributors to this work.

We want to acknowledge the work of all the authors represented here. Their willingness to take time out of their busy schedules to put pen to paper speaks to their commitment to insure the lessons of multidisciplinary, collaborative work to care for our sickest patients are not lost in the day-to-day routine of our healthcare lives.

In addition, there is no doubt in my mind or Jim's that this book would not have been possible without the untiring efforts of our colleague Michele Theiss. Keeping two busy neurosurgeons on task is challenging enough, but to consistently do so with professionalism, grace, style, and eloquence takes a very special person with impressive leadership talents. Michele encompasses all these things and more. Jim and I, the authors, and all readers will be forever in her debt.

Last but certainly not least I have to acknowledge my co-editor. Jim and I have known each other as cadets at West Point, served together as neurosurgery residents, attending neurosurgeons and Chiefs of Neurosurgery at Walter Reed, and shared stories of combat surgery. Jim has always been an extraordinary leader, and he has been able to immensely elevate the level of every program he has led through his vision, hard work, and dogged determination. When Jim Ecklund says he's going to get something done, bank on it. Most of all I have to thank Jim for keeping me around all these years and allowing me to serve beside a leader of such character, integrity, and dedication to his patients and his profession.

Falls Church, USA Leon E. Moores

Acknowledgment

The editors would like to acknowledge the efforts of Inova's Academic Coordinator Michele Theiss, without whom this textbook would not have been possible.

Michele's tireless spirit and optimistic outlook kept all contributors on track and helped to inspire the entire effort.

Thank you Michele

Contents

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Part I

General Principles and Trauma System Management

The Difficult Conversation

1

Leon E. Moores

First, my disclaimer. While I do spend quite a bit of time thinking about these things—and reflecting on how well I'm doing, asking for feedback, and reading (each of which I highly encourage everyone to do)—I certainly do not pretend to have all the answers. Rather, I present this discussion to suggest a framework, perhaps point out some new thoughts, and provide a stimulus to make you want to improve your communication skills.

Sensitivity is an important skill for all physicians. In the abstract, we recognize the importance of good communication with our patients and families, but we sometimes find it hard to put time and energy into this aspect of our many professional responsibilities. Years of difficult and challenging training, a high-stress work environment, and the reality of too much work and too little time contributed to the big screen image of the neurosurgeon rushing up to the family, delivering bad news crisply, and rushing off to save another life. While few of us fit this movie profile perfectly, stereotypes exist for a reason. Additionally, very few physicians I have met make it a point to study and assess their communication skills with the intent to improve.

As we are acutely aware, neurosurgery comprises some of the highest of the highs and lowest of the lows in medicine, for several reasons. The central nervous system is an organ system that people care deeply about, one that has wide-ranging effects on very important functions, and that many patients and a fair percentage of referring physicians find just a bit terrifying. Additionally, many neurosurgical problems present abruptly—one day you are perfectly fine and the next you have a seizure and within hours are told you have a brain tumor. Aneurysmal rupture and cerebral abscesses present without warning and often without prodrome. The lack of ability to prepare for this life-changing event contributes to heightened anxiety on the part of the patient and family. The severely wounded polytrauma patient fits this characterization perfectly. Adding to the stress, an inordinately high percentage of trauma occurs in the young resulting in the loss of youthful vigor or even decades of life.

Under these circumstances, neurosurgeons and other healthcare professionals are often forgiven for being candid, brusque, or downright rude. Patients, families, and staff act as enablers of less than optimal communication on the part of surgeons with comments such as: "but he's a great surgeon, he's just really busy, do not worry about his bedside manner."

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If none of this applies to you, do not be offended. Use this discussion to reinforce your superb bedside communication skills and their importance, and make it a point to model this good behavior and teach and correct others who are not as effective.

If there is a chance it might apply to you, please read on for a few suggested strategies.

Time is one of the obvious barriers to optimum communication during a neurosurgical crisis. There is a finite amount of time available, there are often many tasks that must be accomplished within this short period of time, and we almost always feel the pressure of time and the requirement to quickly move on to the next item on our list.

However, studies have shown that it does not take any more time to give the patient and family the distinct impression that you have been there longer than you actually have [1–4]. Tone of voice, body language, and focus can give your "audience" the impression that they are the only thing on your mind. Conversely, tone, body language, and lack of focus can also give them the impression that they are the least important thing on your mind. If you have not been videotaped during one of these conversations, even with a mock patient, I would highly encourage doing so. It is amazing what you learn when you see yourself outside the moment and you carefully study the reactions of those in the room.

The single most important body language technique is simply to sit. Looking around the room for a chair, moving the chair into a position where you can address the family, and sitting down gives the distinct impression that you have nowhere else in the world to be and you are willing to take as much time as is needed. Open posture, sitting back in the chair, and remaining reasonably still without changing positions every 10 or 15 s magnifies that message. Leaning forward on the edge of the chair, fidgeting, and looking around the room detract from it.

One of my most important if somewhat paradoxical hints is to never appear to be in a hurry. This takes practice, since most of the time we actually are in a hurry. Being in a hurry also makes us feel like we carry some increased psychological size, some air of supreme importance conveyed by the requirement to get to the next appointment. Showing up late, standing in the doorjamb, backing away as you are "finishing" the conversation all convey that the patient you are with right now is not important. Do the opposite, and it will pay off.

Introducing yourself to each and every person in the group is an incredibly effective tool to emphasize that you are there for them. Shaking each hand when practical and culturally acceptable and recognizing their relationship ("you must be the grandfather") sends this message as well. This takes about a minute in a large group of 8–10 family and friends, well worth your time.

Eye contact is critically important. An occasional glance at a team member for confirmation of data is okay; constantly looking around the room, looking at the door, or looking at your watch is not. Focus your eye contact on the principal family members but also take the opportunity to make eye contact with other members of the group perhaps 10–20 % of the time.

When the discussion is wrapping up, focus on the principal family members and ask: "do you have any other questions?" Then ask the group, if there is one: "does anyone else have any questions for me or the team?" These last questions reemphasize the message that you are there for them and, by extension, the loved one you are about to care for. Effective use of these techniques will make the family truly feel that there is nothing else on your mind.

The words you choose have a tremendous impact on the discussion. While we try to avoid using medical jargon, it is such a natural part of our speech pattern that it almost always creeps in at some point. Two communication strategies to ensure clear understanding include asking the listener to repeat back to you in their own words or simply asking if they understood. The former requires more time and can come across as condescending while the latter runs the risk of the family merely nodding assent. More critical

than either of these classic strategies is to give the family the consistent impression that you are open to questions and interruptions and that their education is a critically important part of your job. In fact, I often repeat that statement several times during counseling sessions. If you are sincere, they will be open to asking clarifying questions. If you give them the impression that you are in a hurry and cannot be bothered they are much less likely to ask.

We have all heard the phrase: "laying the crêpe." The concept here is simple—you want to prepare the family for the worst and anything short of that will be a victory. There is nothing inherently wrong with a communication philosophy that leans pessimistic, particularly in a specialty such as neurosurgery—where the patient's status can go from stable to catastrophic in just a few minutes. Personally, I lean perhaps a bit too far to the opposite extreme. I do state that while I cannot predict the outcome, the team is going to do everything we can and I have certainly seen patients make incredible recoveries. However, I pay close attention to the family's reaction and if I get the sense that all they are hearing is: "everything is going to be fine and a miraculous recovery is anticipated," I will circle back to emphasize the severity of the situation and the unpredictability of the outcome. The point here is not to suggest that either optimism or pessimism is superior but rather to suggest that whichever you choose it should be purposeful. As you provide a particular perspective do so intentionally and be sensitive to the reaction of the family. If you sense that you are completely dashing all hope or that you are creating totally unrealistic expectations you may need to adjust to provide balance. Of course this is a very challenging task since every situation is different, every family is different, and every family member within that family is different.

I am convinced that compassionate, effective communication is very important and that during periods of extreme stress and time pressure it is even more difficult to do well. In order to succeed and improve you need to be purposeful, pay attention to how you are perceived, ask for feedback, and read. It's not brain surgery. You can do it.

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2 Communication Between Teams and Multidisciplinary Rounds and Single Primary POC for Family Communication—Lessons Learned and Who's in Charge?

A.B. Weisbrod, R.R. Armola and James R. Dunne

Introduction

Polytrauma patients who sustain neurotrauma are among the most severely injured patients. Optimizing care of each injury must be prioritized within the context of the fragile nature of the neurologic injuries sustained to ensure that interventions do not create a risk of secondary brain/spinal cord injury.

The combination of neurologic and additional multisystem injury is not uncommon. Recent assessments from the Global War on Terrorism conflicts estimate that traumatic brain injury (TBI) occurs in approximately 60 % of service members who are evaluated for other blunt traumatic injuries [1]. Similar injury mechanisms likely occur in civilian motor vehicle injuries, although the number affected by this combination injury pattern is unknown. Despite the frequency and severity of these injuries, this combination is poorly represented in the literature and further research is needed to address epidemiology, outcomes, and best practices to care for this critically injured population.

The Role for Teamwork

Dating back to World War II, medical professionals identified that soldiers were surviving from increasingly complex injuries and living with greater disabilities than could be handled by a single-specialty provider [2, 3]. Therefore, individual providers sought others to collaborate in providing comprehensive care plans that could simultaneously address medical, psychological, and social needs [2]. This initial multidisciplinary concept consisted of a single physician managing and prioritizing the simultaneous input of various specialties [3], and over time this collaborative approach has been shown to improve patient outcomes [4]. Unfortunately, effective multi-specialty collaboration is not seamless. It requires planning, practice, and the commitment of those involved [2]. Specialty providers often practice within single departments with their own unique set of standards, bodies of research, methods of communication, and practice agenda. This isolation creates barriers leading to poor interdepartmental communication which is cited as one of the most common causes of patient care errors [5].

Consequently, healthcare providers have sought to improve multidisciplinary teamwork

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models to improve efficiency. For a common collaborative disease process, departments are often asked to identify the areas of overlap within their respective disciplines where there are shared elements of knowledge and skills, giving rise to the concept of interdisciplinary teams. For example, in the polytrauma patient, orthopedic surgery and general surgery may both require several operative interventions to complete care [6]. If this is identified early in the patient's treatment course, these two specialties can coordinate and share operative time thereby decreasing overall nil per os (NPO) status (affecting patient comfort and nutrition) and making the patient more available for treatment by other specialties (i.e., physical therapy, occupational therapy, and speech therapy) [6]. This model requires increased communication, often manifested in interdisciplinary team meetings. However, once interdepartmental trends are identified, care can be facilitated by establishing interdepartmental checklists, management guidelines, or a shared organized approach for rounding thereby reducing overall resource needs and streamlining care.

One example of this is the Brain Trauma Foundation's (BTF) "Guidelines for the Management of Severe Traumatic Brain Injury" [7]. In 1995, the BTF recognized that the care of the neurotrauma patient necessitates multiple specialties over the patient's longitudinal course. In an effort to improve outcomes, a unified, evidence-based approach was designed as an outline to care for the neurotrauma patient [7]. Several studies conducted by Level I and II trauma centers in the United States and Europe, have shown the merit of this collaboration, resulting in improvements in patient mortality, functional outcome scores, hospital length of stay, and overall cost when adherence to specific BTF guidelines have been documented [8–10].

The Brain Injury Guidelines (BIG) project is a recent attempt to develop collaborative practice guidelines. A cohort of acute care surgeons and neurosurgeons identified a population of patients with TBI that could be managed by acute care surgeons without the need for neurosurgical consultation [11]. Both retrospective and prospective validation of BIG have shown no difference in 30-day outcomes; however, targeted research and better allocation of resources have shown a decrease in both ICU and hospital length of stay, as well as an estimated $5,000 savings in hospital cost and $7,000 savings in hospital charges per patient [12, 13].

Who Should Lead the Multidisciplinary Team?

It has been well-established that polytrauma patients have improved outcomes when evaluation and management occur by physicians within a trauma program that has been verified by the American College of Surgeons Committee on Trauma (ACS COT) [14–16]. The ACS COT has specific requirements for programs to qualify as an ACS verified trauma program [17]. Specifically, the ACS COT requires that in all Level I, II, and III trauma centers "The trauma surgeon must retain responsibility for the patient and coordinate all therapeutic decisions. Many of the daily care requirements can be collaboratively managed by a dedicated ICU team, but the trauma surgeon must be kept informed and concur with major therapeutic and management decisions made by the ICU team." [17].

With this criteria outlined, the polytrauma patient who sustains neurotrauma should therefore be managed primarily by a trauma surgeon. Recent literature has shown that whether neurotrauma is primarily managed by a neurosurgeon or an acute care/trauma surgeon using discretion to consult a neurosurgeon, the quality of care is similar [12, 13, 18–20]. Furthermore, while neurosurgeons are trained to provide neurotrauma care, their availability as a resource, is becoming increasingly scarce due to shortages in this physician specialty [21, 22]. This fact is even more concerning given the documented increased incidence of patients sustaining neurotrauma [21, 22].

In addition, having the trauma surgeon act as the primary multi-specialty manager for the combined neuro and polytrauma injured patient supports patient/family centered care. A common

need identified among patients/caregivers is for consistency of information regarding the plan of care for the day and longitudinally over the hospital course [1]. From the patient/caregiver perspective, it is critical that if several healthcare providers are relaying information, a clear message is communicated consistently [23]. Therefore, it has been recommended that a single provider be assigned to deliver information about treatment plans [24]. Although research is lacking in which discipline is best equipped to perform this task, trauma surgeons may be the most qualified since they already assume the lead role and are integrated in the care of the polytrauma patient throughout the duration of their hospital course.

Communication with the Patient/Caregiver

The involvement of the patient and his/her caregiver(s) has been shown to be critical for the successful treatment of patients sustaining both neurotrauma and polytrauma [1]. However, effective patient-provider communication is faced with many barriers. Often, the patient/caregiver does not have a medical or healthcare background. Moreover, the stress and emotions created by the acute change in the patient's overall health status will interfere with the patient/caregiver's ability to receive, process, and recall new information [23–26]. This mandates that information is transmitted in a clear and concise manner that is both sensitive and empathetic to the recipient [1]. This also highlights the aforementioned need for consistent and clear communication [23].

Recent studies have identified the type of information desired by patients and their caregivers [1]. In the acute phase of care, daily communication is considered ideal [23]. It is important to define all diagnoses and the prognosis for each [27, 28]. Patients/caregivers wish to hear both the best and worst case scenarios for physical, functional, behavioral, and cognitive outcomes [27, 28]. It is desired to know the reasoning behind each diagnostic test, details of monitoring equipment, the purpose of any new medication and both short and long-term treatment plans [27, 28]. Caretakers require information on how their new role will affect their daily life and existing relationships [28]. Transitions of care including discharge from acute care to rehabilitative care, and again from rehabilitative care to home are important intervals to review and update the above information while at the same time providing anticipatory guidance for the next stage of care [23, 28]. Patients and their caregivers find it helpful to review this information again after a change in level of care to address any new problems or questions that arise [6, 26, 29]. Written material handouts are not considered an acceptable substitute for direct education and communication but can be utilized to reinforce education and discussion points [30].

Our Experience Building the Team

Walter Reed National Military Medical Center (WRNMMC) is a tertiary care military medical facility located in Bethesda, Maryland. Throughout the Operation Iraqi Freedom/Operation Enduring Freedom conflicts, WRNMMC functioned as the primary US based facility for neurotrauma patients with polytrauma, requiring a transformation from a 250 bed university-affiliated teaching hospital into an ACS COT verified trauma center [31]. Continuous monitoring of outcomes and process improvements drove the evolution of our multidisciplinary team into its current structure as an interdisciplinary team; a process that would not have been possible without a commitment to interdepartmental communication and respect.

WRNMMC holds multidisciplinary rounds twice a week. All providers involved in the care of polytrauma patients are invited to attend to discuss the current census of trauma patients. A large core staff is involved, including: a trauma attending, who facilitates the meeting; representatives from the surgical teams taking care of the patients (trauma, neurosurgery, orthopedic surgery, oral

maxillary facial surgery/otolaryngology); a provider each from the acute pain service, neurology, psychology; rehabilitation specialists from physical therapy, occupational therapy, speech therapy, nutrition, as well as a physical rehabilitation physician; involved social workers, and case managers; and both the administration and nursing staff to represent the operating room and all involved hospital wards.

To start an efficient discussion, the trauma attending will announce the patient of interest, and then list current prioritized active issues drawn from daily interaction of providers and written notes. The core staff will voice any concerns about the identified priorities or barriers. Examples include the coordination of operative time between services, a concern that psychological needs are hindering physical therapy advancements, or the acknowledgement that the patient's high pain control regimen may affect discharge planning. Next, an estimate is given regarding the expected hospital course (i.e., 2 weeks of operative therapy and 1 week of acute rehab prior to anticipated transfer to an appropriate rehabilitation facility), with an opportunity for discussion. Finally, the expected type of rehabilitation facility is offered, again with a chance for core staff to interject.

At the close of rounds, participants are given an opportunity to discuss any concerns unique to their specialty. Examples include failure to communicate changes in weight-bearing status in a timely/accurate manner to rehabilitation services or if nutritional services identifies that delays in operating room start times are prolonging NPO times and potentially affecting overall nutritional status. Representatives from different services can solve problems immediately or decide to collaborate after the meeting to find an appropriate solution.

While the multidisciplinary meeting covers detailed information, with practice, it flows efficiently. On average, approximately 20–40 patients are discussed in the span of 30–60 min. All participants exit the meeting with a global sense of the patient, the patient's priorities, and the plan of care.

Conclusion

Polytrauma patients with neurotrauma are the most critically injured patients who utilize multiple resources and require a number of specialty services during their continuum of care. Although additional research is needed to determine best practice models for the critically injured patient, the trauma surgeon functioning as the team leader to coordinate and manage the overall plan of care is supported by ACS COT. Having a specific provider drive the overall plan also facilitates patient/family centered care. Development of an interdisciplinary team provides an opportunity for a seamless transition from the acute care phase to the rehabilitation phase while encouraging open communication and mutual respect among the healthcare team members.

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Mass Casualty Events and Your Hospital

3

Erich Gerhardt, Gary Vercruysse and Peter Rhee

Planning

MCE's by their very nature are rare and unpredictable events that can make preparation and planning seem daunting, if not impossible [1–4]. However, it is because of this rarity and unpredictability that one cannot overstate the importance of appropriate preparedness [5]. No two MCE's are exactly alike, but there are certain patterns of injury, resource requirements, pitfalls, and behavior within the response itself that are common to all disasters. These patterns form the centerpiece around which a response plan can be constructed [2, 3].

When developing a plan for a MCE, assumptions are made as to how various aspects of the response will proceed. For the plan to be effective, those assumptions should be based on actual experience and not on what one expects to happen. For example, under normal conditions it is assumed that the most seriously injured patients are the first to arrive at the hospital. However, despite this logical assumption, experience shows that what is most often observed is the least seriously injured arrive first with a significant delay in the arrival of the more severely injured patients who will require the most resources. Knowing that the most injured often arrive later, a significant amount of resources should be reserved, so that they are not exhausted on the less severely injured [2, 3, 5, 6].

Appropriate planning is based on such experience-based knowledge. It starts by looking back at the responses to previous MCE's, both military and civilian, to learn what actually happened, what worked or did not work, and how things could be improved. By doing so, there will be recognition of the previously observed patterns with a directly related plan that can anticipate and accommodate future patterns to lead to a successful outcome [2, 3, 5].

Planning for MCE's should be performed by the people who will actually carry out the response, and should involve all hospital services. This includes not only patient care services such as doctors and nurses, but also food services, maintenance, security, and other vital members. In this respect, every service in the hospital has a role. The plan should be based on an analysis of the known threats within the hospital's particular region, which is known as a Hazard Vulnerability Analysis (HVA). Typically, an HVA will aid in identifying all possible threats or hazards, and provides an estimate of the probability of each occurring along with a defined level of preparedness for that event. When these are identified, rather than developing a set of multiple specific plans to address each type of disaster individually,

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a plan that follows an all-hazards approach should be developed. An all-hazards approach will create a single plan that is generic enough to address the factors common to all possible hazards, but also allows for flexibility to accommodate the specific requirements of a particular event [3, 5].

Once a plan for a MCE has been developed, it must be tested to ensure its effectiveness and to reveal areas of weakness, and it must be familiarized to those who will execute it. In the United States, semiannual training programs and drills are required by law and there are four distinct types: seminars, tabletop exercises, functional exercises, and full-scale exercises. While the first three of these are relatively easy to organize and implement from a cost and resource perspective, their ability to effectively prepare an institution for an MCE has not been reliably demonstrated. On the other hand, while a full-scale exercise provides the best real-time training by coming as close as possible to replicating a true MCE, the overwhelming cost and use of community-wide resources makes them a luxuriously rare event. A novel alternative that is gaining traction is the use of a virtual-world hospital simulation. Computer simulation should be accessible, customizable, and inexpensive enough such that it can be implemented by any institution with standard computers and internet connection. Of all currently available training/testing measures, it is the only simulator with a validated system of performance assessment [3, 5, 7–10].

The final key element of MCE preparation is the analysis and review that follows a training exercise or an actual MCE. This debriefing should occur not just among those at the highest level who are in charge of running the hospital, but also within each division and subdivision. In this way every person at each level who was involved in the MCE or training exercise will be able to review the appropriateness of their individual response. Ideally, debriefing will take place immediately after the exercise while details are still easily recalled. As in the pre-event planning, this comprehensive review should document the actual elements of how the response was carried out, what worked or did not work, and how things could be improved [3, 11].

Perhaps the best most recent evidence demonstrating the importance of intense MCE preparation comes from the Boston Marathon bombings. In this event, bombs were strategically placed in a crowded area and produced 264 casualties. However, there were only 3 deaths, and no patient who was brought to a hospital died. These excellent results have been credited to the training efforts coordinated by The Conference of Boston Teaching Hospitals, which has been conducting simulations and exercises regularly since the 2001 September 11th attacks. By examining the responses to other MCE's, updating their own plans accordingly, and continued training, the hospitals were prepared to efficiently and effectively navigate casualties resulting from the bombings to a successful outcome [12].

Facility Considerations

In an actual MCE, hospital notification of a disaster and the imminent arrival of casualties are by no means standardized or accurate in predicting the number, types, or severity of casualties. In fact, hospitals generally learn of the event from news media or by the arrival of the first wave of injured patients. As mentioned above, the first patients to arrive are usually the least severely injured. These issues make it difficult, if not impossible in the early stages of an MCE to predict the full scope of the response that will eventually be required. If a hospital does receive any pre-arrival notification, it is usually just a few minutes notice. In order to be prepared with an appropriate response, certain facility preparations should rapidly occur during this short time. First, to ensure the security of the hospital and its workers, the building should immediately go on lockdown. Entry should be restricted to casualties requiring treatment (as determined by the triage officer) and necessary staff. This will prevent an influx of unnecessary people (families of casualties, media, nonurgent casualties, worried well, and volunteers) who can place a burden on the triage effort [3, 6, 9].

Simultaneously, the hospital needs to obtain adequate space, staff, and supplies to provide

sufficient care for the incoming patients. The ability to rapidly adapt to a large patient load is referred to as a hospital's surge capacity. During a surge, priority will be given to the most critical areas of ED, OR, and ICU. In order to clear space and secure resources, noncritical surgeries should be canceled and a process of reverse triage will be undertaken in all other areas of the hospital. This is a process in which patients already admitted or still in the ED are evaluated with the goal of downgrading or discharging as many as possible.

After patients have arrived and the emergency response under way, a second issue the hospital will face is how to continue to function as a regular hospital. That is, it must accommodate critical patients arriving during the response who are not involved in the MCE. Routine emergencies such as MI, trauma, and pregnancy/labor will continue to occur during an MCE. To appropriately handle such emergencies without compromising the MCE response, these patients should be triaged and treated along with and according to the same principles as the MCE related casualties [3, 13].

Triage

Triage focuses on sorting and prioritizing casualties according to their needs to achieve the greatest survivability with limited available resources [2, 3, 14]. Though the basic principles may seem relatively simple, the lack of experience most physicians have with triage, and the endless possible scenarios make it challenging to perform successfully, especially for relatively inexperienced clinicians [14]. In discussing the topic of triage, a distinction should first be made between how it is practiced in the field and how it is practiced in the facility. Field triage involves the site of casualty generation and is carried out by first responders. The primary goal is to deliver the patient to their ultimate destination as quickly as possible. This is accomplished by assessing and categorizing patients so it can be determined which ones should be transported to the hospital first, if at all [3, 14, 15]. Since this chapter is intended to address MCE response in the hospital setting, the following discussion will focus on facility triage, though many of the principles pertain to both settings.

The ultimate goal of facility triage is to identify the casualties that require one of the relatively scarce hospital resources (OR or ICU monitoring) [3]. Once the receiving hospital is notified of a MCE, traditionally a designated triage area is quickly established immediately outside the ED to allow continuous patient flow [5]. Because of the very quick assessment required for optimal triage, one person can be assigned the task of triage officer. Typically at a Level 1 trauma center this will be the senior trauma surgeon. If multiple other surgeons are available, he or she can continue to triage until required to take a patient to the operating room. At this point, triage duties should be transferred to the person with the next most triage experience, which is typically the senior emergency department physician [14].

Triage decisions should be based on rapid assessments taking approximately 1 min per casualty. There are multiple triage assessment systems described, but the most widely adopted is the Sort, Assess, Life-Saving Interventions, and Treatment/Transport (SALT) system (Fig. 3.1). This system is based on assessment of ability to walk, respirations, circulation, mental status, presence of hemorrhage, and a consideration of available resources [16, 17]. The intent of the brief assessment is to categorize each patient into one of four categories: expectant (not survivable), immediate (requires intervention immediately), delayed (requires intervention but not immediately), and minimal (walking wounded) [15]. Perhaps a simpler, more intuitive system was developed and used in the recent wars in Iraq and Afghanistan. In these theaters, a three tier system was used which was found to be quicker and more effective. In this system, casualties were categorized as either expectant (dying), urgent (requiring immediate care), or nonurgent (not sick) [14] (Fig. 3.2).

As mentioned above, the triage process should be very quick; approximately 1 min per patient.

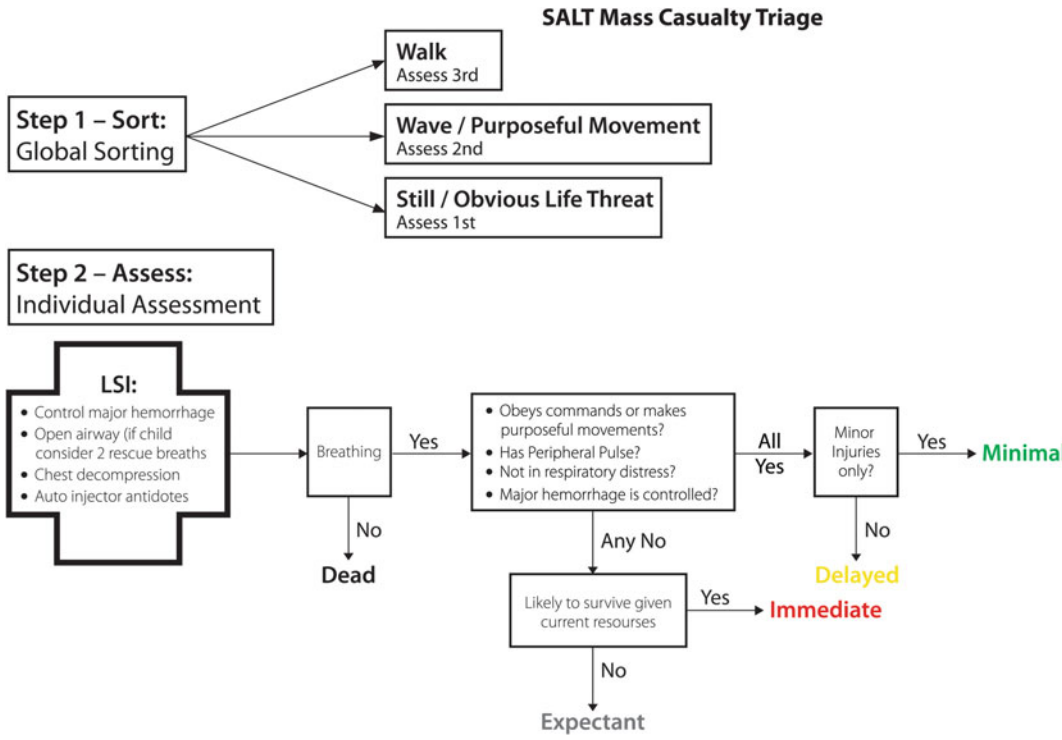

Fig. 3.1 SALT mass casualty triage. *LSI* Life saving intervention

Category	Frequency
Expectant	20%
Urgent	20%
Non-Urgent	60%

Fig. 3.2 Three tiered triage system

Triage is not the time to be hooking patients up to monitors or using blood pressure cuffs/stethoscopes, or even doing a standard rapid ATLS type exam. Furthermore, it should be stressed that the goal of the triage officer is to sort patients and direct their flow to the appropriate destination as they arrive; not to treat them, and not to stack them in one area and then begin triage. The triage assessment consists of a quick look to see if the patient is responsive, if they are breathing, their pulse character (i.e., thready and rapid), estimation of blood loss, and whether the patient is likely to survive given the available resources (Fig. 3.1). If the officer is highly experienced and efficient in triage, he or she can do this as the patient is still on or being pulled from the ambulance. The triage decision is then based on the officer's clinical gestalt [3, 14].

Nonurgent Casualties

Typically, the majority of patients brought in during a MCE will fall into the nonurgent category with minor to moderate injuries not requiring immediate operation [9]. These patients are usually easy to identify in the triage assessment because they will be talking coherently, are

not in cardiorespiratory distress, and are not bleeding significantly. They can be directed to a designated minimal care area of the emergency department and have their injuries partially treated or their care delayed entirely [14]. As resources need to be cautiously reserved, these patients will initially receive only the care required to keep them from deteriorating, allowing resources to be reserved for more seriously injured future patients. For example, a patient with penetrating chest injury may have an empiric thoracostomy tube placed without imaging. A patient with penetrating abdominal injury who is hemodynamically stable will be given analgesia and then triaged to the floor to await possible operation once more resources are available. The intent of this care is to temporize as is possible until casualties are no longer arriving and the full scope of the event is understood in the context of the available resources [9].

Urgent Casualties

Urgent casualties are the most important patients to correctly identify. Typically they will have injuries that require immediate, life-saving intervention, usually in the OR. The most common presentation of an urgent casualty is a patient with active hemorrhage, the source of which is often surgically correctable. This frequently is the result of penetrating gunshot or knife injuries as has been observed in highly publicized domestic mass shootings and the 2014 China subway knifings. However, the Boston Marathon bombings demonstrated that explosive attacks producing hemorrhagic extremity injuries and traumatic amputations typical of the military setting are also an unfortunate reality in the civilian world.

Correct identification of urgent casualties is the cornerstone of successful MCE management because accurate triage of this cohort saves the most lives. The underlining principle of facility triage is to divert resources away from nonurgent and expectant patients so that medical care can be rendered to the urgent patients at or near the level that would be under normal conditions. When triage is performed correctly, this will be done without overtaxing available resources [9, 14].

Expectant Casualties

An expectant casualty can be difficult to identify because what specifically constitutes expectant will not be clearly defined prior to the arrival of casualties. How the triage officer decides what meets criteria to categorize as expectant depends on the characteristics of the MCE itself. It will be based not solely on the condition of a particular patient, but also the number and condition of other casualties, and the resources available. In other words, expectant in a certain set of circumstances may be a patient whose injuries are so severe they will die regardless of the available resources, or a patient whose survival requires such a large share of the valuable limited resources that several other patients will die if those resources are used in an attempt to save this casualty.

An example of the former is a patient in extremis with a devastating open head injury and significant visibly damaged brain tissue. Though the patient has not yet succumbed to the injury, it is clear that chances of survival, much less meaningful recovery, are not realistic. An example of the latter is a victim of blast injury in extremis with multiple sources of hemorrhage. Under normal conditions, this patient might be salvageable if a mass transfusion protocol is undertaken while a trauma surgeon, vascular surgeon, and neurosurgeon operate simultaneously. However, as previously stated, in MCE's the patients outnumber resources. And in this example, multiple resources that could be used to save several lives would be used inappropriately in attempt to save one life, thus violating the principle of doing the greatest good for the greatest number.

The definition of expectant in any MCE is dynamic and may change significantly as resources become more or less available and the inflow rate or complexity of incoming casualties change. Typically, when a patient is deemed expectant they are given comfort care in an area away from the main hospital, perhaps a chapel or

cafeteria, so as not to utilize valuable resources and space that might otherwise be utilized for salvageable patients. At a later time if the characteristics of the MCE have changed so as to allow the opportunity, patients initially deemed expectant can be re-triaged and their status changed to be consistent with the current MCE conditions [2, 3].

Patient Identification

To facilitate identification, accurate delivery of patients, and communication of triage assessment to other care providers, the triage officer should have at his or her disposal an assistant tagger during the triage process. Patients should be clearly tagged or marked with a patient ID, their intended destination, and status determined by triage. All of this information should also be logged by the tagger. Additionally, some minimal form of documentation of type of injury and any interventions undertaken should accompany the patient as they move from one location to the next. This will allow providers to give the appropriate care and avoid redundancy in subsequent settings [3, 14, 18].

Undertriage and Overtriage

The two most critical aspects of triage are the correct identification of the urgent casualties and reservation of resources for their immediate treatment. In this regard there are two major errors that can occur: undertriage and overtriage. Undertriage occurs when critically injured patients who should be assigned to the urgent category are instead deemed non-urgent and have their medical treatment delayed. The obvious implication of this is preventable mortality due to medical resources being withheld from what would otherwise be a salvageable injury if treated. Overtriage occurs in one of two ways. The first is when non-urgent patients with mild to moderate injuries who could tolerate delayed treatment are assigned to the urgent category for immediate intervention. The second is when expectant patients with a dismal at best chance of survival are assigned to the urgent category and undergo intervention. In either case, valuable resources are being utilized for inappropriate patients.

Under normal non-MCE conditions, overtriage is more of a financial issue in which there is an economic loss due to the unnecessary consumption of a valuable, yet easily replaced resource. In this situation, the use of the resource does not influence mortality because there is an abundant supply available for the next patient who requires them. But as previously stated, in a MCE, patients outnumber the resources. As such, the resources need to be stretched as thin as it is possible. Their use on someone who either does not need them or would not survive despite their use means that other patients whose survival are dependent on these resources may die.

These errors reinforce the principle that triage accuracy is essential to reducing casualties in an MCE and underscores the importance of the triage officer being the most experienced trauma surgeon available [3, 9, 14, 19]. However, no matter what level of experience the triage officer has, mistakes will be made. Fortunately, research from the Boston Marathon bombings has shown that in addition to triage officer gestalt, objective findings may be of utility in identifying urgent casualties. In one study, loss of heart rate variability and complexity were shown to correlate with injury severity and could predict which patients required life-saving interventions. At this time, implementation of such monitoring may be difficult in the context of a 1 min patient evaluation, but it does provide hope that useful adjuncts may be of use in the future [20].

Pitfalls

No matter how comprehensive or well organized a plan seems to be, there are certain pitfalls that are common to all disaster responses. These pitfalls can be discussed as they pertain to the entire large-scale coordinated response that involves multiple agencies and institutions, or as they relate to the response within a single hospital. For the purposes of this chapter, we will focus on how some of the major pitfalls affect the hospital.

One of the most common and often first failures in a MCE is communication. This can result from damage to telephone lines thereby limiting the hospital's ability to communicate externally on land lines, damage to cell phone towers which limits internal and external communication, or simply overload of cellular phone networks by the community, media, and health care workers trying to obtain information. Redundant systems that have worked in the past to overcome this include handheld radio transceivers and even ham radios.

Failure of security at the hospital is another pitfall that can keep a response from running smoothly. Media, worried families of injured, and well-meaning volunteers can inundate an ER and should have restricted access to triage and treatment areas.

Uncertainty of who is in charge of running the response is another major pitfall frequently involved in MCE's. There should be predesignated individual or small group assigned the authority to oversee and coordinate all divisions involved in the response. If there is failure to pre-designate this command position, then multiple individuals could attempt to assume the lead role. This will lead to a loss of the coordinated effort necessary to achieve interoperability between all the disciplines and divisions involved in the response [3, 5, 9].

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Rural and Austere Environments

4

Jeffrey M. Lobosky

Rural and Austere Environments

The dawning of the twentieth century brought with it a major transformation in American society. There began a massive exodus of the traditional agrarian population to the growing urban centers across the country. The appearance of the automobile and a myriad of other technological advances further encouraged this shift and provided Americans with a plethora of powerful and efficient tools. At the same time, those very advances provided more powerful and efficient sources of injury and death. By the 1950s, trauma had become a significant cause of death and serious disability across the U.S. and in many communities, both rural and urban, survival of such injuries became the exception rather than the rule.

In 1966, the National Academy of Science published a scathing report entitled "Accidental Death and Disability: The Neglected Disease of Modern Society" [1]. The expose quickly captured the attention of the press, the public, the medical establishment, and Congress and as a result the Emergency Medical System (EMS) was conceived. Soon the concept of regionalized trauma centers, standardized protocols for the management of the severely injured patient and a nationwide 911 access network emerged. As a consequence of such efforts, victims of trauma now received efficient and timely treatment and survival became the *rule* rather than the exception.

A half century later, America's trauma system continues to thrive as designated trauma centers throughout the American landscape are staffed by board certified emergency room physicians, fellowship trained trauma surgeons, and critical care intensivists who man highly sophisticated and specialized ICUs. These frontline physicians are supported by air and ground transport teams which essentially bring the emergency room to the trauma victim while still in the field. Despite the widespread establishment of such networks there remains a significant population of our citizens who are well beyond the reach of one of these lifesaving institutions.

Patients in remote and rural areas often find that their local hospitals have a paucity of specialty coverage and limited access to the technological advances that most of us take for granted. How can these patients be best served when in need of competent care as a result of a major traumatic event? What options are open to provide lifesaving treatments in environments that have inadequate resources? The answers to these and other questions are the responsibility of not only the providers in the austere communities, but also of those of us who are integrated in the greater trauma care networks. In addition, successful solutions require

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the commitment of local, regional, and national political decision-makers.

First and foremost, it is essential to educate the physicians and mid-level practitioners who most often provide the care in remote facilities. It is the responsibility of the tertiary specialist to initiate the lines of communication between the rural providers and the larger facilities and to assure that the care the patient receives at the local hospital is appropriate. As a neurosurgeon, I have often times visited the medical staffs of outlying hospitals and lectured on the stabilization of the head or spinal cord injured patient. Discussing a common nomenclature such as the Glasgow Coma Score or advising when to give Mannitol or Methylprednisolone can be of enormous value to a physician or nurse practitioner inexperienced in treating severely traumatized patients. As important however, can be sharing with these colleagues *what not to do* in these situations as the principle "primum non nocere" must prevail.

On the other hand, it is incumbent upon the local practitioners to be open to these educational opportunities and willing to provide the expertise to stabilize the patient until transfer can be arranged. I attempt to make these first line providers competent in performing a brief but meaningful neurological examination and comfortable with initiating therapies which may keep open the window of opportunity for more sophisticated intervention as the "golden hour" is extended.

As regional medical centers become increasingly burdened with an influx of victims of traumatic injury we are finding more and more of these institutions unable to accept appropriate transfers because of bed availability. For this reason it is essential that the smaller facilities take a more active role in the management of less critically injured patients who may not require such tertiary care. Unfortunately, many of the providers in remote emergency rooms have learned the magic catch phrase "we don't feel comfortable" managing a given trauma patient and thus the Emergency Medical Treatment and Active Labor Act (EMTALA) compels hospitals and physicians to accept in transfer a patient who could be well managed in their home facility [2].

For the system to function appropriately, smaller hospitals in remote and rural regions must accept the responsibility for the care of those patients. This "culture change" requires a strengthening of the relationship among the regional hospital and its many smaller referring facilities. The first piece of such a relationship is the educational component discussed in the previous paragraphs. But making them comfortable requires much more than sharing with them when to give an osmotic diuretic or how to calculate the Glasgow Coma Score. One of the major concerns of providers in remote regions is the rare patient who does deteriorate beyond the capabilities of the local hospital. The fear, not totally unfounded, is that when they call back asking for transfer they will find that now there are no beds available or that since the victim is now an "inpatient" and no longer in the emergency room EMTALA does not apply and the receiving consultant is free to refuse the transfer.

In those institutions with which we have attempted to establish a more symbiotic relationship, we have assured the providers that if a patient they have agreed to manage locally deteriorates, we guarantee that we will accept the immediate transfer regardless of bed availability. The problem justifiably becomes ours to solve and thus offers a degree of assurance that the local provider is not left managing a patient beyond his or her capability because they agreed to our advice to keep the patient initially. This policy is not an easy one to establish and requires a degree of trust on both sides that often takes years of familiarity and experience to emerge.

An additional piece of the puzzle that is essential for such a relationship to work is access by the regional trauma center to the diagnostic studies, however, limited of the outside institutions. Not infrequently, patients are transferred with a diagnosis that is not supported once the patient has been helicoptered in and the "outside" CT scan is reviewed locally. I have had patients airlifted to our institution with an "interhemispheric subdural hematoma" only to find simply

a calcified falx cerebri misread at the outside facility. Another elderly female, wide awake and asymptomatic after a fall, was transferred with a "6 cm epidural hematoma" when in fact she harbored a calcified meningioma that was present and unchanged on a CT scan 5 years prior. Having access to the PACS system of the referring hospital would have spared these patients an unnecessary transfer. Recently, my partners and I have been meeting with our referring hospitals' radiology departments and obtaining access to their internal PACS systems on our home desktop computers. This allows us to view the X-rays and CT scans from several (but not all) of our feeding hospitals and can often times result in a local hospital admission and preclude transfer to a tertiary facility.

Rural practitioners can now be greatly aided with the emergence of *telemedicine* as an option to any facility with access to a computer. The definition of "telemedicine" is used rather broadly in the medical literature and most often refers primarily to "tele radiology"—the ability to review radiological studies over web based platforms. In the preceding paragraph I described our experience with "telemedicine" but the potential goes far beyond reviewing CT or MRI scans remotely and giving advice as to the necessity of transferring the patient to a tertiary center [3, 4]. For years, cardiologists and dermatologists have utilized real time technologies, to meet remotely with patients, render a diagnosis and prescribe a treatment plan. Using computer interfaces for live treadmill testing, cardiac auscultation, and real time images of patients has resulted in specialty access for individuals who previously were unable to obtain such consultations without long travel that many found prohibitive [5, 6].

The development of robotics now allows surgeons and interventional cardiologists to operate from a control console far removed from the actual patient. There is little doubt that in time such technology will allow specialists in the tertiary setting to perform procedures on patients many miles distant from the consultant. Although such intervention may be anticipated in the future, the internet currently allows physicians to monitor patients and enter orders remotely. At our institution, for example, I am able to access the minute–minute changes in a patient's vital signs and neurological status. From my desktop computer at home or in the office, from my i-Phone or i-Pad, I am able to evaluate a patient, order and view a CT or MRI and enter changes in the rate of hypertonic saline infusion or ventilator settings without being physically present in the hospital. There is no reason that the same technology cannot be applied to the care of a patient in a remote setting without the luxury of neurosurgical expertise immediately at hand. Thus, it is feasible that a patient deemed not to have a mass lesion requiring evacuation could remain at the local hospital while the neurosurgeon hundreds of miles away provides continuous active intervention as if they were housed in his or her own tertiary NTICU.

Of course, such participation will require navigating a number of potential barriers. The transmission of personal data across the internet is always at risk for exposure and HIPAA regulations continue in force within the realm of telemedicine [7]. The consultant must be credentialed to the medical staff of the rural hospital to allow him or her to provide treatment orders either by phone or computer entry. As anyone who cares for patients in a NTICU appreciates, it is critical that physicians trust the information relayed by competent nurses. Additionally, those same nurses must be able to trust and respect the input of the treating physician and it takes time and experience for both parties to reach such an understanding.

Finally, the necessary expansion of telemedicine will only occur if Medicare, Medicaid, and the commercial insurance providers acknowledge the importance of this emerging technology and reimburse the providers at a rate commensurate with the time, expertise, and risk of the given service. Few specialty consultants will be willing to review diagnostic studies and provide management recommendations for a given patient in a remote location if they are not adequately compensated for their input. If I review an outside CT scan and advise the local ER physician that he may provide the expected

care locally, my name is entered into that physician's narrative and I become liable from a medico-legal standpoint for the advice I rendered. I should not have to assume only risk without being fairly reimbursed [8, 9].

There will be instances where, despite competent providers in these austere environments and extraordinary input from the specialty consultants at the tertiary facilities, the nature of the patient's injuries will necessitate rapid transport to a higher level of care. Indeed, the mainstay of emergency medical transport remains the ground ambulance. Over the last four decades, these vehicles have become increasingly more sophisticated; so much so that they are able to provide trauma victims with all the technology and expertise available in most emergency rooms. Thus, it is now possible to initiate critical interventions at the scene which can not only save lives but prevent the deleterious effects associated with secondary insults of hypotension and hypoxia. Those who man these transports are no longer the local sheriff's deputies or funeral directors associated with ambulances in the mid twentieth century. The paramedics and emergency medical technicians (EMT) of the modern era are highly trained and exceedingly competent practitioners [10].

However, in many remote settings, time is of the essence and the distance between the trauma victim and his or her necessary care is often times too great to be covered by ground. Fortunately, over the last century, air transport has become increasingly available to rescue those in locations far removed from the tertiary trauma centers. The transfer, via air, of patients with medical emergencies has been around for as long as man has flown. In World War I, the French began transporting injured soldiers in fixed winged aircraft and such practices expanded in each ensuing conflict. The American military experience with air ambulances began in earnest in World War II where it was estimated that more than one million patients were transported to military hospitals during the conflict [11].

The Korean and the Vietnam Wars which followed saw the emergence of the more versatile helicopter as the mode of transport in medical emergencies. However, because of limited size, maneuverability and the expertise of the flight crews, these transports primarily *transported* and treatment was limited until arrival at a military medical facility. In the early 1990s, the United States Air Force initiated the Critical Care Air Transport Team (CCATT) which is a highly sophisticated cadre of physician specialists, critical care nurses and respiratory therapists able to deploy on a moment's notice and provide a mobile ICU on board any available transport aircraft. In general, the efforts of the CCATT teams are restricted to military personnel in combat arenas but during times of natural disasters they have occasionally provided the same services to the civilian population [12].

The utilization of air ambulances to transport civilians was first established at St. Anthony's Hospital in Denver in 1972 [13]. Since that time, tertiary centers across America have added air ambulances to their arsenal of tools directed to the care of trauma victims in all geographic venues. These fleets of helicopters and fixed wing aircraft can be especially supportive to those in the remote and rural settings where access roads may be limited and distances from major trauma centers prohibitive. According to the Association of Air Medical Services, approximately 550,000 patients are transported annually by air; 400,000 by helicopter and 150,000 by fixed wing [14].

Such technology is life saving and the use of these aircraft have resulted in a significant reduction in the mortality rates associated with trauma across the U.S. We must not forget, however, that air transport can have dangerous consequences for both the patient and the crew. As the use of these aircraft has increased, there has been a disturbing increase in the number of accidents associated with air ambulances. In 2013 alone, there were 13 crashes involving air transports in the U.S. resulting in 23 patient and crew fatalities and numerous injuries [15].

The use of aircraft to transport patients must not be undertaken without serious consideration as to the true necessity for such flights. From both a safety as well as an economic perspective, it is essential that the personnel in remote settings

access air transportation wisely. This reinforces the role that telemedicine can play in the management of the trauma victim in rural regions, at times allowing the patient to be cared for locally and thus precluding the expense and the risk of a medical flight. It is imperative that referring physicians think carefully before requesting flight care and convince themselves that such intervention is absolutely necessary in the care of the patient rather than just using this precious resource out of convenience.

Probably the most controversial issue to enter the realm of trauma management in remote or rural settings is the use of non-neurosurgeons to insert intracranial pressure monitors, perform burr holes or even craniotomies to evacuate an epidural or subdural hematoma. Much of this debate has been the result of military trauma surgeons performing occasional lifesaving craniotomies in combat arenas where a patient is deteriorating rapidly and access to neurosurgical expertise is not readily available. Additionally, an increasing number of neurosurgeons are opting out of call responsibility at civilian trauma centers across the country for a variety of reasons—diminishing reimbursement, skyrocketing malpractice premiums, inconvenience, burnout among a "graying" neurosurgical workforce and an expanding interest in elective spine surgery as a greater proportion of neurosurgical practice. This often times leaves remote facilities and occasionally traditional receiving facilities with a lack of neurosurgical coverage. In a 2001 survey of American Association for the Surgery of Trauma membership, a surprising 40 % of respondents were comfortable with non-neurosurgeons placing intracranial pressure monitors and 14 % thought it reasonable to have them perform craniotomies! [16].

Some general surgeons in rural practices are suggesting that they be allowed to perform such procedures under emergent conditions where patients are rapidly deteriorating and the distance to available neurosurgical expertise is hours removed. Indeed, there is evidence to suggest that early decompression results in better outcomes, but the decompression must be appropriately performed [17]. There is little rationale for "burr holes" in an acute subdural or epidural hematoma as the clot is thick and gelatinous and requires a generous craniotomy to effect adequate decompression. In addition, burr holes alone make it virtually impossible to identify and control the bleeding source. Craniotomy, under any circumstance, is not an easy undertaking. The technical skills involved in accessing the intracranial compartment are just the tip of the iceberg. Controlling the bleeding source, repairing torn large venous sinuses, managing large contusional hemorrhages or malignant cerebral edema present challenges that cannot be adequately addressed by non-neurosurgeons.

However, with appropriate training and commitment it is possible to provide a skilled general or trauma surgeon in a rural setting the tools to perform trauma related craniotomies when the option is allowing the patient to succumb to their head injury for a lack of neurosurgical expertise. These cases should be few and far between and every attempt should be made to transport the victim to a tertiary facility with neurosurgical availability. Rinker et al. reported his experience at a Level III rural trauma center [18] and others report similar acceptable outcomes in the absence of immediate neurosurgical consultation [19]. However, what constitutes an "acceptable outcome" is debatable in a trauma system as advanced as ours. The paper by Schecter and his colleagues discussing their experience in American Samoa described using burr holes as a diagnostic tool [20]. Certainly few of us would find it acceptable to return to those days prior to CT scanning when "woodpecker" surgery was performed to identify a possible mass lesion.

Young and Bowling reported similar complication rates between neurosurgeons and mid-level practitioners in ninety-two trauma patients requiring the insertion of an intracranial pressure monitor. They concluded that the use of mid-levels for such intervention was safe [21]. In 2014 Ekeh et al. published their outcomes at Wright State School of Medicine utilizing trauma surgeons to insert ICP monitors. Again, there were no appreciable differences in the complication rates between the trauma surgeons and the neurosurgeons [22]. However, both of these studies were done at a busy Level I trauma center

and should not be extrapolated to suggest similar outcomes could be realized in a setting with much smaller volumes of experience.

The data suggests, without demeaning the training and skills of neurosurgeons, that under certain circumstances non-neurosurgeons may be able to perform limited neurosurgical procedures with acceptable outcomes. The guidelines under these conditions must be stringent and it is imperative that neurosurgical input for training and monitoring of non-neurosurgeons be extensive and ongoing. Such practices should be designed to save lives in remote settings where immediate neurosurgical expertise is unavailable and the time and distance to a tertiary center is prohibitive. They should not be implemented to save neurosurgeons the inconvenience of getting up in the middle of the night to provide needed care to a head injured patient.

Once again, the use of telemedicine in such circumstances can be invaluable. Ideally, when a rural practitioner is required to perform a craniotomy, intra-operative cameras might allow the neurosurgeon at the tertiary facility to "assist" by giving real time advice as the surgery proceeds and provide much needed guidance in the presence of an unexpected event. This would allow the neurosurgeon, who will eventually receive the patient in transfer, a better opportunity to understand the extent of the injury and the details of the surgery performed.

When inclement weather and distance may preclude the safe transport of a patient to the regional trauma center, the use of local mid-level practitioners and general surgeons to insert ICP monitors might be a reasonable course of action. Again, using the technologies of telemedicine, the patient can be managed in the local ICU with real time neurosurgical input until conditions allow a safer transfer. However, I cannot emphasize more strongly the importance of adequate training and experience of the non-neurosurgeons if such a program were to succeed.

The management of patients with traumatic neurosurgical conditions in remote or rural settings, with limited resources and medical expertise, presents a multitude of challenges for both the rural practitioner and the tertiary consultant. Fortunately, technological advances in the diagnosis, treatment, and transport of these victims allow the opportunity to initiate invaluable care in the local hospitals and at times provide ongoing care for these patients without transfer to the tertiary facility. Coordination of such care is a complex process that by necessity requires the input and commitment of all parties involved in the treatment of the polytraumatized patient. Only through such efforts can we assure that patients in every corner of the American landscape have access to the lifesaving marvels afforded by our trauma care system.

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5 Prehospital Care and EMS Considerations in the Polytrauma Patient with CNS Injuries

Dan B. Avstreih and Scott D. Weir

Much of modern prehospital Emergency Medical Services (EMS) arose directly from efforts to advance the care of severely injured trauma patients. The 1966 National Academy of Sciences white paper "Accidental Death and Disability: The Neglected Disease of Modern Society" is considered the seminal document in EMS systems, driving, along with lessons from the battlefield and concurrent but unrelated advances in emergency cardiac care, the mandates and funding that shaped prehospital medical care over the next 50 years [1].

Opportunities for the favorable outcome in the brain-injured polytrauma patient can be influenced far before the patient hits the doors of the emergency department, or even has first contact with medical provider of any type. Legislative actions such as helmet laws, law enforcement efforts in driving under the influence (DUI) prevention and safety innovations by automotive and civil engineers are all pre-event factors that can markedly affect patient outcomes, or even whether the event occurs at all. However, once an injury occurs, it is the mission of the diverse web of public safety, logistics and medical specialists to provide critical medical care until the patient is delivered to the hospital [2].

In the United States, most civilian trauma victims will access the emergency medical system via 911. Though the specific details of call processing and dispatch can vary significantly in different locales, generally this process involves a public safety answering point (PSAP) and responder dispatching process [3]. Depending on the resources and sophistication of the system, this may include emergency medical dispatch (EMD) with pre-arrival instructions [4].

The medical assets deployed to an event will be a function of both the design and resources of the system and the nature of the specific incident. A roofer injured in a 40 foot fall may only need paramedics and an ambulance, where a victim of a high-speed motor vehicle accident may require assets capable of vehicle extrication, fire suppression, and traffic control.

Care of the trauma patient in the prehospital environment brings unique challenges rarely encountered in the hospital environment. Simply the act of responding to the scene involves risks for both ground-based and air medical providers. Vehicle crashes are the leading cause of mortality

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among EMS providers and the second leading cause of death in firefighters [5]. Non-fatal injuries in vehicle crashes account for almost 10 % of morbidity as well [6]. Multiple factors contribute to this including but not limited to the use of warning lights and sirens (WLS), fatigue associated with shiftwork, the presence of multiple communication distractions in the driver compartment and the only recent emphasis on crashworthiness in the patient care compartment [7–16]. Response by air ambulance is also associated with significant risk [17–19]. The NTSB calculated air ambulance crash rate was 4.75 accidents per 100,000 flight hours from 1998–2004 and, in the most deadly year (2008), five crashes resulted in 21 fatalities [20]. Though it is the goal of the 2014 FAA Final Rule on Helicopter Safety to prevent these accidents, the difficulties faced in helicopter emergency medical services (HEMS) operations including nighttime visibility, weather, and terrain will remain part of the challenge, particularly in scene response [6, 21].

Depending on the mechanism of injury, operations once on the scene of the polytrauma patient can also present challenges to rescuer safety. Approximately 6 % of firefighter deaths involve being struck, many of which are related to roadway operations at accident scenes [5, 22]. Other threats to provider safety can include hazardous materials, electrical wires, or even active shooter scenarios. Providing rapid, potentially even lifesaving, care must always be balanced with provider safety. A similar thought process must be applied to patient safety. Interventions that should be undertaken prior to patient movement such as cervical motion restriction may need to be foregone in vehicle fires or impending structural collapse.

The specific levels of training and scope of practice for prehospital providers is set by individual states and therefore varies across geographic areas [23]. For simplicity's sake EMS care can be divided into two categories: basic life support (BLS) and advanced life support (ALS). Basic life support involves primary assessment and stabilization by noninvasive means such as spinal motion restriction, splinting, oxygen administration, and noninvasive positive pressure ventilation. The scope of practice for advanced life support providers can include more comprehensive knowledge and assessment, invasive procedures including vascular access, endotracheal intubation, and needle thoracostomy, and a variety of emergent medications including narcotics for pain management, benzodiazepines for TBI associated seizures or agitation [24]. The topic of rapid sequence intubation is complicated enough to warrant its own discussion later in this chapter, but some agencies do carry induction and paralytic agents for this purpose. The scope of practice of flight nurses is governed differently and some air medical programs have additional capabilities including central access and blood products [23].

There are two commonly used programs for the trauma education of prehospital providers —"Prehospital Trauma Life Support" and "International Trauma Life Support." These standardized curricula are similar in large part to the Advanced Trauma Life Support (ATLS) program utilized by hospital-based providers, though they are tailored to the unique aspects and perspective of prehospital care [25–27]. The two programs are very similar apart from minor variations. Both emphasize initial scene assessment followed by an initial rapid patient assessment. Limited interventions are applied at the point of first contact to stabilize immediate life threats, after which the patient is moved to the transport unit for secondary trauma assessment, vital signs, vascular access, and further management as indicated, ideally with rapid transport to definitive care occurring in parallel. The shared goals of these programs is the thorough patient assessment completed in a rapid, efficient manner to identify and stabilize immediate life threats and effect timely transport to definitive care, providing all reasonable additional stabilizing measures during transport. While some interventions have demonstrated value in the hospital-based setting, their application in the prehospital phase may not add value and/or even critically delay the greater value of hospital-based care—time-dependent treatment effects carry greater weight than treatment effects alone.

Prior even to patient contact, prehospital providers can discover crucial clues about potential

injury patterns or even coexisting medical factors that hospital staff may not have otherwise accessed. A single vehicle accident involving an elderly patient with no evidence of an attempt to stop can identify the need for a syncope evaluation, seizure workup, or ongoing cardiac event. Certainly the only thing more challenging than taking care of the polytrauma brain-injured patient is when that patient is also having an acute myocardial infarction. The presence of prescription medicines or illegal drugs can be clues to a medical etiology masquerading as severe traumatic brain injury. A quick fingerstick blood glucose check or a single dose of naloxone can prevent an unnecessary intubation and ICU stay. There is a broader resource management role to the initial scene size-up as well. Inherently dispatch information can never be complete, and the assets needed to manage a simple two car accident can be markedly different depending on whether each car contains five adults or just a driver. It is difficult for laypersons to predict the nature of injuries from the state of vehicles. Modern automotive designs such as crumple zones can cause accidents to look very bad but dissipate forces away from intact passenger compartments. The National Highway Safety and Traffic Administration (NHTSA) Crash Injury Research and Engineering Network (CIREN) program continues to study the injury patterns that accompany certain crash data, and the future of postcrash automotive data transmission may greatly aid emergency responders in predicting the severity of injuries they will encounter on arrival [28].

Prehospital priorities in the management of trauma patients focus on rapid identification and stabilization of life-threatening injuries, prevention of physiologic deterioration, and transport to closest appropriate facility for definitive care. Prioritization is essential as these goals may be in conflict with each other, particularly balancing on-scene treatments with care during transport. In that sense, the primary goal of EMS is to minimize the prehospital phase of care while still addressing everything that matters. While there are whole textbooks devoted to prehospital medical care and Emergency Medical Services is now a board-certified medical subspecialty, several key areas of intervention play an important role in the management of these patients. After describing the general approach to prehospital trauma patients, we will discuss these areas in depth.

Once the initial scene assessment reveals the mechanism of injury, the primary survey of the patient reveals the nature and extent of injuries, and prioritizes immediate interventions. Immediate threats to life are identified and addressed in the order of priority at the site of wounding. To maintain the judicious balance between competing objectives—between addressing identified injuries and minimizing delays on scene—assessments and interventions are limited to those warranting immediate action prior to patient packaging and movement to the EMS transport unit. These are:

- Uncontrolled external life-threatening hemorrhage.
- Occluded airway and/or inadequate ventilation.
- Tension pneumothorax.
- Open pneumothorax.
- Unstable pelvis—because application of pelvic circumferential compression device is best applied while placing the patient on the backboard.
- Impaled objects—stabilization to prevent further injury with movement [25, 26].

The remaining injuries are generally addressed during the secondary survey and transport phase. Patient movement is itself a therapeutic intervention. The benefit of patient movement, from the point of first contact to the EMS transport unit and from the scene to the trauma bay, should be balanced against the benefit of other interventions considered. This perspective guides decisions about clinical priorities in the multiply injured trauma patient—when and where to do the things needing to be done. In general, a critically injured trauma patient (see Table 5.1) should be identified upon completing the primary survey; which frames the goal of keeping on-scene delays as brief as achievable and less than 10-min. Vital signs are not done at the point of initial contact; perfusion is assessed by skin

Table 5.1 Critically injured trauma patient—warranting rapid transport < 10 min

(1) Inadequate or threats to airway
(2) Impaired ventilation or respirations
(3) Significant external or suspected internal hemorrhage
(4) Abnormal neurologic status
a. Glasgow Coma Score (GCS) < 14
b. Seizure
c. Neurologic deficit
(5) Penetrating trauma to head, neck, torso, or extremities proximal to knee/elbow.
(6) Amputations or near-amputations proximal to fingers/toes

color, temperature, and assessment of peripheral and central pulses for presence, rate, and character. Vital signs and vascular access are deferred until the patient has been moved to the transport unit with rare exception when movement to the transport unit is delayed, usually due to prolonged extrication, or not achievable. Once in the unit, vital signs are obtained and vascular access is established and a secondary survey is completed, likely during transport [25, 26].

Despite the widespread use of GCS for assessment of the multisystem trauma patient with traumatic brain injury, there is significant concern, particularly among EMS physicians, regarding comparative value, accuracy and reproducibility of this and other assessment classification scores for head injury [29–38]. Both PHTLS and ITLS include determination of Glasgow Coma Score during the primary and secondary trauma survey, though one utilizes a rough assessment of the level of responsiveness on an Alert-Verbal-Pain-Unresponsive scale (AVPU scale) at the point of initial contact as a rapid gauge of neurologic status.

Numerous authors have noted the limitations of the GCS and the p-GCS in particular. The GCS is difficult for EMS personnel to consistently remember and accurately apply without ready references and frequent experience with its use—particularly in the highly stressful context of a multisystem trauma patient in the prehospital setting [32, 34, 39]. The GCS was not intended to be used as a single score but rather the expanded components are more valuable [29, 40]. The GCS is less reliable in the mid-range of scores from 9–12 [29]. The predictive value of the GCS for mortality is less sensitive in elderly patients at traditional threshold values [41]. Hypotension, hypoxia, and language barriers all impact the GCS [29]. The Brain Trauma Foundation (BTF) Guidelines recommendation for the use of the GCS is a weak recommendation based on low quality, Class III evidence [42]. The BTF EMS guidelines also call for the correction of hypoxia and hypotension prior to obtaining GCS, which is rarely the case with the initial p-GCS [42]. Although the guidelines suggest that the prehospital GCS is a reliable indicator of severity of TBI, evidence suggests p-GCS lacks prognostic value although observed trends in GCS are more predictive [35]. In the multiply injured trauma patient, the interpretation of GCS is even more complex.

Notably once acquired, many guidelines stratify GCS into ordinal categories of injury severity—mild brain injury with a GCS 13–15, moderate brain injury with a GCS 9–12, and severe brain injury with a GCS 3–8. The AVPU scale produces a similar stratification by injury severity (Table 5.2)

It has been suggested that simpler and more reproducible measures may perform equally and with greater consistency than the GCS. Some suggest that the 6-point motor score alone provides adequate performance to replace the 15-point full GCS [29–31, 43]. The KISS principle and reproducibility under stress would favor utilization of even simpler scales such as the Simplified Motor Scale (also called the TROLL exam with a built-in scoring mnemonic

Table 5.2 AVPU scale and corresponding GCS range and injury severity

AVPU responsiveness category	Likely associated GCS	Classification of severity of injury
Alert	13 (E4/V4+/M5+)	Mild GCS 13–15
Verbal	12 (E3/V4+/M5+)	Moderate GCS 9–12
Painful	6 (E2/V2+/M2–4)	Severe GCS 3–8
Unresponsive	3 (E1/V1/M1)	

Source Adapted from Braithwaite, AVPU versus GCS: Which is better for EMS? presented at the Gathering of Eagles Conference 2014

for EMS—Test Responsiveness: Obeys—Localizes—or Less) [43, 44].

Simplified motor score (SMS)	TROLL exam
2—Follows commands	2—Obeys commands
1—Localizes painful stimuli	1—Localizes painful stimuli
0—Withdraws to pain or less	0—Less than localizes painful stimuli

The SMS has been validated in two independent studies in both the ED and the prehospital setting [43–45]. It provides the same relevant information as GCS. It was statistically derived and shows better inter-rater reliability than the GCS [32, 33, 45].

While GCS likely will still play a role in the trauma bay and ICU, strong consideration for less complex and more reproducible scoring systems such as SMS or AVPU should be considered for prehospital providers and the unique prehospital phase of care, at least in the early phases of patient assessment and stabilization.

Despite being a pillar of ATLS guidelines for hospital-based treatment, airway management is one of the most complicated and controversial in the prehospital arena [27, 46–48]. Numerous studies have failed to demonstrate any survival benefit in moderately to severely injured trauma patients undergoing prehospital intubation [49–55]. Several authors have found an increased mortality, though more recently there have been studies that showed an outcome benefit [51, 56]. There are several reasons why prehospital intubation may not be in the best interest of the patient, even in the setting of severe TBI. First, while seasoned medics may tell "war stories" about intubating an entrapped patient upside down in a dark, muddy ditch, none would argue that these are ideal conditions for a high-risk procedure, and even the best prehospital conditions are nowhere near those of the trauma bay or operating room [46–48, 57–59]. The ability to obtain and then maintain proficiency in endotracheal intubation is also a challenge for many EMS systems. The studies that have been able to demonstrate outcome improvements in the setting of prehospital rapid sequence of the patient used small, highly practiced cohorts of prehospital providers that perform intubations frequently [51, 60]. This does not describe the vast majority of EMS systems. Though it is possible that advances in high fidelity simulation can compensate to some degree, regular access to the operating room may be both necessary and increasingly uncommon [61–64]. It is likely that paramedics need to intubate 12–15 times per year to maintain proficiency [65]. This number can be difficult to achieve in systems with either low call volumes or a high number of advanced life support providers. Using blinded pulse oximetry and ETC02 data, it has been shown that EMS providers frequently underestimate both the difficulty and time involved during an individual intubation, which is particularly relevant as maximizing physiologic parameters to prevent secondary injury is a current mainstay of brain injury treatment [66, 67]. Single episode of hypoxia has been associated with a worse outcome, and the circumstances involved in a severely brain-injured patient often do not allow for ideal intubation conditions [66, 68–72]. A relatively new concept of delayed sequence intubation, which involves procedural sedation with ketamine followed by aggressive preoxygenation prior to paralysis and endotracheal tube placement, has been studied among altered mental status patients in medical setting, but

currently there is no published study on its use in trauma [73–77].

To some degree, the older prehospital rapid sequence intubation (RSI) literature needs to be interpreted in the context of changes in technology. Video assisted laryngoscopy has replaced direct laryngoscopy in many systems, and research has shown that paramedics can obtain intubation proficiency quicker with these devices [78–81]. A number of supraglottic rescue devices have replaced surgical cricothyroidotomy as backup for failed intubation and this too may influence success rates [82–86]. Concerns about decreased cerebral perfusion in the setting of supraglottic airways have been raised in animal models [87]. However, a recent radiologic study showed no decrease in carotid flow in humans [88]. Unrecognized esophageal intubation or tube dislodgment during transport can be mitigated by routine use of waveform capnography [89, 90].

Even if intubation is successful and uncomplicated, there are significant risks that still must be managed. Inadvertent prehospital hyperventilation is well-documented, even in experienced providers [69, 91, 92]. This can lead to cerebral vasoconstriction, decreased cerebral perfusion, and ultimately increased injury to at risk areas of brain [71, 93]. This again can be potentially mitigated by strict use of continuous and EtCO2 monitoring, ventilation timing devices, and transport ventilators [89, 92]. While end-tidal CO2 is an unreliable index of PaCO2 in the hemodynamically unstable, multisystem trauma patient, it is the only available means to guide ventilations [94–96]. Maintaining end-tidal in the 35–45 mm Hg range is recommended for the intubated patient though no recommendations are available for the nonintubated patient supported by supraglottic airway or bag valve mask ventilation [89, 97].

The introduction of positive pressure ventilation, particularly over-ventilation, can decrease effective perfusion by decreasing thoracic venous blood return. This has been associated with poorer outcomes even in the setting of normal CO2 levels, a concept widely referred to in the prehospital setting as “death by hyperventilation [98].” We will discuss the concept of therapeutic hyperventilation in the setting of suspected herniation syndrome later in this chapter.

The management of volume status in the trauma patient has evolved greatly in the last 30 years. While we have largely moved past the days of 2 large bore IVs run wide open in every trauma patient regardless of presentation, balancing resuscitation goals in the brain-injured polytrauma patient remains quite challenging [99]. The benefits of controlled resuscitation are most well established for penetrating injury with noncontrollable source of blood loss [99–103]. The role of controlled resuscitation in blunt multisystem trauma is still evolving and questions remain regarding which patients, how low, and how long [102, 104–106]. In blunt trauma with brain injury the optimal strategy, and detailed thresholds remain unclear [51, 70–72, 99, 103]. Strategies appropriate for isolated brain injury may not directly apply to brain-injured patient with uncontrolled bleeding from an extracranial injury. Similarly, controlled resuscitation strategies reasonably considered for torso injury, may be harmful in the patient with associated severe TBI [101, 102, 104, 107, 108]. In fact, many of the controlled resuscitation studies excluded head injured patients. Studies including patients with intracranial injury show increased mortality in head injured patients in whom fluids were withheld in the setting of hypotension, and a single episode of early hypotension has been associated with up to a 150 % increase in mortality [70, 72, 107, 109].

Studies which included head injured patients show a trend toward benefit with IV fluid administration and correction of hypotension [107]. However, the appropriate resuscitation endpoint remains ill defined. Interestingly, the 2007 BTF guidelines use a SBP of <90 mm Hg as the definition of hypotension [42]. Some authors and evidence suggests increased mortality at threshold of SBP <110 mm Hg [105, 109–111]. While it may be that mean arterial pressure is a more appropriate measure to guide resuscitation and to achieve and maintain an adequate cerebral perfusion pressure in the face of presumed elevations in intracranial pressure, the studies showing adverse outcome reported SBP

rather than MAP. For these reasons most guidelines present their recommendations in terms of SBP rather than MAP.

In the prehospital environment, there are significant limitations that impact end points for resuscitations. Blood pressure is most frequently obtained by a noninvasive oscillometric automated cuff, and accuracy of devices in the setting of hypotension may be variable [112, 113]. The manually auscultated blood pressures that are often used upon arrival in the trauma bay can be limited in feasibility due to noise during air or ground transport. Palpated blood pressures and pulse oximetry wave form systolic blood pressure may be variably utilized when circumstances preclude auscultation. The precision and reliability of such measures are unclear and the evidence on thresholds for targeted resuscitation does not address the method of monitoring [114].

Currently, utilizing the proposed thresholds by alternative monitoring methods is also not validated. As continuous capnographic monitoring has become common, there have been suggestions to use EtCO2 as a marker of perfusion [94–96]. While this appears to have utility in medical cardiac arrest patients, in the multisystem trauma patient, dynamic changes in both ventilatory and hemodynamic variables are likely to impact the observed values and the correlation to PaCO2 is less reliable and less predictable [59–61]. The validity of this measure in nonintubated patients and patients with supraglottic airway devices is unknown.

Possible clinical endpoints such as palpable radial pulses and mental status rather than numerical endpoints may be best suited for the prehospital setting, though distinguishing alternations in mental status due to inadequate perfusion as opposed to primary TBI (or even simply alcohol intoxication) is challenging.

Strategies for diagnosing and managing herniation syndromes in the prehospital setting is an area warranting particular discussion, as the recommendation of limited hyperventilation of the patient with suspected impending herniation —"targeted or therapeutic hyperventilation"—by BTF, ITLS, and PHTLS influences not only the individual patient but also may unintentionally impact on the care of the population of brain-injured patients as a whole.

The BTF prehospital guidelines suggest that clinical signs such as dilated and unreactive pupils, asymmetric pupils, abnormal motor response with extensor posturing or unresponsiveness, or deteriorating GCS from a starting score of 9 be used to identify herniation, though they stipulate that ventilation, oxygenation and hemodynamics be normalized before considering targeted hyperventilation and that it be discontinued when signs are no longer present [42]. However, the success of a targeted strategy presupposes the reliability of the clinical signs. That is not clearly established to be true in the prehospital setting. This is concerning since herniation protocols rely on accurately identifying the population that may benefit from hyperventilation and distinguish it from the non-herniating population known to be harmed by hyperventilation.

It is reported that as much as 17 % of the population has anisicoria and was noted to be pronounced in 4 % of the studied population [115]. A retrospective analysis found that pupil asymmetry had a positive predictive value for an intracranial lesion of only 30 % and even with asymmetry greater than 3 mm the positive predictive value was only 43 % [116]. The authors note "a single measurement of pupil asymmetry is neither a sensitive nor specific finding in either identifying or localizing an intracranial lesion." [116] A fixed pupil is defined in the guidelines as less than 1 mm of response to bright light. The accuracy of estimates in a field environment is unknown and, because metabolic and cardiovascular abnormalities including hypotension, hypoxia, and hypothermia all may be associated with dilated pupils and decreased reactivity, guidelines state that pupils should be assessed after the patient is resuscitated and stabilized [117]. The BTF prehospital guidelines on pupillary exam note that the relation between prehospital pupillary findings and outcome have not been evaluated and recommendations are based on studies from in-hospital studies where pupillary findings have prognostic value predicting mortality, and studies have found that while pupillary function may be an indicator of brain

injury after trauma, it is not a specific indicator of severity [116, 117].

When hyperventilation is utilized in the hospital setting the guidelines recommend using it in conjunction with ICP monitoring to guide therapy. The prehospital environment substitutes clinical measures out of necessity but this almost certainly decreases the accuracy of appropriate patient identification. The use of a targeted strategy on a population level also supposes that the intervention has a high likelihood of benefit in the appropriate population compared to the magnitude and frequency of harm with which it will be applied to the non-herniating population. This is a function of both the size of the populations of interest and the size of the harm/benefit in the respective populations. The incidence of cerebral herniation has been estimated to occur in 40 % of cases of severe TBI although the frequency with which it occurs within the prehospital phase of care is likely even lower [51, 72, 118]. For these reasons, the majority of cases of severe TBI that prehospital providers encounter are likely to involve TBI without cerebral herniation.

Hyperventilation reduces ICP at the expense of cerebral blood flow (CBF) and cerebral perfusion pressure (CPP). The effects on CBF are compounded in the multisystem trauma patient with TBI whose injuries place them at greater risk for superimposed hypotension [51, 72, 103]. The beneficial effects of hyperventilation are at best short-lived and predicated on delaying herniation to allow more definitive interventions. Although weak recommendations from BTF advocate limited short-term hyperventilation in narrowly selected patients facing imminent risk of herniation, no outcome studies establish its effects [69, 93, 97]. In light of the adverse effects associated with hyperventilation when applied to non-herniating patients, it is reasonable to consider more narrowly defined selection criteria as well as pursue alternative treatments with less potential for adverse impact. These may include simple measures such as elevation of the head of the bed to 30°, keeping the head midline and avoiding compression of venous drainage.

Hyperosmotic agents are variably utilized in the prehospital setting, more commonly by air medical providers and critical care interfacilty transport services than ground-based emergency response services. The majority of evidence comes from hospital-based studies including the use of hypertonic saline (HTS) as a hyperosmotic agent in the management of elevated ICP, which will be addressed elsewhere in this text. Since high concentration HTS requires central venous access for administration, it is not suited for prehospital application. However, lower concentrations can be administered through peripheral venous access, as can 8.4 % sodium bicarbonate, which is readily available and familiar to all tiers of prehospital providers and been reported to reduce ICP in TBI patients for 6 h [51].

With all strategies for management of possible herniation, the best possible care for the individual patient in ideal circumstances must be balanced against the likelihood that the variables to inform such decision-making will be available in the prehospital phase of care and the potential downsides of misapplication of the strategy to a patient that is not suffering from the condition.

Transport modality and destination choice are the final major treatment decisions. The need to balance the logistics of patient movement with time sensitive medical intervention is one of the greatest challenges in trauma care, especially in the prehospital phase. Just as traumatologists must decide if a patient can be stabilized for arterial embolization in interventional radiology or needs to go directly to the operating room, prehospital providers must make multiple decisions that balance care priorities with speed to hospital. As we routinely tell our providers, all decisions, including logistical ones, are medical decisions. The thinking on when to transport has evolved considerably since the concept of the Golden Hour was first introduced. What started as “diesel fuel and cold steel” had swung considerably in the other direction of two large bore IVs prior to transport by the time a seminal 1996 study found that victims of penetrating trauma had a higher survival rate if they arrived in the ED via private vehicle as opposed to by EMS [119–122]. The seemingly simple decision of when to place an IV access needs to take into account what will be given through the line and

what effect will it have on the patient's overall outcome, balanced against delaying transport for the procedure and the likelihood of successful placement (and possibility of provider injury) in the back of a speeding ambulance.

The "right answer" continues to evolve with our knowledge treatment options. The data on tranexamic acid infusions from the CRASH studies has added more value to an IV, and the development of a successful blood replacement product could markedly rebalance the equation [123–127]. Regardless, because much of our current strategies for management of acute traumatic brain injuries involves maximizing physiology to prevent further damage, a thoughtful, multidisciplinary approach with active EMS engagement is most likely to result in the best logistical medical decisions.

When considering mode of transport, three main variables come into play. The first, and likely most important in the vast number of severely injured patients, is time to definitive care. In the civilian setting, this usually represents a choice between ground ambulance and HEMS transport. Ground assets are much more prevalent. In 2011, air medical transports represented approximately 2 % of all ambulance transports in the US, with only 1/3 being scene runs [23]. Availability of air assets is a function of geography, but also of weather conditions, appropriate landing zones, and other flight safety conditions. While one might assume that medical helicopters, with average cruising speeds of 135–150 mph and largely straight, traffic-free flight paths would be the quickest way to the hospital, the scene logistics play are often much more complicated [60, 128–135]. In most geographic areas, air assets are not routinely dispatched as part of EMS response, and once requested, there are still inevitable delays for weather/route checks and spin-up time [136, 137]. Additional delays can occur if a landing zone cannot be safely established immediately proximal to the scene, and thus requiring ground transportation to another location to meet the aircraft. At the aircraft, beyond the necessary pauses for patient report and physical transfer, noise, lighting and physical space limitations can necessitate patient assessments and invasive procedures, especially endotracheal intubation, be completed prior to on-loading. In situations where patient access is delayed due to entrapment or environmental barriers and the aircraft can be on the ground prior to packaging, many of these potential delays no longer apply. A conceivable gross rule of thumb could be, with regards to speed of arrival, patients benefit from air ambulance transport if the trauma center is greater than 30 min away [23]. In general, research seems to show improved outcomes with HEMS transport in patients with a moderate injury severity score (ISS). Patients with severe ISS are unlikely to survive in any mode of transport, and HEMS resources seem to be unnecessary, from the physiologic standpoint, in patients with low ISS [60, 128–133, 137, 138].

Aside for the potential for more rapid transport to the trauma center, HEMS assets can also be utilized to bring providers with advanced training and protocols. Depending on the nature of the injuries, a time delay in transfer to definitive care may actually increase the chances of a good outcome [60, 131, 133]. Most would argue that a delay in transport to RSI a burn patient with the potential for significant airway involvement would be justified, while delaying transport in penetrating thoracoabdominal trauma is rarely in the patient's interest [108, 122, 139]. Many of our brain-injured polytrauma patients fall somewhere in between these bookend cases. As referenced earlier, rapid sequence intubation in cases of suspected TBI may be associated with survival benefit. With a small number of providers with advanced training and regular practice, it is plausible that flight programs may better be able to manage the risks associated with RSI than EMS systems with less regular exposure to critical trauma [60, 128, 133].

The third variable—the impact on resource availability and population health—is less within the scope of this book, other than to acknowledge that the complexity of some logistical decisions. For example, the choice to drive a patient by ground 60 miles to the closest trauma center must

be balanced by the risk to the population of taking the town's only ambulance out of service for 2 h [60, 140–142].

The choice of destination hospital is a product of national recommendations, state legislative requirements, local trauma system guidance, hospital and EMS resources, and the specific injuries and/or mechanism of the individual patient. The National Expert Panel on Field Triage provides a decision algorithm through the CDC Trauma Triage Guidelines. It is recommended that patients with substantial alterations in level of consciousness or vital signs or with anatomically severe injuries such as penetrating thoracic trauma or two or more long bone fractures are transported to the highest level of trauma center available in the specific local trauma system [143]. Patients with a high-risk mechanism of injury but that does not meet the vital sign or anatomic criteria higher in the algorithm should still be transported to a trauma center but may not need the highest level of trauma care [143]. Local factors can have significant impact on destination decision as well. In 2005, 84 % of all US residents have access to a Level I or II trauma center within 60 min, though over one quarter would require HEMS to achieve timely access [140]. Depending on the region of the country, there maybe multiple Level I trauma centers in a five-mile radius or one in the entire state [135, 141, 144, 145]. EMS resources, both in terms of certification level and transport resources, can also vary considerably. Situations can arise where direct transport to a local non-trauma hospital is indicated for stabilization of a critical airway or tube thoracostomy prior to transfer to a trauma center for definitive care. These decisions can be complicated but may also have significant impact on individual patient outcome. A regional approach to trauma care involving perspective and expertise from all aspects of the care continuum is most likely to lead to good decision-making at the side of the patient [146, 147].

The last phase of EMS care for the trauma patient (other than the post-event analysis, debriefing, and feedback for which we strongly advocate), is the patient report and handoff. There are several points worth emphasizing during this phase. Despite numerous studies documenting the challenges on in-hospital sign-outs, there has been less formal study of EMS-ED handoffs. Research has generally found that between 25 and 50 % of EMS report is not acquired by the ED team [148–152]. This can be addressed in several ways. It is likely that simple awareness may lead to better communications. The nature of the problem lends itself to practice in cross-disciplinary simulation settings. It is possible that communications could be improved if EMS report follows a scripted format though the research has found mixed results [152]. One such tool is the "DeMIST" format—Demographics, Mechanism, Injuries identified, Signs (objective data like vital signs, EtCO2), Treatments and response to interventions [152]. Special attention should be paid to accurate and reliable information—vitals should never be "stable" and normal vitals must be entirely normal. Particular attention should be paid to trends over transport. A blood pressure on arrival of 110/60 may not be particularly alarming, but if it was 180/90 on-scene and 140/70 just prior to the hospital, the value is much less reassuring. Similar diligence should be paid to neurological findings particularly level of consciousness and pupillary exam. Related, if a patient has undergone prehospital rapid sequence intubation, communication of a field neurological exam, time and type of paralytic, time of last sedative, and evidence of patient motion since pharmacological paralysis can all help guide the care of the severely brain-injured patient.

The development of an integrated, coordinated, and effective trauma system that delivers high quality, well-researched, and evidence-based care across the continuum of providers is now a goal more than 50 years in the making. The 1966 National Academy of Sciences white paper, the 1996 "EMS Agenda for the Future" and the 2006 Institute of Medicine "EMS at the Crossroads" report all have broadcast calls to action to continue to improve the care of trauma patients in this country [1, 146, 147]. Continued interdisciplinary collaboration, whether at the side of a specific

patient, in after-action discussions, regional steering meetings or books such as this will remain foundational in advancing our care of these complex and challenging patients.

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Part II
Arrival at Facility

AIS Versus ISS Versus GCS—What's Going on Here?

6

Mayur Jayarao and Shelly D. Timmons

Introduction

Assessment of traumatic brain injury (TBI) severity is of critical importance to the subsequent appropriate clinical management of patients who suffer trauma. Over the years, numerous scales and scores have been developed in order to describe head injury severity in the acute setting and ultimately to predict patient outcomes. The most frequently used are the Glasgow Coma Scale (GCS) , and for polytrauma, the Abbreviated Injury Score (AIS), and Injury Severity Score (ISS). These assessments serve as major building blocks upon which trauma databases, clinical trials, and patient outcome studies have been designed.

When patients initially arrive at a treatment facility after sustaining a traumatic brain injury, their early assessment is focused on the identification of all systems of injury (taking mechanism of injury and field assessment and treatment into account), maintenance of airway and circulatory status, and identification and stabilizing treatment of immediately life-threatening followed by limb- and function-threatening injuries. Once this has been accomplished, secondary, tertiary, and quaternary assessments are done along with ongoing radiographic and laboratory testing to further refine the injury profile. During the course of these early assessments and stabilization procedures, the need for accurate neurological assessment has resulted in the evolution of scoring systems to allow emergency providers to rapidly determine the severity of brain injury. Intervention can then be employed to prevent or mitigate the cascade of secondary injury physiological processes that begin at the instant of impact. Furthermore, the need for easily recordable scores for the conduct of large-scale predictive modeling and research has contributed to the variety of trauma scores in common usage.

Glasgow Coma Scale (GCS)

The most widely used measure of head injury severity in the acute setting is the GCS (Table 6.1), a physiological measure of injury severity that was described by Teasdale and Jennett in 1974 [1]. There is a valid correlation between the post-resuscitation GCS and prognosis [2]. However, frequent use of sedatives and paralytics prior to arrival at the emergency room can make early GCS measures inaccurate and scores can rapidly improve after the effects of these agents abate. Additionally, the GCS can suffer from interobserver variability in certain settings and premorbid acute intoxication may render the

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Table 6.1 Glasgow coma scale. Adapted from: Teasdale, Jennett Lancet 1974

Eye opening (E)	Verbal response (V)	Motor response (M)
4—spontaneous	5—oriented	6—spontaneous
3—to verbal command	4—confused	5—localizes to pain
2—to pain	3—inappropriate words	4—withdraws to pain
1—none	2—incomprehensible sounds	3—flexor/decorticate to pain
	1—none	2—extensor/decerebrate to pain
		1—none
Total = E + V + M		

GCS unreliable [3–5]. Field medication impact was highlighted by Stocchetti et al. [6] who found a number of patients were mistakenly classified as severe due to the effects of sedatives and paralytics, as has been demonstrated in multiple other clinical trials. The motor component of the GCS (GCS-M) has also been shown to be equally as sensitive as the total GCS [7] in the acute setting. The fact is, though, that the GCS is a clinical exam-based assessment of brain function that infers some degree of anatomical localization, but it does not take into account the severity of injuries from a purely anatomical or radiographic basis nor does it consider operative findings.

Abbreviated Injury Score (AIS) and Injury Severity Score (ISS)

The AIS was described in 1971 after being developed jointly by the American Medical Association (AMA), the Association for the Advancement of Automotive Medicine (AAAM) and the Society of Automotive Engineers [8]. The development was consensus-driven and was initially devised to classify injuries sustained in motor vehicle crashes with the aim of improving vehicular safety, but has now expanded to include other mechanisms of injury. The score provides a simple numerical method that is anatomically based (head, face, neck, thorax, abdomen, spine, upper and lower extremities, and external). It has no physiological contribution. The head AIS ranks injuries from 0 to 6 (Table 6.2) using neuroradiologic and operative findings. In addition, it has been expanded to include intracranial injuries based upon location, number, and size. Hence the scoring is often performed after the fact, commonly at discharge from hospital.

The ISS [9] is a composite measure derived from the AIS score that rates the three most severely injured body regions out of six (head or neck, face, chest, abdomen or pelvis, extremities or pelvis, and external). ISS can range from 0 to 75 and is calculated by summing the squares of the highest three component values. A patient with an AIS score of 6 in any anatomic region is automatically assigned an ISS of 75. Major trauma or polytrauma is defined by a total ISS greater than 15 [10]. The ISS score correlates linearly with several markers and surrogates for severity, such as mortality, morbidity, and hospital stay.

Table 6.2 Abbreviated injury score (AIS). Adapted from JAMA 1971

AIS Code	Injury
1	Minor
2	Moderate
3	Serious
4	Severe
5	Critical
6	Maximum/not survivable

GCS, AIS, and ISS Combinatorial Predictive Value

There have been numerous attempts to combine anatomic (and thereby radiographic) scores (AIS, ISS, Marshall CT grading) with physiological or clinical data (GCS, Revised Trauma Score) to predict outcome after trauma. The New ISS, the Acute Physiology and Chronic Health Evaluation (APACHE), and the Trauma and Injury Severity Score (TrISS) have also been utilized for predicting trauma mortality. However, the use of these scores has been demonstrated to be limited due to frequent misclassification and false positives or negatives [11, 12]. On the other hand, studies have demonstrated that utilizing combined physiological data (GCS or GCS-M) and anatomic scores (AIS or ISS) can improve outcome predictions, although this has been inconsistent. Furthermore, the fact that the determination of AIS and ISS are determined over time, as radiographic and other injury progression information becomes available, makes their utility in the acute phases of resuscitation limited.

Assessment of the literature must take into account the durability of prognostic value as well as the accuracy. Furthermore, care must be taken in interpretation of predictive scores for groups in the early clinical stages of treatment for an individual patient. Scores predicting finite outcomes measures (such as mortality) are limited in their utility in the resuscitation phases of clinical decision-making, because in retrospective clinical studies, decisions to treat or not to treat are not random, and in randomized trials, intention to treat may impact the outcomes of select patient groups. Therefore, the self-fulfilling prophecy of early mortality in those with worse "predictive scores" will select out patients who, had they been treated aggressively and survived, may have had a broad spectrum of outcomes but who would likely have fared poorer.

That being said, some information is available in the literature regarding the combination of scoring systems. A recent study by the senior author [2] and colleagues was conducted to predict early (two-week) cumulative mortality analyzed data from 2,808 blunt TBI patients utilizing GCS, GCS-M and head AIS. TBI was categorized as severe (GCS 3–8), moderate (GCS 9–12) or complicated mild (GCS 13–15 with positive CT findings). GCS and GCS-M were found to be stronger predictors of 2-week mortality than head AIS alone with no benefit in combining GCS and head AIS. In addition, as seen in other studies, older age was associated with mortality: age ≥ 60 was an independent predictor of mortality after controlling for both GCS and head AIS.

In an effort to identify a surrogate for GCS when unattainable, Walder et al. [13] compared AIS and worst GCS with Glasgow Outcome Score (GOS) at 6 months in 109 severe TBI patients. They found that head AIS based on initial CT served as a useful prognostic indicator (for the grossly divisible five measures of functional outcome delineated by the GOS) in patients where the initial GCS scores were not accurately assessable. In a larger study, Demetriades et al. [5] analyzed 7,764 patients with head injuries using GCS and head AIS ≥ 1. While they found that head AIS, GCS, and age (over 55 years of age) were significant independent predictors of death, there was no good correlation between GCS and head AIS with respect to impact on overall mortality. Of note, in the system under study, the emergency responders were not allowed to administer sedative or paralytic agents in the field, so GCS assessment at admission would theoretically have been more frequently accurate.

In contrast, Foreman et al. [14] prospectively evaluated 410 patients with TBI utilizing GCS, AIS, and ISS for even longer-term outcomes assessments. Twelve month functional outcomes utilizing the Glasgow Outcome Scale-Extended (GOS-E) were reviewed. They concluded that GCS, AIS and ISS weakly correlated with 12-month outcomes, with anatomic measures outperforming GCS as predictors of GOS-E. Additionally, the combination of GCS and AIS/ISS correlated better than if either one was used alone.

Conclusions

There is evidence that GCS and AIS or ISS, either individually or in combination, are useful in predicting mortality and outcomes for TBI patients. Nonetheless, there are differences in data depending on the outcomes chosen, the timeframe under study, and likely other systematic influences, such as the routine use of sedatives and paralytics in the field. This highlights the difficulty of using limited data points in a complex injury in a complex organ with complex outcomes in a complex clinical setting. Extreme caution should be used in the resuscitative phase when making decisions of futility or aggressiveness based upon these scores and they should never be used in isolation for any given patient. Further studies incorporating additional clinical data points will be required for more accurate early prognostication after TBI, because much of the variance in outcome is not accounted for by parameters measured to compute these scores. As data capture and analyses improve with strides in computing and electronic medical record-keeping, more sophisticated models of prediction in TBI are emerging. While more sophisticated prediction models are a necessary and important part of advancing the field, they will not likely supplant the shorthand scoring methods that have been in use for decades now. Rather, a variety of data sets and means of communicating patient status and injury severity will be shown to compliment one another to better define TBI.

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Trauma Resuscitation and Fluid Considerations in the Polytrauma Patient with CNS Injury

7

George P. Liao and John B. Holcomb

Introduction

Polytrauma that includes the central nervous system, especially cases involving traumatic brain injury (TBI) presents a challenge to both surgical and neurocritical care teams due to potential competing interests during the resuscitative period. Trauma resuscitation involves the infusion of fluids to help decrease bleeding, reverse and prevent coagulopathy, support cardiovascular integrity in order to maintain organ, tissue, and cellular function. Recently these goals have been met while decreasing edema formation. In the brain, the blood brain barrier (BBB) normally maintains immunologic privilege as well as tight autoregulatory fluid control. However, following TBI, BBB dysfunction leads to vasogenic and cytotoxic edema, which contributes to intracranial hypertension [1]. TBI in return has been shown to have systemic implications in physiology such respiratory compromise as well as derangements in the hypothalamic pituitary adrenal axis such as acute glucocorticoid deficiency and diabetes insipidus [2]. This chapter will discuss current practices as well as preclinical and clinical studies aiming to answer the question about the optimal fluid resuscitation strategy.

In trauma patients without TBI, resuscitation goals include relatively low mean arterial, urine output and central venous pressure until definitive hemostasis is obtained, reversal of coagulopathy as well as the clearing of a base deficit. These "hypotensive" goals are utilized until definitive hemostasis is obtained, usually within 2–3 h of admission. In neurocritical care, adequate cerebral perfusion is paramount, with goal pressures of at least 60 mmHg, achieved by balancing intracranial pressure (ICP) and systemic mean arterial pressure of at least 90 mmHg. Especially early in the resuscitation of a polytrauma patient, it is obvious that these goals may seem contradictory. Intracranial pressure is reduced in a tiered fashion, with first tier treatments typically including sedation, establishing an ICP threshold, cerebral perfusion monitoring, neuromuscular blockade, cerebral spinal fluid (CSF) drainage, and hyperosmolar therapy [3]. Second tier treatments include hyperventilation, barbiturates for pharmacological coma with electroencephalogram monitoring for burst suppression, hypothermia, and surgical decompression. Mean arterial pressure is commonly supported by the use of vasoactive pressors norepinephrine and phenylephrine because they have the least effect on cerebral vasomotor tone, but overaggressive hypertension may increase the risk of acute respiratory distress syndrome [4]. Up to one-third of

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TBI patients have abnormal cerebral autoregulation. As the result of the loss of cerebral autoregulation, cerebral blood flow and capillary hydrostatic pressure increases, exacerbating edema and ICP. CSF circulation and clearance of metabolites is also impaired following TBI.

Fluid Balance

Only a handful of clinical studies have been designed to specifically address trauma resuscitation and fluid balance in cases that include traumatic brain injury, and none have found any association to benefits of fluid balance management and neurologic outcome [5]. Inferences have been made from other studies such as the North American Brain Injury Study: Hypothermia II (NABIS:H II) suggested that the higher incidence of intracranial hypertension was likely associated with resuscitation in the first 96 h aimed at countering hypotension encountered during the hypothermic protocol. Adjusting for injury severity, TBI patients were shown to have modestly increased odds of death after receiving resuscitative intravenous fluids in the prehospital setting. A retrospective cohort TBI study examined total fluid balance over the first 10 days of intensive care admission and the association with refractory intracranial hypertension despite first tiered therapies (defined as ICP >20 for 30 min or ICP >15 for 15 min in patients status post decompressive craniectomy). The study found that there was no difference between cumulative fluid in patients that did or did not develop refractory intracranial hypertension [6].

Crystalloids Versus Colloids

Crystalloids have long been first line therapy for resuscitating the trauma patient but the pattern of distribution of specific crystalloid products has implications on the degree of interstitial edema. Colloids such as albumin have the potential of raising intravascular oncotic pressure, thereby reducing interstitial edema to tissues such as the brain. However, studies such as the Saline versus Albumin Fluid Evaluation (SAFE) trial found that the clinical effect of colloids such as albumin have been much less than estimated [7]. Ad hoc subgroup analysis of the SAFE TBI trial found that the use of albumin was associated with increased treatment intensity in order to control ICP [8]. Reviewers of the SAFE trial have suggested that the albumin was either leaking into the brain interstitial tissue thereby exacerbating the edema or that the albumin solution was slightly hypoosmotic compared to normal saline [9]. In another study, albumin combined with neutral or a slightly negative fluid balance was associated with low mortality in severe TBI, but was associated with high rates respiratory failure [10]. To date, other colloids including synthetics have not produced convincing evidence to alter clinical practice.

Hyperosmolar Therapy

Hyperosmolar therapy includes mannitol, which is administered at 0.5–1 g/kg and produces effect within 15–30 min. This can be administered every 6 h to a target serum osmolaritiy of 310–320 Osm/L. In addition to lowering the intracranial pressure, mannitol also has been shown to improve cerebral blood flow (CBF) [11]. 23 % hypertonic saline can be used for hyperacute ICP elevations and for herniation syndromes and can reduce the ICP by up to 50 % within minutes and produce a durable response over hours [12].

Osmotic agents, including mannitol and hypertonic saline have been shown to be well tolerated and effective in the reduction of intracranial hypertension, but to date, no study has shown improved survival nor improved neurological outcomes. While both mannitol and hypertonic saline are both considered first tiered therapies, the dosing and administration practices vary between and within institutions and thus the power of systematic reviews are limited [13]. The Saline versus Albumin Fluid Evaluation Translation of Research Into Practice Study (SAFE TRIPS) trial was a global cross-sectional study that looked at 391 intensive care units and found

that the choice of resuscitative fluid varied considerably and was associated more with local practice then the clinical scenario [14].

In the case of the trauma patient with polytrauma, hypertonic saline has found applications in reducing bowel edema in damage control surgery. In a retrospective study, the use of 3 % sodium chloride at 30 mL/h as maintenance fluid compared to isotonic fluids at 125 mL/h in damage control laparotomies was associated with 100 % primary fascial closure by day 7 compared to 76 % with isotonic fluids ($p = 0.010$). Retrospective studies have suggested that mannitol and hypertonic saline boluses (23.4 %) are equivalent in reducing ICP [15]. It is evident however, that in practice, the use of mannitol has become more limited to situations where quick reductions in ICP is required as the potential for diuresis complications are more prevalent than with hypertonic saline [16]. Rapid diuresis in the hypovolemic polytrauma patient can be especially deleterious, causing precipitous drops in blood pressure. Thus in theory, hypertonic saline can be considered one of the optimal fluids to be administered in a scenario of a patient with TBI undergoing damage control laparotomy. Although hypertonic saline is a common agent used for intracranial hypertension, patients experience worsening of their hypocoagulability and hyper-fibrinolysis, which may complicate the initial resuscitation of patients with polytrauma [17–19]. In a randomized control study evaluating single 250 mL bolus administration of 7.5 % saline, 7.5 % saline/6 % dextran, or normal saline in the prehospital setting for severe TBI patients not in hypovolemic shock, no differences were seen in 6 month Extended Glasgow Outcome Scale scores or disability rating scores. A follow-up study examining the same prehospital strategy of treating severe TBI patients with hypovolemic shock also did not show any differences in 28 day survival (although the study was stopped early due to increased early mortality in a subset of hypertonic saline and hypertonic saline/dextran groups that did not receive packed red blood cells in the first 24 h).

Other Crystalloids

Investigators have also explored the use of lactate containing solutions and sodium bicarbonate in small clinical studies. Lactate is a preferred energy substrate in TBI, increasing cerebral blood flow and in a small study, reduced intracranial hypertension to a similar degree as equimolar mannitol [20]. Half molar sodium lactate was applied in a randomized double blinded study versus normal saline and was found to significantly reduce the number of elevated ICP episodes as well as total fluid and chloride balance over the first 48 h post TBI [21]. Equiosmolar 8.4 % sodium bicarbonate was investigated in a small, randomized trial versus 5 % hypertonic sodium chloride and was found to have equal reductions in ICP [22]. The use of sodium bicarbonate may reduce the incidence of hyperchloremic metabolic acidosis commonly seen with repeated doses of hypertonic sodium chloride and may provide an advantage in critically ill trauma patients where acidosis already exists [23].

Blood Products

Blood products are increasingly becoming a standard addition to the trauma resuscitation algorithm starting in certain cases in the prehospital setting [24]. Optimal resuscitation using blood products has been shown through the Prospective Observational Multicenter Major Trauma Transfusion (PROMMITT) and Pragmatic Randomized Optimal Platelet and Plasma Ratios (PROPPR) studies to be best performed using balanced red cells, fresh frozen plasma (FFP) and platelets. Many leading trauma centers now use plasma as the primary resuscitation fluid in hypovolemic trauma patients. These centers are also placing this approach into the prehospital environment [25]. Of interest in TBI is the potential therapeutic benefit of FFP due to the known endotheliopathy that occurs in trauma. One TBI population that may particularly benefit

from FFP is the pediatric population, which is prone to developing coagulopathy following injury than adults and also demonstrate acute phase dysregulation of fluid and electrolyte balance [26].

Plasma repairs the systemic endothelial injury and dysfunction that leads to coagulation disturbances and inflammation [27]. This protective property has been shown in the pulmonary endothelium as well as in studies on platelet function, and thus may play an important role in treating the endothelial dysfunction that occurs following TBI at the level of the blood brain barrier [28]. Compared to normal saline, FFP has been shown to cause less activation of coagulation, natural anticoagulation, and endothelial systems in porcine polytrauma models of TBI [29].

Initial porcine studies by the Alam group comparing FPP, 6 % hetastarch and normal saline in a combined controlled TBI and hemorrhage model (mimicking the polytrauma patient) demonstrated superiority of FFP over 6 % hetastarch and normal saline in reducing lesion size and edema. The volume of normal saline required to resuscitate the animals was three times that of FFP [30]. Further studies demonstrated decreased excitotoxicty through decreased levels of glutamate and glycerol as well as improved energetics with higher levels of mitochondrial pyruvate dehydrogenase complex activity with FFP resuscitation compared to normal saline [31]. More recently, the investigators were also able to demonstrate improved levels of brain oxygenation, cerebral perfusion pressure and endothelial nitric oxide synthase [32].

The roles of blood products such as FFP and component factors become critical with the increased incidence of trauma patients arriving on anticoagulation including warfarin, clopidogrel and others. The reversal of anticoagulation is often part of the initial resuscitation process and may be even more essential to survival in TBI patients than non-TBI trauma patients [33]. Investigators have suggested that the use of recombinant factor VIIa can reduce the amount of FFP required and may help reduce length of stay and intensive care required in the coagulopathic TBI patient [34]. In the most challenging cases where direct thrombin inhibitors such as Dabigatran, Etexilate are not easily reversed, monitoring with thrombelastography and treatments such as activated prothrombin complex concentrates, recombinant factor VIIa and other factors may need to be employed, along with possible emergency dialysis [35, 36].

Other Considerations

In the effort to move resuscitation to the prehospital setting, investigators have studied the potential of "on demand" versions of plasma and red cells. Lyophilized plasma product was found to be just as effective as FFP preclinical swine models of combined TBI and hemorrhagic shock [37]. The hemoglobin based oxygen carrier HBOC-201 was found to improve cerebral perfusion pressure and brain tissue oxygen versus lactated ringers [38, 39]. While some high volume centers in the US have placed liquid plasma and RBCs on their helicopters, the dried plasma products will facilitate wide spread adoption. Although increasing oxygenation should theoretically protect the injured brain, a recent randomized trial found that neither the administration of erythropoietin nor establishing a transfusion threshold of 10 g/dL resulted in any improvements in a dichotomized Glasgow Outcome Scale at 6 months post TBI [40]. Additionally, the incidence of venous thromboembolisms increased in the treated groups. In the design of such studies, the choice of the outcome measure may need to be tailored to the proposed mechanism of the treatment in order to find clinically significant and relevant associations.

Neurocritical Care Targets of Resuscitation

The monitoring and treatment of ICP is a major target in the treatment of TBI. However, controversy exists in the impact of ICP directed therapy on outcomes. The multicentered, randomized Benchmark Evidence from South

American Trials: Treatment of Intracranial Pressures (BEST TRIP) study reported no difference in functional/cognitive outcome, mortality, median ICU stay, and serious adverse events between maintaining ICP at or below 20 mmHg to imaging and clinical examination alone [41, 42]. Critics of the trial argue that the study varied from established guidelines and did not specifically look into ICP monitor use for the management of intracranial hypertension, thereby limiting external validity and generalizability. The average ICP during the acute neurointensive period has been used as an early target for therapy in hopes that this indicator could correlate with long-term outcome. However, studies have reported that average ICP during the first 48 h do not correlate with 6-month functional nor neuropsychological outcomes [43]. Some suggest that, these studies generally do not reflect continuous monitoring trends, number of spikes and waveforms, and are thus likely limited by design. Despite these findings, recent evidence looking specifically at large databases and studies following the Brain Trauma Foundation (BTF) guidelines suggest that ICP monitoring contributed to improved outcomes [44–47].

The debate regarding ICP monitoring and outcome has led investigators to seek additional, multimodal approaches to guide resuscitation for the injured brain and include brain oxygen monitoring and microdialysis. Poor short-term outcome is associated with hypoxia measured by $pBrO_2$ (partial pressure of oxygen in brain tissue) independent of elevated ICP, low CPP, and injury severity [48]. Studies have suggested that $pBrO_2$ directed therapy can lead to improved Glasgow Outcome Scores (GOS) at 6 months versus standard ICP directed management [49]. The multicentered Phase II Brain Tissue Oxygen Monitoring in Traumatic Brian Injury (BOOST 2) trial, will further evaluate whether $pBrO_2$ levels below the critical threshold of 20 mmHg can be reduced with monitoring, in addition to the evaluation of safety, feasibility and GOS extended scores 6 months post injury. Despite the potential benefits of an additional metabolic indicator of resuscitation, judicial use of monitoring equipment may be necessary as using $pBrO_2$ monitors have also been shown in a study to be associated with higher cumulative fluid balance, vasopressor use, pulmonary edema and refractory intracranial hypertension [6].

Microdialysis has the ability to provide information regarding the metabolic status of penumbral brain tissue, and includes real-time glucose, lactate, glycerol, and glutamate measurements although robust randomized clinical trials have not yet been pursued. Studies have suggested that metabolic derangements can be detected by microdialysis prior to increases in ICP [50]. Investigators have also demonstrated that metabolic crisis, defined by brain glucose <0.8 mmol/L and lactate/pyruvate ratio > 25 can occur at an incidence of 74 % despite adequate resuscitation and controlled ICP [51].

While the use of $pBrO_2$ monitoring and microdialysis has not been widely adopted in clinical use, these two devices provide investigators valuable tools beyond simple ICP measurements when evaluating emerging therapeutics. Combined microdialysis and positron emission tomography in patients following severe TBI demonstrated that metabolic crisis can even be present without cerebral ischemia as measured by oxygen extraction fraction and cerebral venous oxygen content [52].

Future Directions

The solution to effective resuscitation for the polytrauma patient with TBI will likely be in the form of a multimodal approach that will include FFP, hyperosmolar agents, as well as other emerging fluid options such as lactate and hypertonic bicarbonate solutions and other therapeutic adjuncts. Optimizing resuscitation by decreasing blood loss and edema seems to be a reasonable approach. Clinical strategies have even included case reports where continuous renal replacement therapy was shown to normalize intracranial hypertension in TBI patients within 48 h of initiation through a hypothesized mechanism of gentle removal of fluid, solutes and

inflammatory cytokines [53]. Preclinical studies have suggested that valproic acid can improve energetics, reduce lesion size, and edema [54]. Cell therapy with bone marrow derived mesenchymal stromal cells has been shown to inhibit inflammation and preserve vascular endothelial integrity in lungs after hemorrhagic shock and preserve vascular endothelial barrier proteins [55]. Clinical trials are underway in both pediatric and adult populations using autologous bone marrow derived mononuclear cells intravenously delivered within 48 h of injury [56, 57].

Controversy still exists in the extent of which ICP directed management impacts short and long-term outcomes, thus other strategies, new targets are necessary. Clinical trials should be designed to test therapies against clinically relevant outcome measures such as neurointensive length of stay, short and long-term neurocongitive outcomes and neuroimaging, in addition to standard long-term function. Neurophysiological outcomes, such as BBB dysfunction can be assessed by CSF-plasma albumin quotient and may be the key to validating and translating preclinical studies to the intensive care unit [58]. Even the amount of resuscitative fluid and adequacy on a per patient basis can be optimized. For example, limited transthoracic echocardiogram has been shown to be effective in guiding fluid resuscitation [59]. Also, plasma levels of longitudinal midregional pro-atrial naturetic peptide has been studied as a prognostic tool of GOS outcome at 6-months post injury [60].

Polytrauma that includes central nervous system injury and hemorrhagic shock presents a complicated challenge for trauma and neurocritical care teams during the resuscitative period. The choice of fluid administrated during the resuscitative period has direct impact to the central nervous system. The adequacy of resuscitation in regards to TBI must look beyond ICP and CPP management adherence to include clinically relevant indicators of outcome. To date, small studies and post hoc analysis have not yielded convincing support towards any single clinical management strategy. Although plasma and other fluids have emerged as effective agents in preclinical studies, robust clinical trials or retrospective studies using trauma registries must be designed to correlate preclinical physiologic as well as functional improvements to clinically measureable outcomes.

Today, trauma and neurocritical care teams must approach the TBI patient with coexisting hemorrhagic shock with a tailored approach, using multiple systemic and neuromonitoring modalities while applying judicious selection of resuscitative fluids. Balanced blood products should be given for hemorrhagic shock and early ICP monitoring established with frequent neurologic checks. The delay to ICP monitoring or neurosurgical intervention should be reduced. Retrospective studies suggest that hemorrhagic complications infrequently occur when international normalized ratio (INR) levels of 1.6 or less [61]. The increased usage of thrombelastography to assess the functional clotting status may reduce the delay that moderately elevated INR values causes to neurosurgical interventions [62]. Early stabilization of both systemic and cerebral endothelia with FFP may influence the course of resuscitation. The choice of additional resuscitative fluids may depend on the clinical scenario. FFP can be given when patients present with multiple derangements such as hypovolemia, coagulopathy, and possibly cerebral edema due to endothelial dysfunction of the BBB. Hyperosmolar agents can be used for episodes of intracranial hypertension, but can be beneficial when applied to counter systemic as well as cerebral edema in TBI patients undergoing damage control laparotomies. Other fluid options such as lactate and hypertonic bicarbonate solutions should be considered as additional therapies for neuroprotection if clinically indicated. These resuscitative efforts should ideally be directed using prospectively designed service guidelines and thoroughly captured for analysis.

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Initial Imaging Considerations, Repeat Imaging Frequency

8

Krzysztof M. Bochenek

Overview of Trauma Imaging

Trauma is the major cause of death in individuals younger than 45 years and a leading cause of morbidity and disability. Trauma victims are frequently brought in with multiple undiagnosed injuries and need urgent evaluation and lifesaving interventions. Traditionally, radiological assessment consisted of plain radiography of the chest, pelvis and focused ultrasound of the abdomen, followed by targeted evaluation with a CT. Additional radiographs of the spine and extremities could be obtained as needed. While many patients with lesser injuries are still evaluated this way, whole body CT (WBCT) has become the study of choice for more severely injured patients in many centers.

A representative protocol consists of a helical scan through the head and the cervical spine with the arms positioned along the sides of the body performed without intravenous contrast. This is followed by a contrast enhanced scan of the chest, abdomen and pelvis performed in a venous phase with arms above the head. For patients suffering from severe polytrauma, CT angiography is frequently incorporated into the initial WBCT scan. This modified protocol consists of an unenhanced head CT, CT angiogram (CTA) of the neck, chest, abdomen, and in some cases the pelvis. Venous phase images of the abdomen and pelvis can alternatively be obtained. Images of the cervical, thoracic and lumbar spine are reconstructed from the CTA and or CT datasets.

It is accepted that WBCT saves time compared to traditional radiological evaluation. It allows for earlier treatment, fewer missed injuries, and was shown to result in decreased mortality [1]. Utilization of WBCT may lead to fewer overall scans and shorter hospital stays [2].

Imaging of the Brain

Indications for Imaging

Most polytrauma victims suffer from moderate or severe head injury and require head imaging. There is, however, a subset of patients with mild traumatic brain injury for whom imaging may not be indicated, allowing for minimizing radiation exposure and resource use. The exact definition of mild traumatic brain injury varies in literature, but is frequently described as an injury to the head and brain resulting in a brief alteration of mental status such as confusion, disorientation, brief loss of consciousness or amnesia. A Glasgow Coma Score (GCS) of either 14–15 or 13–15 is commonly used to define mild traumatic brain injury [3].

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Table 8.1 New Orleans criteria and the Canadian head CT rule

New Orleans criteria	The Canadian head CT rule
Age > 60	**High risk for neurosurgical intervention:**
Vomiting	Age > 65
Headache	Two or more episodes of vomiting
Drug or alcohol intoxication	GCS < 15 at 2 h after injury
	Suspected open or depressed skull fracture
Persistent anterograde amnesia	Any sign of basal skull fracture
	Medium risk for brain injury detection by CT:
Visible trauma above the clavicle	Retrograde amnesia > 30 min
Seizure	Dangerous mechanism (pedestrian struck by a motor vehicle, occupant ejected from a motor vehicle, fall from a height of at least 3 ft or 5 stairs)

Based on reference (8)

Two major predictive rule sets were devloped to determine which patients with mild traumatic brain injury need imaging (Table 8.1). In the New Orleans's Criteria headache, vomiting, age older than 60 years, persistent anterograde amnesia, drug or alcohol intoxication, visible trauma above the clavicle, and posttraumatic seizures were found to be independent predictors of abnormalities on a head CT [4]. Head imaging is only needed for patients with any of these 7 risk factors. The Canadian CT Head Rule consists of 5 high risk and 2 moderate risk factors [5]. Head CT is needed if the patient meets at least one of the following criteria: GCS < 15 two hours after trauma, open or depressed skull fracture, sign of a skull base fracture, age > 65, retrograde amnesia of more than 30 min, more than 1 episode of vomiting, dangerous mechanism (pedestrian struck by motor vehicle, occupant ejected from motor vehicle, or a fall from a height of at least 3 ft or five stairs). Both sets of criteria have been validated in multiple studies [6] and offer near 100 % sensitivities for detection of a clinically significant injury. In general the Canadian CT Head Rule seems more specific with pooled specificity of 39–51 % [7] and has a better potential for cost saving [8].

Imaging Findings

CT is the modality of choice for rapid evaluation of the head. It allows for easy identification of both extraaxial (epidural, subdural, subarachnoid, intraventricular) and intraaxial (surface contusion, intraparenchymal hematoma, shear injury) hemorrhages. An intracranial hemorrhage is seen as an increased density on the CT thanks to its highly proteinaceous nature. There is a linear relationship between the attenuation observed on the CT and hematocrit concentration. The density of the whole blood (hematocrit of 45 %) is about 56 HU. The attenuation of normal gray matter is about 37–41 HU, whereas the density of the white matter is about 30–34 HU [9]. These properties make blood usually easily identifiable on a CT. CT, however, has its limitations. In patients who are severely anemic blood may not be sufficiently dense to be detected. Small hemorrhages near bone are subject to volume averaging artifact. This is particularly common along the floor of the anterior and middle cranial fossae as well as near the convexities. In such cases reformatted coronal, and if needed, sagittal images are very helpful. Blood may be obscured by beam hardening artifact related to dense bones, radiopaque foreign bodies, or support structures outside of the patient. Acute blood gradually decreases in density becoming isodense in subacute stage (8 days–1 month) and hypodense in chronic stages (over 1 month) [9]. Small amounts of subarachnoid hemorrhage may become diluted and inapparent after 1 or 2 days.

An epidural hematoma usually occurs at the coup site. It can result from an injury to a meningeal artery or vein, diploic vein, or a dural venous sinus. It is usually associated with a fracture of the adjacent skull. It is classically lentiform in shape located between the dura and the skull. Epidural hematomas do not cross the suture lines as the periosteal layer of the dura

adheres closely to the suture. They, however, can cross midline (underneath the falx cerebri) or between the supratentorial and infratentorial compartments (behind the tentorium cerebelli) as the periosteal layer of the dura forms the outer wall of the adjacent major dural venous sinus which is displaced by the hematoma from the inner table of the skull. Epidural hematomas are usually uniformly dense, however, can contain heterogeneous areas of lower density in cases of rapid bleeding or coagulopathy.

A subdural hematoma occurs at the contrecoup and slightly less commonly the coup site. It represents blood accumulation between the meningeal layer of the dura and the arachnoid. It is caused by injury to the superficial bridging veins. It is crescentic in shape, can cross the suture lines, however, unlike the epidural hematoma, does not cross underneath the falx cerebri or the tentorium cerebelli. The subdural hematomas are usually homogenously dense, and when small, may occasionally be difficult to separate from the adjacent bone. Evaluation with subdural CT window is usually helpful. They may be lesser or mixed density in cases of rapid bleeding, particularly in coagulopathic patients, in patients who are anemic or in cases of acute on chronic subdural hematomas. A rare, but potentially confusing mixed density subdural hematoma can be seen in cases of an arachnoid tear resulting in cerebrospinal fluid mixing with subdural blood or in cases of a subdural hematoma extending into an arachnoid cyst.

Subarachnoid hemorrhage can result from tears of small arteries and veins along the surface of the brain in the subarachnoid space, blood extension from a cortical contusion, or blood extension from the ventricular system through the foramina of Luschka and Magendie. On a CT, an acute subarachnoid hemorrhage has an appearance of linear densities in the sulci and basilar cisterns. It is frequently located near the convexities or near the areas of parenchymal contusions. Redistributed subarachnoid hemorrhage can often be found in the interpeduncular cistern.

Cerebral contusions occur on either the coup or the contrecoup side and result from brain striking the irregular inner surface of the skull during acceleration-deceleration injuries. They are commonly seen in the low anterior frontal and anterior and lateral temporal regions. They can be hemorrhagic or non hemorrhagic. When non hemorrhagic, they appear as areas of low density. Hemorrhagic components result in foci of density within a larger area of hypodensity. In areas of a more severe injury, small hemorrhages may coalesce to form a larger intraparenchymal hematoma. Most contusions increase in size during the initial 12–24 h and it is typical for them to become more hemorrhagic. In one study just 84 % of traumatic intracranial hematomas reached maximal size by 12 h [10].

Diffuse axonal injury, also called shear injury, represents strain of the axonal cytoskeleton due to acceleration/deceleration and rotational injuries. Disruption of axons occurs not only during the actual trauma, but also during the subsequent days, weeks and even years due to a cascade of biochemical events and Wallerian degeneration [11]. Typically milder injuries involve the parasagittal white matter near the grey-white junction, particularly in the frontal lobes. More severe injury also involves the corpus callosum. Severe injuries, particularly related to rotational forces, also affect the brainstem, mainly the dorsolateral midbrain. Shear injury is thought to be responsible for most of the global cognitive impairment seen in severe head trauma patients.

On a head CT scan diffuse axonal injury is seen as punctate hemorrhages at the lobar gray-white junction, in the corpus callosum and brainstem (Fig. 8.1a). CT, however, is not sensitive as the injury is to a large degree microscopic [12] and only up to 20 % of lesions are hemorrhagic.

Secondary effects of trauma develop as a result of several factors, chiefly cerebrovascular flow dysregulation, excitotoxicity, oxidative stress related to free radical formation, energy failure and inflammation. Several of these factors result in brain swelling which is thought to be directly caused by both hyperemia and cerebral edema [13]. Studies demonstrating decreased blood volume following trauma suggest the cerebral edema may the major component of brain swelling. It is thought that the edema is initially mainly vasogenic with cytotoxic edema becoming more

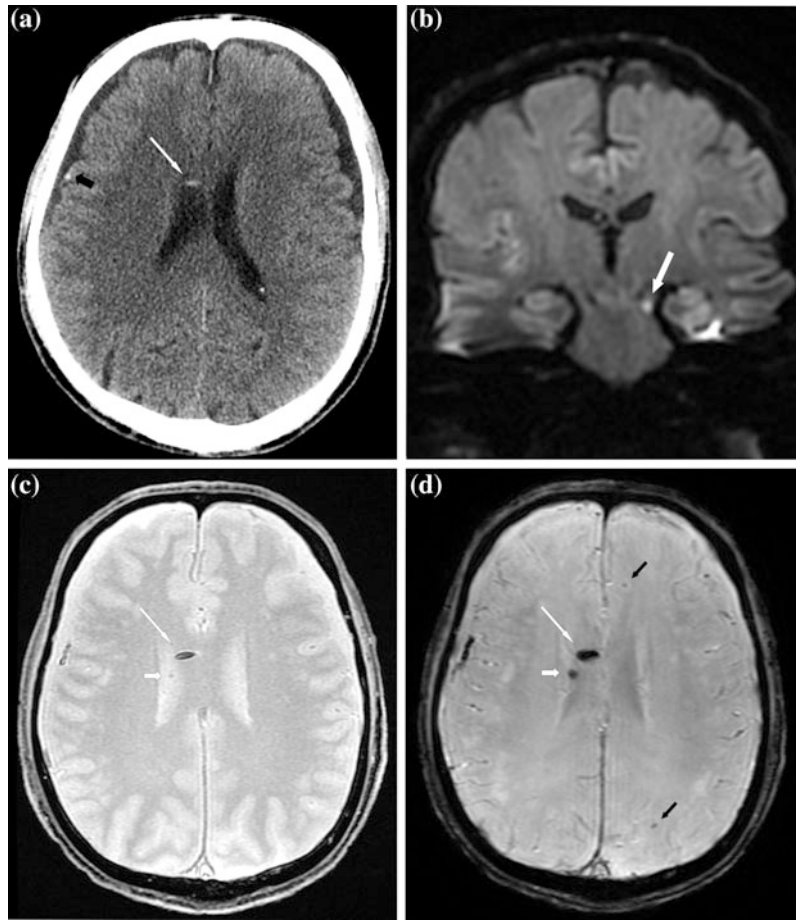

Fig. 8.1 DAI in a 63-year-old trauma victim. **a** Head CT shows small linear hemorrhage in the corpus callosum consistent with hemorrhagic focus of shear injury (*long white arrow*). Small amount of subarachnoid hemorrhage is seen along the surface of the brain on the *right* (*short black arrow*). **b** Diffusion weighted sequence shows additional focus of nonhemorrhagic injury (*white arrow*) involving the brainstem. **c** T2*-weighted gradient echo image confirms findings seen on the CT and reveals an additional small focus of hemorrhagic shear injury (*short white arrow*). **d** Foci of hemorrhagic DAI are more apparent on the susceptibility weighted sequence (*white arrows*). Several foci visible on that sequence (*black arrows*) are not visible on the T2*-weighted gradient echo images (**c**)

prominent over the subsequent hours and days [14]. On CT, cerebral swelling related to hyperemia is seen as effacement of the sulci, the basilar cisterns, and the ventricular margins. Areas of vasogenic edema are low attenuation, while cytotoxic edema results in loss of grey white differentiation. Severe brain swelling leads to increased intracranial pressure and decreased cerebral perfusion pressure which can result in an infarction. Children and young adults are particularly susceptible to post traumatic cerebrovascular flow dysregulation with incidence of brain swelling being nearly twofold higher in children than adults [15].

Brain swelling can lead to brain herniation. A subfalcine herniation occurs when the cingulate gyrus herniates under the falx cerebri. An uncal herniation represents herniation of the medial temporal lobe through the tentorial incisura. A compression of the oculomotor nerve by the displaced temporal lobe can present as “blown pupil”. A direct central transtentorial herniation results from diencephalon and midbrain being forced through the tentorial incisura. Mass effect

in the posterior cranial fossa can result in upward transtentorial herniation in which the cerebellar tissue herniates through the tentorial incisura, or in cerebellar tonsillar herniation which occurs when the cerebellar tonsils extend down through the foramen magnum.

Decreased cerebral perfusion pressure can lead to cerebral ischemia. Additionally, ischemia can also be caused by vasospasm, vascular injury in the neck, and mechanical compression of blood vessels related to brain herniation. Infarction in the anterior cerebral artery territory is typical following subfalcine herniation, while infarction in the posterior cerebral artery territory is frequently seen as a result of an uncal herniation. CT usually demonstrates hypodensity in the territory of the affected vessel.

CT is the imaging modality of choice for detection of cranial fractures. They are usually readily identified as linear lucencies extending through the calvarium. Non-displaced fractures which are oriented in an axial plane may be difficult to detect without reformatted multiplanar images or 3D rendering. Fractures extending to the paranasal sinuses, the mastoid air cells, or the middle ear cavity may allow air to enter the intracranial compartment. Pneumocephalus usually resolves over time, but persistent pneumocephalus raises possibility of a CSF leak.

Role of MRI

A typical MRI scan of the brain in a trauma patient includes T1-weighted, T2-weighted, fluid attenuated inversion recovery (FLAIR), diffusion weighted (DWI) and gradient echo T2*-weighted or susceptibility weighted (SWI) sequences. Although contusions frequently demonstrate enhancement, contrast is usually not needed, as it does not increase the conspicuity of lesions related to an acute brain injury. MRI is more sensitive than CT for detecting extra-axial hematomas, both hemorrhagic and nonhemorrhagic contusions, and foci of diffuse axonal injury.

Epidural and subdural hematomas have a variable appearance on MRI depending on the age of the hemorrhage and the amount of protein. In addition, arachnoid tears, areas of rapid bleeding, and presence of an underlying chronic extraaxial hematoma contribute to a heterogeneous appearance of subdural and epidural hematomas. For that reason MRI may not be reliable in determining the age of an extraaxial hematoma. They are, however, readily identifiable on MRI due to intrinsic high soft tissue resolution and multiplanar capabilities of MRI. In a study where 62 consecutive patients with moderate or severe head injury were imaged in an acute phase with CT and MRI, MRI revealed SDHs in 37.1 % of cases while CT in only 6.5 % [16].

MRI is also more sensitive than CT for detection of an acute SAH and intraventricular hemorrhages. FLAIR and SWI sequences are particularly useful with SAH usually seen as linear increased signal intensity on a FLAIR sequence and linear decreased signal intensity on a gradient echo T2* weighted or SWI sequence. The sensitivities of both sequences for detection of SAH vary in literature, but both have been reported to be more sensitive than CT [17, 18] with modern FLAIR sequence performing better than the GRE T2* weighted sequence.

MRI is very sensitive for detection of contusions. They appear as areas of parenchymal T2 prolongation and frequently demonstrate increased signal intensity on the diffusion weighted images. The hemorrhagic component is seen as foci of low signal intensity on the gradient echo and susceptibility weighted sequences.

MRI is significantly better than CT in demonstrating shear injury lesions. The nonhemorrhagic lesions are best seen as small foci of increased signal intensity at the lobar gray-white junction, in the corpus callosum and brainstem on the FLAIR and DWI sequences (Fig. 8.1b). In a study comparing FLAIR, T2-weighted, DWI and T2* weighted gradient echo sequences [19] DWI sequence detected the most lesions showing particular robustness for nonhemorrhagic lesions. Most DWI positive lesions (65 %) showed restricted diffusion. In that study DWI was, however, less sensitive for the detection of hemorrhagic lesions than the T2* sequence. Small bleeds are well delineated on the gradient echo and susceptibility weighted sequences (Fig. 8.1c, d).

They are particularly well seen on the newer 3 T scanners which can reveal nearly twice as many lesions as the 1.5 T scanners [20] (Fig. 8.1d). DWI is very useful in detecting the secondary effects of trauma such as an acute infarction.

MRI has clear limitations in an acute trauma setting. It is not always readily available and may not be compatible with support apparatus and metallic foreign bodies. The patients are at risk of airway dislodgment during transport and are at risk for hemodynamic instability during long scan times. The images are frequently degraded by motion. Despite its sensitivity for detection of additional injuries, acute MRI rarely offers additional information that would alter the medical or surgical management. In a study by Manolakaki in which MRI was performed within 48 h of admission [21], one third of MRI studies detected additional findings or described the lesions better than the initial CT. The findings, however, were not clinically significant and did not lead to a change in management.

MRI may, however, play a role in patients in whom minimizing ionizing radiation is desired, for example pregnant or pediatric patients. It can also help in evaluation of patients who have a normal brain CT but demonstrate persistent abnormal neurological findings on the examination.

Follow Up Imaging

Widespread availability of CT has led to its increased utilization in a follow up of trauma patients. The compelling argument for a repeat brain CT for stable patients with brain injury is based on the premise that it could allow for identifications of patients who would benefit from early medical or surgical intervention to minimize secondary brain injury. The counter-argument is an increased cost, risks related to transferring the patients within the hospital, and exposure to a potentially unnecessary radiation. The challenge is to utilize a repeat head CT enough to detect progressive injury before symptoms develop, yet without overutilization in patients at low risk of progressive injury.

Multiple studies attempted to define a subset of patients for whom a scheduled repeat head CT would be beneficial. In patients with mild head injury (GCS 13–15) and no neurological deterioration, routine follow up head CT is not indicated [22]. Wang et al. in a systematic review of literature [23] found that in 30 studies they reviewed, progression of injury was shown on a follow up CT in 36 % of trauma patients. A neurosurgical intervention following a repeat head CT occurred in 11 % of patients with 6 % of patients undergoing an surgical intervention based on the results of a head CT. They found that 32 % of patients with progression on CT underwent a change in medical management compared with 4 % without progression on a head CT. The review was hampered by differences in studied populations, inconsistencies in definitions of progression of CT findings and the neurosurgical intervention. They found that coagulopathy and overall injury severity were the most commonly reported risk factors for progression of injury on a CT and were also associated with the need for a neurosurgical intervention.

Subsequent studies further characterized subgroups that benefit from follow up imaging. Park et al. investigated the need for a repeat brain CT in patients with traumatic intracranial hemorrhage [24]. He found that patients with progression of lesions on a CT had lower initial GCS score (mean 14.6 in stable group vs. mean 11.9 in group demonstrating progression) and were more likely to be males. Among various types of intracranial hemorrhages, patients with epidural hematomas, intraventricular hematomas, and multiple lesions were more likely to have progression on the follow up CT (59, 80, and 77 % respectively). In that study no patients with stable scans required neurosurgical intervention and 47 % of patients with worsening scans required intervention. More importantly, of the patients who showed radiological worsening on the repeat head CT, 37 % underwent neurosurgical intervention despite lack of significant neurological deterioration. In a separate study Carlos et al. concluded that routine follow up head CT is indicated in patients with GCS ≤ 8 [25] as results may lead to intervention before neurological deterioration. In addition to low GCS, coagulopathy, male

sex, epidural hematoma, multiple intracranial lesions, other risk factors for progression of findings include hypotension and elevated intracranial pressure [26].

Repeat head CT is also indicated in patients who are deeply sedated limiting physical examination. Wurmb et al. found worsening of intracranial pathology on a follow up CT in 54 % of deeply sedated polytrauma patients on mechanical ventilation [27]. In 54 % of these patient the therapy was changed due to results on a follow up CT.

The optimal timing of a follow up head CT varies with the type and extent of injury. Sullivan et al. found that enlargement of epidural hematomas occurred early, detected on average within 8 h of injury and within 5 h of initial diagnosis [28]. Other traumatic intracranial hematomas, however, evolve slower. Yamaki found that just 84 % of traumatic intracranial hematomas reached maximal size by 12 h [10]. In a pediatric population deterioration tends to be caused by cerebral edema which mostly develops over the 48 h after head injury. Timing of the follow up head CT thus needs to be individualized.

A routine head CT in critically ill patients are not without risks with complications occurring in 17 % of patients in one study [29]. The most common complications are hemodynamic instability and dislodgement of the airway. Ionizing radiation related to scans in childhood has been linked to future cognitive effects in adults as well as increased incidence of leukemia and brain tumors [30].

While CT is useful for diagnosis and prognostication of outcome in patients with hemorrhagic injuries, there is a subset of patients with normal or near normal head CTs who fare poorly exhibiting profound cognitive impairment frequently remaining comatose long time after the initial injury. These patients usually demonstrate findings of shear injury on MRI. Areas of shear injury are well visualized on T2*-weighted gradient echo images which are sensitive to local field inhogeneity related to presence of blood products. SWI is a newer variant on a gradient echo sequence in which both the magnitude component of the T2* data and the phase of the MR signal are utilized to increase sensitivity for detection of microhemorrhages. It is able to detect four to sixfold more hemorrhagic shear injury lesions than the standard gradient echo sequence [31]. In addition, the phase images of the SWI can differentiate between diamagnetic and paramagnetic susceptibility effects of calcium and blood, respectively [32].

Since shear injury occurs to a large degree at a microscopic level, it is not fully depicted with conventional MRI techniques. The integrity of the white matter can be better evaluated with diffusion tensor imaging (DTI). This MRI technique characterizes directionality of water diffusion by assessing diffusion in at least 6, frequently 25–30 directions. Within a coherently organized white matter, water diffuses preferentially along the direction of white matter fibers, which is known as diffusion anisotropy and is quantified by a DTI measure called fractional anisotropy (FA). In patients with head trauma the microstructural integrity of the white matter tracts is impaired with resulting decreased FA values [33]. Abnormalities of FA are commonly analyzed by two different methods. In a voxelwise statistical analysis the DTI scan is spatially warped in a way that its white matter tracts coincide with those of a 3D white matter atlas or "mean FA skeleton". Multiple voxels are analyzed without a priori assumptions. In the region of interest method, specific white matter tracts are a priori designated and DTI derived values such as FA can be calculated in these areas. DTI studies have shown that in patients with brain trauma, injury commonly occurs in frontal association pathways, in particular the anterior corona radiata, uncinate fasciculus, the genu of the corpus callosum, and the inferior longitudinal fasciculus [34]. The extent of microstructural damage as evaluated by DTI in the above mentioned regions which may frequently appear normal on conventional MR imaging correlates with impaired cognitive function [34]. Both methods, however, are best at demonstrating group differences between patients with traumatic head injury and controls and are not practical at this point for evaluation of individual patients.

Functional MRI (fMRI) allows for detection of areas of increased neuronal activity. It is based

on blood oxygen level dependent (BOLD) effect. Since the neurons do not have substantial energy stores, increased neuronal activation leads to increased blood flow and increased oxygen extraction. Increase in paramagnetic deoxyhemoglobin should theoretically result in decreased signal on the T2* weighted sequence, however, since there is disproportionate increase in inflowing diamagnetic oxyhemoglobin the net result is an increase in BOLD signal [35]. This allows for creation of activation maps, which are usually superimposed on structural brain images. There has been recent interest if fMRI can help better assess the state of consciousness of patients who seem to be minimally conscious or in a persistent vegetative state. Monti et al. performed fMRI on 54 patients who were either in vegetative or minimally conscious state [36]. They found willful modulation of brain activity in 5 patients, all victims of a traumatic brain injury, 4 of whom were thought to be in a persistent vegetative state based on clinical evaluation. In one case they were able to elicit yes and no answers to questions utilizing their fMRI technique. If further studies confirm these promising early results, fMRI may become an adjunct to clinical evaluation that may help in classifying the state of consciousness of trauma patients with severe brain injury. It could perhaps someday be useful in establishing basic communication with some patients who appear unresponsive.

Outcome Prediction

Compression of basilar cisterns, presence of subarachnoid hemorrhage, midline shift, traumatic intracranial hemorrhagic lesions are predictors of poor outcome [37]. Due to sensitivity of CT for detection of such findings multiple researchers investigated its potential for prediction of outcome. One of the early, widely recognized systems is Marshall classification. It utilizes the status of the basilar cisterns, the degree of midline shift, and the presence or absence of high density lesions to define 4 types of diffuse head injury. Additional 2 diagnostic categories depend on presence of an evacuated or nonevacuated mass lesion. Patients can be classified into one of these categories and their mortality at discharge can be predicted [38]. The system, however, has limitations in classifying patients with multiple injury types and is nonlinear thus limiting its application to use as a severity scale. Maas et al. developed refined classification system [39] which relies on status of the basilar cisterns, presence of midline shift, intraventricular or subarachnoid hemorrhage, or an epidural mass lesion. This system, called Rotterdam score (Table 8.2), is well standardized, validated, and permits a more clear differentiation of a prognostic risk, particularly in patients with mass lesions.

Table 8.2 Rotterdam score for the probability of mortality in patients with traumatic brain injury according to their CT characteristics

Predictor	Score
Basal cisterns	
Normal	0
Compressed	1
Absent	2
Midline shift	
No shift of shift ≤ 5 mm Shift > 5 mm	0 1
Epidural mass lesion	
Present	0
Absent	1
Intraventricular or subarachnoid hemorrhage	
Absent	0
Present	1
Sum score (add 1 to the score)	+1

The sum score predicts the 6 month mortality as follows: 1 = 0 %, 2 = 7 %, 3 = 16 %, 4 = 26 %, 5 = 53 %, 6 = 61 %
Based of reference (39)

Brain Death

Diagnosis of brain death allows for withdrawal of care and potential organ donation. Although there is some worldwide variability in required observation period, training and number of required

evaluating physicians, there is general agreement on clinical evaluation to asses for cessation of brain function. Occasionally, however, the clinical examination is not reliable or apnea test has to be interrupted due to developing hypotension. Sometimes confirmatory tests are required by local guidelines [40]. In such cases brain death can be confirmed utilizing electroencephalography or somatosensory evoked potentials to demonstrate absent electrical brain activity. Alternatively, imaging can be performed to demonstrate absence of cerebral blood flow. Both digital subtraction angiography (DSA) and cerebral scintigraphy are well established for that determination. DSA is, however, invasive and both modalities are often not practical.

CTA has been proposed as an accurate modality for confirming brain death [41]. Multiple studies, however, have shown that the sensitivity and specificity of CTA is dependent on which vessels are evaluated. In contrast to DSA where contrast opacification is imaged in real time, in most cases, CTA is performed after a set delay following contrast injection. Opacification of the arteries can be seen in brain dead patients due to stasis filling, dilution of contrast into more distal vessels, and due to better sensitivity of CT for detection of contrast compared with DSA [42]. Several scales have been proposed depending which vessels are evaluated for opacification. The most common are 10 point, 7 point, and 4 point scales [43]. The 4 point scale which evaluates the bilateral M4 middle cerebral artery branches and the internal cerebral veins (lack of opacification of all 4 vessels being the positive result) seems the most sensitive reaching a sensitivity of 85 % in one meta-analysis [44]. The specificity of this and other scales is, however, not well established as most studies do not include patients who are not brain dead [44, 45]. CTA, in addition, requires iodinated contrast which is potentially nephrotoxic to the kidneys that could be donated. Although CTA can be used with caution in select cases when its sensitivity and uncertain specificity are taken into account, it cannot be recommended as a standard confirmatory test in evaluation for brain death at this point.

Imaging of Blunt Cerebrovascular Injuries

Indications for Screening

Blunt cerebrovascular injury (BCVI) is defined as damage to extracranial or intracranial cerebrovascular structures resulting from blunt trauma. Injury to the neck vessels is significantly more common than the injury to the intracranial vessels [46]. Historically, injury to the neck vessels was considered rare with early studies quoting 0.08 % incidence among blunt trauma victims [47]. As more aggressive screening became prevalent it became apparent that BCVI is frequently occult and more common, with newer studies quoting up to 1.6 % incidence among the blunt trauma patients [48]. The incidence is even higher in severely injured patients with Mutze reporting an incidence of 2.7 % in patients with Injury Severity Score > 16 [49]. BCVI is significantly more common in adults than in children [50] with reported incidence of 0.03–0.3 % [50, 51] in pediatric blunt trauma victims. Injury to the carotid arteries is more common than to the vertebral arteries. Injury occurs to more than one cervical internal carotid artery in 18–38 % of cases [46]. Injury to both vertebral arteries has been found to occur in 28 % of cases [52] in one study.

Stroke is a dreaded complication of BCVI. The stroke rates related to BCVI vary in the literature with Eastman et al. [53] reporting a representative rate of 15.2 % which decreased to 3.8 % after a change in screening and modification of treatment strategies. Stroke rates as high as 67 % have, however, been reported [54]. BCVI may result in stroke by several mechanisms. Vessel injury results in damage to the intima and frequently the deeper layers of the vessel wall. Thrombus formation near the exposed collagen or in a pseudoaneurysm [55] may lead to a thromboembolic stroke. Alternatively, brain ischemia can be caused by vessel occlusion or severe stenosis related to large thrombus formation, or a blood column dissecting into the vessel wall.

Neurologic sequelae of BCVI are frequently delayed and potentially preventable with treatment. Although it has been suggested that screening of asymptomatic patients may be futile [56], most experts agree that screening during the asymptomatic period before the stroke onset is critical, as stroke rates are lower in treated patients and screening has been found to be cost effective [57, 58].

Extracranial internal carotid artery dissections most commonly occur in their distal cervical portions due to neck hyperextension and rotation with resulting stretching of the carotid arteries over the lateral masses of C1–C3. Neck hypeflexion may result in compression of the carotid arteries between the mandible and the cervical spine. Vertebral artery dissections occur most commonly as a result of cervical spine fractures extending to the foramina transversaria or due to subluxations and frequently involve the V2 and V3 segments.

Based on work performed to a large degree by investigators from Denver and Memphis, high risk criteria for BCVI have been identified (Table 8.3) [59, 60]. Some of the most important include cervical and skull base fractures, severe facial fractures, ischemic stroke, severe head injury, Horner syndrome, and intraoral trauma. Additional studies have demonstrated a 4-fold to 8-fold increase in risk for BCVI in patients with chest trauma. This is particularly true in pediatric population where a non-basilar skull fracture is a significant risk factor as well [51]. An isolated seatbelt sign without other risk factors and with normal physical examination is, however, no longer considered an independent risk factor and should not be used as the sole criterion to elect to screen the patient [61]. The screening protocols have led to a significant increase in detection of BCVI. Nevertheless, it is estimated that more than 20 % of BVCIs occur without any of the established risk factors [62, 63]. Some experts thus advocate more liberal screening which can be accomplished by inclusion of a neck CTA into a whole body CT scan performed for severely traumatized patients.

Imaging of BCVI

BCVI grading is based on a scale developed by Biffl et al. (Table 8.4) [64]. The scale was originally developed for grading of carotid injuries based on their appearance on DSA and was rapidly adopted for grading of both carotid and vertebral injuries based on CTA. When applied to the carotid injuries the risk of stroke increases with the injury grade with reported stroke prevalence of 3, 11, 33, 44, 100 % associated with injury grades of I, II, III, IV, V [65] respectively. Grade I lesions are most common with higher grades progressively less common. For vertebral arteries, stroke and mortality rates are not linear with the injury grade. The highest rate of stroke (40 %) is associated with grade II injuries and the lowest rate of stroke (13 %) is associated with grade III injuries.

Table 8.3 Screening criteria for blunt cerebrovascular injury

Denver criteria	Memphis Criteria
Cervical spine fracture	Cervical spine fracture
Unexplained neurological deficit	Unexplained neurological deficit
Basilar skull fracture with carotid canal involvement	Basilar skull fracture involving the foramen lacerum
Le Fort II or III fracture	Le Fort II or III fracture
Cervical hematoma	Horner syndrome
Cervical bruit	Neck soft tissue injury
Stroke on secondary CT	
Diffuse axonal injury with GCS < 6	
Near hanging with anoxic brain injury	

Denver criteria based on reference (59), Memphis criteria based on reference (60)

Table 8.4 BCVI grading scale

Injury grade	Description
I	Luminal irregularity or dissection with < 25 % luminal narrowing
II	Dissection or intramural hematoma with ≥ 25 % luminal narrowing, intraluminal thrombus, or raised intimal flap
III	Pseudoaneurysm
IV	Occlusion
V	Transection with free extravasation

Based on reference (64)

BCVI has a wide range of appearances on CTA. Minimal intimal injury has an appearance of mild luminal irregularity which does not result in stenosis. It is best seen on reformatted coronal or sagittal images. It may be difficult or impossible to differentiate from vasospasm [66]. A raised intimal flap has an appearance of a linear filling defect extending from the vessel's wall into its lumen. It is seen well on axial images (Fig. 8.2b) with reformatted coronal and sagittal images allowing for better characterization of the lesion (Fig. 8.2a). A dissection with intramural hematoma is usually characterized by variable degree of narrowing of the lumen of the vessel. The wall of the vessel is thickened in either circumferential or eccentric pattern due to the hematoma. Occlusions demonstrate lack of enhancement in the lumen of the vessel. Larger vessels, such as the common or internal carotid arteries, frequently demonstrate gradual tapering of the lumen best seen on the multiplanar reformatted images. Smaller vessels, such as the vertebral arteries usually demonstrate more abrupt narrowing. Pseudoaneurysms have an appearance of a focal outpouching extending from the lumen of the artery which may sometimes narrow the native vessel (Fig. 8.2c). Transection with active contrast extravasation appears as a non-contained collection of contrast surrounding the injured vessel. The exact point of vessel disruption may, however. not be easy to identify. Arteriovenous fistulae may also be difficult to recognize. A typical early opacification of the vein may not be apparent on CTA depending on the phase of the contrast bolus. Enlargement of the draining vein may be the only finding.

Common pitfalls in CT angiographic evaluation of BCVI include streak artifact related to patient's dental hardware, spinal hardware, or dense foreign bodies in the neck. Sometimes suboptimal contrast bolus timing, which can be related to patient's hemodynamic state, can hinder the evaluation for BCVI. Artifact related to gross body motion or swallowing may degrade the images. Atherosclerotic disease and sometimes degenerative spine disease may result in lumen irregularity which may mimic vascular injury. These are, however, usually recognized as such upon more careful review. Congenital variants such as internal carotid artery loops can occasionally mask or mimic vascular injury on the axial images. This is easily rectified by review of multiplanar or 3D rendered images. Congenital hypoplasia or aplasia of the internal carotid artery may be difficult to differentiate from an injury. It is, however, rare and can be recognized by small or absent carotid canal. Asymmetry in caliber of the vertebral arteries is more common and may sometimes present a diagnostic dilemma.

A relatively low prevalence of BCVI calls for a screening modality which is very sensitive and at the same time readily available and inexpensive. DSA is considered a gold standard in evaluation for BCVI. It is, however, an invasive, resource intensive study, not without risks with stroke being a major complication. A 1 % incidence of a transient neurological deficit with 0.5 % incidence of a permanent neurological deficit is commonly quoted [67]. The risk, however, varies widely depending on patient selection and the indication for angiography with a risk of a permanent neurological deficit as low as 0.07 % for some patients [68]. The true risk for trauma patients who are generally young is likely quite low.

Duplex sonography is inexpensive, portable, and noninvasive. It, however, lacks sensitivity which has been reported to be as low as 37.5 % [49]. It is technically limited in evaluation of the frequently injured portions of the neck vessels, such as the distal cervical internal carotid arteries and long segments of the vertebral arteries as they course through the foramina transversaria.

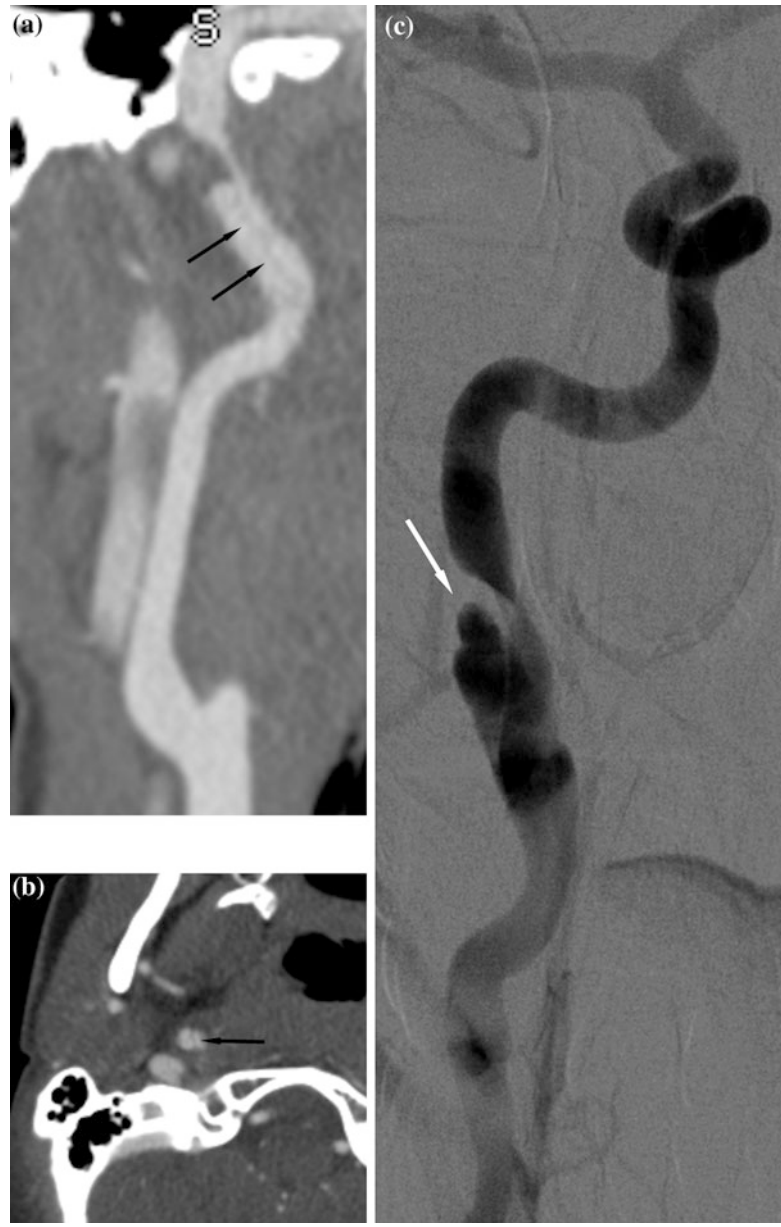

Fig. 8.2 Vascular injury in a 34-year-old trauma victim. **a** Curved multiplanar reformatted image demonstrates dissection with marked lumen narrowing. An intimal flap is seen as a thin linear lucency (*black arrows*). **b** Source axial image shows the intimal flap as well (*black arrow*). **c** Image from DSA performed 24 h later reveals pseudoaneurysm formation (*white arrow*)

Magnetic resonance angiography allows for simultaneous evaluation of both internal carotid and vertebral arteries. It can be performed without contrast and does not involve ionizing radiation. Fat suppressed T1-weighted images allow direct visualization of an intramural hematoma, and the unenhanced time of flight and contrast enhanced images allow for detection of luminal irregularity, pseudoaneurysm, and vessel occlusion [69]. Diffusion weighted images allow for detection of an early stroke. MRI, however, is usually difficult to perform in an acute trauma setting, particularly in critically ill patients who frequently require extensive support apparatus and orthopedic hardware. Motion artifact can be problematic as findings of vascular injury are often subtle and scan time of the fat suppressed T1-weighted sequence is long. MRI was found to perform moderately well

in detection of a traumatic dissection with Biffl et al. reporting a sensitivity of 75 %, specificity of 67 % [70] and Miller et al. reporting a sensitivity of 50 and 47 % and specificity of 100 and 97 % for detection of carotid and vertebral dissections respectively [60]. More recent studies comparing MRA to CTA confirmed superiority of CTA [69].

CT angiography is a noninvasive, readily available, and cost effective [71] tool for BCVI screening. Its sensitivity varied widely in multiple studies. Early studies showed low sensitivity and specificity [60, 70]. With improvement in technique, particularly the increase in the numbers of detectors in CT scanners, the diagnostic performance has improved. It was also shown that experience of the radiologist plays a role with more experienced radiologists and neuroradiologists performing better. Nevertheless, a recent meta-analysis found a pooled sensitivity of CTA for detection of BCVI below 80 % among studies that used scanners with 16 or more slices and in which CTAs were interpreted by neuroradiologists [72]. Although most injuries missed on CTA are lower grade, CTA still may miss substantial proportion of higher grade lesions. Considering this, for high risk patients with a negative CTA, additional screening with DSA has been advocated by some [72]. This, however, should be counterbalanced with limitations of DSA which include its invasive nature, cost, logistic constraints and potential complications. The specificity of CTA for detection of BCVI is 95–98 % with specificity closer to 98 % in larger centers with better equipment and more experience. Confirmation of a positive CTA with DSA is not needed, particularly for higher grade lesions which are confidently diagnosed with CTA.

Follow up Imaging

BCVI is a dynamic process. In a study by Biffl, grade I and II lesions frequently healed, but progressed to pseudoaneurysms in 8 % of grade I and 43 % of grade II lesions. Interestingly, the grade III and IV lesions seemed more stable, remaining unchanged in 93 and 82 % of the cases respectively [48]. In that study follow up angiography changed management in 61 % of dissections by allowing for either discontinuation of therapy or leading to stenting of pseudoaneurysms. Follow up imaging is recommended in 7–10 days [61, 73].

Intracranial BCVI

The intracranial cerebrovascular injuries are substantially less common than injury in the neck. They primarily consist of dissections, aneurysms, and arteriovenous fistulae. A fracture extending into the carotid canal is associated with an internal carotid artery injury in 11–35 % of cases [74, 75] and commonly prompts a search for a carotid artery injury. Multiple other CT findings can be seen in patients with internal carotid artery injury, such as other basilar skull fractures which do not extend to the carotid canal, cerebral contusions, intracranial hemorrhages [75] indicating that severe head trauma in general, is a risk factor for an internal carotid artery injury. Injury to the internal carotid artery may lead to vessel narrowing, occlusion, pseudoaneurysm formation, or development of an arteriovenous fistula.

Traumatic intracranial aneurysms are rare comprising about 1 % of all intracranial aneurysms. They are more common in pediatric population [76]. The mechanism of injury is different in different anatomical locations. The proximal intracranial internal carotid and basilar artery aneurysms are linked to basilar skull fractures. Aneurysms arising in the supraclinoid internal carotid artery are related to a transition of the artery from being relatively fixed to mobile as it exits the cavernous sinus. Severe deceleration can result in either vessel stretching or its direct injury against the anterior clinoid process. Aneurysms arising from the branches of the circle of Willis usually involve the anterior circulation. They are thought to occur due to direct injury against stationary structures such as the falx cerebri and the tentorium cerebelli in case of anterior and posterior cerebral artery branches respectively, or injury against depressed skull fractures in case of

distal cortical branches. The traumatic aneurysms differ from non-traumatic aneurysms as they frequently do not occur at the branch points and histologically are most commonly pseudoaneurysms. They typically appear days or weeks after the initial injury [77], and are prone to rupture with one study reporting 50 % rupturing within first week of after diagnosis [78]. Traumatic intracranial aneurysms can be identified with CTA which is usually a first line study. MRA can also depict the more proximal aneurysms. The aneurysms, however, are frequently small and involve more distal branches. In these cases, the diagnostic performance of CTA and MRA is low and conventional catheter angiography is needed.

The traumatic carotid cavernous sinus fistulae (CCF) are almost always direct type and frequently demonstrate a single communication involving the horizontal portion of the cavernous internal carotid artery and the cavernous sinus [79]. They commonly result from cranial base and facial fractures [46]. Bilateral CCF are rare constituting 1–2 % of traumatic CCF [80]. A direct fistula allows for high pressure arterial blood to be transmitted to the cavernous sinus with resulting revision of flow patterns leading to expansion of the cavernous sinus and the draining veins. Carotid cavernous fistulae are commonly diagnosed with noninvasive techniques, but conventional angiography is often used for better delineation of the fistula and the flow dynamics. Doppler ultrasound usually reveals dilatation of the superior ophthalmic vein which has a pulsatile, reversed or bidirectional flow. CT also reveals an enlarged superior ophthalmic vein in addition to proptosis, enlargement of the extraocular muscles, and bulging of the cavernous sinus. CTA better depicts smaller draining veins. Careful analysis of the source images can reveal the fistula itself, which may sometimes be difficult to visualize on DSA in patients with rapid filling of the cavernous sinus when the fistula is large [81]. MRI and MRA usually demonstrate findings similar to the ones seen on CT and CTA, and may additionally reveal abnormal signal in the cavernous sinus related to altered flow. MRI is better than CT in demonstration of intraorbital edema. MRA may demonstrate the fistula itself, although not as reliably as the CTA [81].

Imaging of the Spine

Indications for Imaging

Spine or cord injury is estimated to occur in 1–4 % of trauma patients [82]. A missed injury is an important medical and legal issue as spinal injuries can result in significant mortality, morbidity, or need for prolonged care. Low yield of imaging coupled with concerns about cost and unnecessary radiation exposure led to multiple studies to determine which patients are at risk and require imaging for cervical spine clearance. Among them there were two prospective observational cohort multicenter trials: the National Emergency X-ray Radiography Utilization Study (NEXUS) and the Canadian Cervical Spine Rule (CCR). The NEXUS study [83] enrolled over 34,000 patients. According to it, alert, non-intoxicated patients without distracting injury who have no posterior cervical midline tenderness or focal neurological deficit are deemed to be low risk for a cervical spine injury (Table 8.5). The CCR [84] identifies patients who are at high risk for cervical spine injury and should undergo imaging, and patients who are at low risk for injury, who should undergo assessment of active range of motion (Table 8.6). The low risk patients who are able to actively rotate the neck 45° to the right and left without pain are deemed cleared without imaging. Both studies have been validated and

Table 8.5 NEXUS criteria

No midline cervical tenderness
No focal neurological deficit
Normal alertness
No intoxication
No painful, distracting injury

Based on reference (83)

Table 8.6 Canadian cervical spine rule criteria

High risk factors that mandate radiography	Low risk factors that allow safe assessment of range of motion
Age ≥ 65 Dangerous mechanism (fall from height ≥ 1 m or 5 stairs, axial load to the head, high speed motor vehicle collision, rollover, ejection, motorized recreational vehicle, bicycle collision) Paresthesias in extremities	Simple rear-end motor vehicle collision Sitting position in the emergency department Ambulatory at any time Delayed (not immediate) onset of neck pain Absence of midline cervical spine tenderness

Radiography is needed for patients with any of the high risk factors or none of the low risk factors. Patients with any of the low risk factors should undergo active neck rotation 45° to the right and left. Those who are unable to rotate the neck without pain should undergo radiography
Based on reference (84)

showed high sensitivities and specificities, with several studies indicating better performance of CCR.

Imaging Modalities

The patients who do not meet clinical criteria for clearance of the spine should undergo imaging. Radiography is not a sensitive modality for evaluation of a spine injury. It is particularly limited at the cervicothoracic and craniocervical junctions, where many injuries occur. A meta-analysis of 7 relevant studies revealed pooled sensitivity of radiography for detection of a cervical spine injury of 52 % [85]. Wintermark found a 32 % mean sensitivity of radiographs for evaluation of thoracolumbar fractures [86]. In one study one third of the cervical spine fractures missed on the radiographs were unstable or clinically significant [87]. In contrast, a CT is highly accurate with a reported 90–99 % sensitivity and 72–89 % specificity for a cervical spine fracture detection [88]. It allows for better characterization of the fractures. In a study by Campbell et al. in which CT findings were the standard for comparison, 20 % of unstable burst fractures of the thoracic and lumbar spine were misdiagnosed as stable wedge compression fractures by plain films [89]. In addition, CT allows for faster triage and was found to be cost effective, particularly for higher risk patients [90, 91]. The CT is thus the modality of choice for evaluation of cervical, thoracic and lumbar spine in adult trauma patients who require imaging [92, 93]. Plain radiographs should be reserved for patients who are not able to be examined by CT.

Pediatric patients deserve special consideration. In children younger than 10–12 years old the majority of injuries occur in the upper cervical spine. This is explained by the fact that the fulcrum of motion in children is at the C2–C3 level while it is at the C5–C6 level in adults [94]. The immature spine is hypermobile due to ligamentous laxity and shallow facet joints. This, coupled with relatively large head and weak muscles, makes a pediatric spine more predisposed to instability. The children, particularly those younger than 5 years old are, however, more prone to development of ionizing radiation induced malignancies. The choice of radiographs or CT for the initial evaluation should thus be individualized with radiographs more appropriate for younger, lower risk patients and CT reserved for older children with higher likelihood of injury. In a polytrauma setting when head CT is performed and imaging of the cervical spine is indicated, CT should be performed for initial evaluation. In patients who undergo CT of the chest, abdomen, and pelvis reformatted images of the thoracic and lumbar spine with sagittal and coronal reconstructions are optimal for injury evaluation. Children older than 14 years of age should be treated as adults for purposes of spine imaging [92].

The exact incidence of pure ligamentous injury without osseous defects to the cervical spine in trauma victims is difficult to ascertain, but it is thought to be 0.04–0.6 % [95]. Although fractures

are well delineated by CT, soft tissues, such as the ligaments and joint capsules, are not. Traditionally ligamentous injury in the cervical spine has been evaluated with flexion and extension (FE) radiographs. Their adequacy has been primarily extrapolated from cadaver and volunteer studies some of which were performed in 1970s [96, 97]. Patients with a subluxation of more than 3.5 mm (and according to other studies, 2 mm) on the FE radiographs are considered to have ligamentous injury. The FE radiographs often, however, do not allow for proper visualization of the lower cervical segments. In addition, in many examinations sufficient range of motion cannot be obtained, frequently due to muscle spasm. In various studies the adequacy rate of FE radiographs was determined generally to be 31–60 % [98, 99], with some reporting an adequacy rate as low as 5 % [97]. The FE radiographs do, however, have a role in patients with negative CT and MRI, treated with collar for neck pain. In these patients, FE radiographs performed after resolution of pain can add to assessment of spinal stability prior to discontinuation of the collar.

Due to excellent soft tissue resolution MRI is considered superior to FE radiographs in detecting ligamentous injury. Multiple studies described patients with negative radiographs who had ligamentous injury detected by MRI [100–102]. For example, Duane in a study of 271 patients found that FE radiography failed to identify any ligament injuries, while MRI found eight [103]. The patterns of injury seen on MRI include signal abnormality in a ligament, ligament elevation or disruption (Fig. 8.3), signal abnormality in a disk, disk widening, T2 prolongation involving the facet joint, and facet joint widening. There are, however, no established criteria for distinguishing significant from inconsequential abnormalities on the MRI. Goradia et al. in a study comparing MR imaging findings with intraoperative findings found good MR sensitivity for detection of injury to the posterior longitudinal ligament, the disk, and the interspinous soft tissues, but generally poor correlation between findings on the MR and at surgery. They concluded that MR may overestimate the degree of disruptive injury [104].

The role of MRI in evaluation of cervical spine instability in unreliable or obtunded trauma patients is controversial. Some authors conclude that the cervical spine in such patients can be cleared given a negative CT. In particular Panczykowski in a large meta-analysis found a negative predictive value of a normal cervical spine CT to be 100 % [105]. Others, however, found that MRI can depict abnormalities not detected on CT that alter management. In a meta-analysis, Schoenfeld et al. found that MRI identified injuries that altered management in 6 % of patients [106]. The heterogeneity of literature is to a certain degree related to varying definition of an "unreliable clinical examination". In some studies patients merely "obtunded" were deemed to have an unreliable clinical examination. In a recent review of literature James et al. concluded that in the obtunded blunt trauma patient with unreliable clinical examination and negative CT scan, there is a role for cervical spine MRI, as it can detect unstable injury [107]. For patients with intact gross motor function on a reliable clinical examination MRI may not be necessary. MRI is also not indicated for detection of ligamentous disruption in the thoracic or lumbar spine if CT is normal. In such cases the chances of unstable ligamentous injury are extremely low.

MRI is important in evaluation of injury to the cord and nerve roots. It can well depict cord compression due to disk herniation, displaced bony fragments, or an epidural hematoma. It can help in predicting outcome by characterizing the degree of cord injury, such as the extent of edema, intramedullary hematoma or presence of a cord transection. It has a role in determining the cause of neurological deterioration in subacute or chronic stages by detecting developing myelomalacia, syrinx, or adhesions with cord tethering. Traumatic nerve root avulsions were traditionally evaluated with myelography and CT myelography. Newer MR techniques can offer similar diagnostic performance without exposure to unnecessary ionizing radiation or intrathecal contrast injection [108]. In addition, MR neurography can image the nerves more peripherally and characterize brachial plexus injuries better than CT [109].

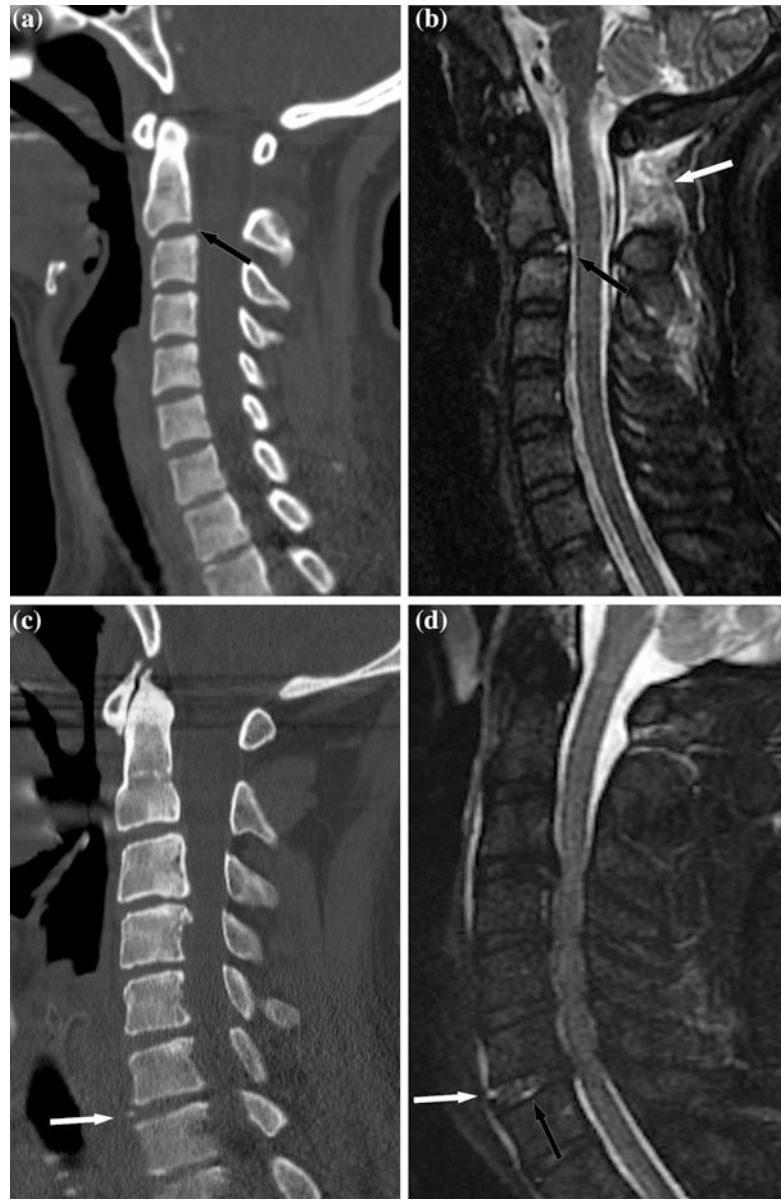

Fig. 8.3 Ligamentous injury in a 31-year-old (a,b) and a 54-year-old (c,d) trauma victims. **a** CT demonstrates subtle widening of the posterior C2–C3 disc space (*black arrow*) and the distance between the C1 and C2 posterior arches. **b** STIR image shows disruption of the posterior longitudinal ligament and posterior annulus injury (*black arrow*). There is also injury of the posterior ligamentous complex (*white arrow*). **c** CT shows a small avulsed bony fragment near the anterior aspect of the C6–C7 disc space (*white arrow*). **d** STIR image demonstrates disruption of the anterior longitudinal ligament (*white arrow*) and disc injury (*white arrow*)

Injury Types

Various injury mechanisms result in different injury patterns. Hyperflexion injury is the most common occurring in 50–60 % of cases [110]. Narrowing of the anterior disk space, widening of the interlaminar and interfacet spaces is frequently seen. It can result in a ligamentous injury such as hyperflexion sprain. Addition of a rotational component can result in a unilateral facet dislocation. Bilateral facet dislocation can occur due to severe hyperflexion and result in a severe neurological injury. Fractures include a simple vertebral body compression fracture, clay shoveler's fracture, and a flexion teardrop fracture which is frequently associated with spinal cord injury. An additional axial loading component may result in a burst fracture. Hyperflexion injury to the thoracolumbar spine occurs usually at the thoracolumbar junction or in the upper

lumbar spine where it can result in a Chance fracture.

Hyperextension injuries occur more commonly in the cervical spine than the thoracolumbar region and occur in 19–38 % of cervical spine injuries. Widening of the anterior aspect of the disk space due to injury to the anterior longitudinal ligament or anterior disk disruption can be seen. Fractures include an extension teardrop fracture, hangman's fracture of C2, various combinations of pedicle and laminar fractures, and fracture dislocation of the facet joints. Hyperextension dislocation injury can result in cord compression between the posteriorly subluxed vertebral body and the ligamentum flavum. This type of injury may, however, on imaging demonstrate only minimal translation of the vertebral body and was traditionally difficult to recognize on radiographs [111]. Anterior vertebral body dislocations in hyperextension injury occur when there is failure of the middle column and posterior elements. In the upper cervical spine hyperextension injury results in posterior arch of C1 fractures; severe hyperextension can result in an atlantoaxial distraction.

Rotational injuries frequently happen in the upper cervical spine and are more common in children. They may lead to C1–C2 rotatory fixation or dislocation. Shearing injury commonly occurs at the craniocervical junction and can result in an atlantooccipital dislocation, which is often fatal. Axial loading with lateral bending can result in occipital condyle fractures. More complex forces result in odontoid fractures.

Spinal Stability

Spinal stability is commonly determined using the 3 column classification model proposed by Denis [112]. The model was originally developed for thoracolumbar injuries and was promptly applied to cervical spine injuries as well. According to it, the spinal column is divided into 3 columns. The anterior column consists of the anterior longitudinal ligament, the anterior annulus, and the anterior portion of the vertebral body. The middle column is composed of the posterior longitudinal ligament, the posterior portion of the annulus, and the posterior portion of the vertebral body. The posterior column contains the neural arch, facet joints, as well as the posterior ligamentous complex. In this model, the injury to the middle column is of critical importance as injury to 2 columns renders the spine mechanically unstable. Subsequently it was, however, recognized that many injuries involving two columns with an intact posterior ligamentous complex can be treated nonsurgically.

The recognition of the role of the soft tissue structures and the need for a classification system that would better assist in management contributed to development of a Thoracolumbar Injury Classification and Severity Score [113] and shortly thereafter the Subaxial Cervical Spine injury Classification System [114]. These systems assign score based on the morphology of the injury, the neurological status of the patient, and the integrity of the posterior ligamentous complex in case of the thoracolumbar injury and the discoligamentous complex in case of a cervical injury (Tables 8.7 and 8.8). A calculated composite injury score stratifies patients into surgical and nonsurgical treatment groups. Patients scoring less than 4 points are managed nonsurgically, more than 4 points surgically, and those scoring 4

Table 8.7 The thoracolumbar injury classification and severity (TLICS) score

Feature	Points
Injury morphology	
Compression	1
Burst	2
Translational/rotational	3
Distraction	4
Posterior ligamentous complex	
Suspected/indeterminate	2
Injured	3
Neurologic status	
Nerve root involvement	2
Complete cord injury	2
Incomplete cord injury	3
Cauda equina involvement	3

Based on reference (113)

Table 8.8 The subaxial cervical injury classification (SLIC) system

Feature	Points
Morphology	
Compression	1
Burst	2
Distraction	3
Rotation/translation	4
Discoligamentous complex	
Indeterminate	1
Disrupted	2
Neurologic status	
Root injury	1
Complete cord injury	2
Incomplete cord injury	3

Based on reference (114)

points managed either surgically or nonsurgically. Both systems have demonstrated validity in early investigations [115, 116], but with improved understanding of spinal stability, modifications or new systems will likely be proposed.

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Evidence-Based Review of the Use of Steroids in Neurotrauma

9

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Inflammation and edema is poorly tolerated by the central nervous system (CNS) because it can result in secondary injury through the release of local and systemic cytotoxic inflammatory mediators [1]. Secondary injury can be the sequela of traumatic, infectious, auto-immune, or neoplastic processes in the CNS. Steroids such as dexamethasone and methylprednisolone have anti-inflammatory properties that consequently may be beneficial adjuncts for patients with these diseases. A recent meta-analysis and Cochrane review concluded that both adults and children have reduced neurologic morbidity and mortality when steroids were used as adjuncts in bacterial meningitis [2, 3]. Steroids have been used in the treatment of bacterial meningitis to reduce secondary injury for over 60 years; therefore, many authors have also extrapolated this modality for treatment of traumatic brain and spinal cord injuries [4].

Traumatic brain injury (TBI) is a leading cause of premature death and disability in the world with the majority of TBIs resulting from road injuries [5, 6]. As road related TBIs decrease in industrialized nations, a much steeper rise has afflicted the developing world with the increasing popularity of motorized vehicles [7, 8]. In the United States the estimated incidence of TBI related disability is 33 cases per 100,000 persons per year [9]. In the developing world, this number is thought to be significantly higher with an estimated incidence of over 200 cases per 100,000 persons per year [10]. Even this number is thought to be underestimated as motorized vehicles are on the rise in Asia. TBI has become a critical public health and socioeconomic problem with the majority of TBI cases affecting younger persons resulting in early death or long-term disability [9]. Various attempts have been made to identify interventions that may provide even a moderate reduction in the morbidity and mortality associated with TBI.

Steroids were investigated in the 1960s as a therapeutic option for reducing cerebral edema after Galicich et al. reported significant improvements in patients suffering from increased intracranial pressure secondary to brain tumors or from post-operative swelling [11]. Additional experimental evidence has accrued since then confirming and elucidating the mechanisms through which steroids reduce vascular permeability and free radical production in cerebral edema [12–15]. Although the clinical benefit of steroid use in reducing vasogenic cerebral edema has long been established, it was not until years later when authors first reported the potential

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benefit of steroids for cytotoxic edema in the setting of TBI [14–18].

In 1976 Faupel et al. conducted a prospective double-blind review comparing dexamethasone to placebo in 95 patients suffering from severe TBI [19]. In their review, the authors found a significant decrease in mortality in the treatment group but noted no overall improvement in outcomes as the surviving patients in the control group were more likely to be severely disabled or in a persistent vegetative state [19]. A subsequent prospective double-blind randomized clinical trial comparing low dose and high-dose methylprednisolone to placebo was conducted in 88 patients with severe TBI by Giannotta et al. in 1984 [20]. While the authors found no significant difference in 6 month outcomes in the treatment groups, subgroup analysis showed improved survival and speech function in patients under the age of 40 with high-dose methylprednisolone [20].

While the early reports were promising, multiple subsequent studies were conducted and none showed substantial benefit [20–24]. Cooper et al. performed a prospective double-blind study involving 97 patients with severe TBI treated with high-dose dexamethasone or placebo. The authors found no significant difference in outcomes, serial neurological examinations, or intracranial pressure at 6 month follow-up [23]. Gaab et al. performed a similar study in 1994 with high-dose steroids given early after injury (within 3 h) and found no significant difference after 12 month follow up [25]. Low dose methylprednisolone was also evaluated in a similar fashion and similarly showed no significant difference in outcome after 6 months follow up [21].

Despite these findings, in 1995 a survey was conducted regarding the management of patients with TBI indicating that steroids were being used in 64 % of trauma centers in the United States [26]. This was likely because the results of the National Acute Spinal Cord Injury Study (NASCIS) were published in the early 1990s concluding that treatment with extremely high doses of methylprednisolone is indicated for acute spinal cord injury (this recommendation has since been discouraged by the CNS/AANS guidelines) [27, 28].

In 1997 Alderson et al. performed a systematic review of all randomized control trials evaluating steroids for the treatment of TBI. The result of their extensive review was a lack of benefit for the use of steroids in the treatment of TBI. Although the results were convincing, the authors maintained that the lack of benefit was uncertain and emphasized the need for a larger randomized double-blind clinical trial [19].

In 2004 the results of such a trial was published. The Corticosteroid Randomization After Significant Head Injury (CRASH) trial was an international randomized double-blind study evaluating the effects of methylprednisolone for the treatment of TBI [29]. This study involved the enrollment of over 10,000 patients from 239 hospitals in 49 countries. Each patient presenting to the hospital within 8 h of injury with a GCS of 14 or less was randomized to receive methylprednisolone for 48 h or placebo. The protocol of this study was similar to the NASCIS trial in order to capture any potential benefit from early intervention. The study was concluded early by the data monitoring committee after over 5 years of enrollment when an interim analysis showed not only no benefit but a higher 2-week mortality in the steroid group [29]. While the exact mechanism is uncertain, the increase in mortality seemed to be related to additional extra cranial injuries.

One such extra cranial injury associated with TBI is acute spinal cord injury (SCI) . Just as cerebral edema occurs after TBI, spinal cord edema occurs with both primary and secondary insults to the spinal cord in an acute spinal cord injury (SCI). In fact, much of the excitement regarding the use of steroids in TBI has stemmed from the data published from studies regarding the use of steroids in SCI. Despite more recent evidence suggesting the lack of efficacy of steroids in TBI, the data regarding the use of steroids in SCI has not been so clear-cut.

Spinal cord injuries may occur from a variety of high-energy accidents, predominantly affecting the young adult patient population. Traumatic SCI incidence is approximately 40 new cases per million population, with over half of these patients younger than 30 years of age [30]. The WHO reports as many as 40–80 new cases

per million per year worldwide. The etiology of SCI in developed nations is predominantly seen after motor vehicle accidents. In countries with lower GDPs, falls are the predominant cause of SCI, with motor vehicle accidents less common [31]. The high level of morbidity leading to long-term disability, combined with the limitations of current medical and surgical treatment, makes prevention of SCI the most effective management. Despite having many recent advances in the prehospital transfer of patients at risk for SCI, little progress has been made in the treatment of SCI once a neurologic injury has occurred.

Neurological injury after acute SCI was found in animal studies to occur as a result of cell membrane breakdown at the site of trauma, peaking by the 8 h post-injury time period. Methylprednisolone has been shown in these same animal model studies to inhibit lipid peroxidation and hydrolysis, thus limiting the breakdown of the phospholipid bilayer after SCI. As lipid peroxidation is believed to cause further vasoactive processes within the metabolism of arachidonic acid, prevention of this pathway was theorized to improve vascularity of the injured spinal cord [32].

Standard practice in the mid-late 1900s included the administration of steroids to patients presenting with evidence of acute spinal cord injury, a practice based predominately on animal models. A national study (National Acute Spinal Cord Injury Study, NASCIS) was undertaken in the early 1980s to analyze outcomes in patients receiving steroids following acute SCI [33]. This was the first of several multicentered, double-blinded randomized controlled trials to review steroid use following SCI.

NASCIS I randomized 330 patients into 2 groups based on varying dosages of methylprednisolone. Patients were eligible for randomization if presentation was consistent with an acute traumatic spinal cord injury as assessed by an attending neurosurgeon within 48 h of injury. The high-dose group received 1000 mg methylprednisolone bolus on admission, followed by 250 mg every 6 h for 10 days; the standard dose group received 100 mg bolus on admission, followed by 25 mg every 6 h for 10 days. Detailed neurological exams were performed and documented on admission, at 6 weeks, 6 months, and 1 year. Examination was directed for outcome assessments of motor function, response to pinprick and light touch, with each graded in both an expanded score and a 5-point scale. Results were reported based on right side neurological exam only. Analysis of follow up scores at both 6 weeks and 6 months revealed improvements in all aspects of the neurological exam, without statistically significant difference between the two groups. In regard to morbidity and mortality, wound infection was found to occur 3.6-fold more often in patients in the high-dose group, with $p = 0.01$. Although not reaching statistical significance, mortality was three times more common at 14 days and twice as common within 28 days in the high-dose group. Given the increased risk and lack of benefit, the NASCIS I trial was closed early [33].

The second national trial regarding treatment of acute spinal cord injury patients investigated the dose of steroids, as well as the use of naloxone. Animal models had revealed that the dose of methylprednisolone used in the original NASCIS study may have been subtherapeutic, leading NASCIS II to utilize a much higher dose but only for a 24 h period. The addition of naloxone therapy was also included in this trial based on positive results in animal models suggesting neurological benefit to treatment with naloxone therapy. The study performed randomization on 487 patients by the 12 h post-injury mark, where patients received either methylprednisolone + placebo for naloxone, naloxone + placebo for methylprednisolone, or placebo for naloxone + placebo for methylprednisolone, in a double-blinded fashion. Patients were again assessed at admission, 6 weeks and 6 months for pinprick, light touch, and motor function [32].

Overall evaluation of patients receiving methylprednisolone revealed initial improvement in regard to sensory function over the placebo and naloxone groups. In addition, when the methylprednisolone group was stratified for patients receiving treatment within 8 h post-injury, there

were statistically significant improvements seen in regard to both sensory and motor function at the 6 month assessment. By the one-year mark however, these sensory gains equilibrated and were no longer significant. Again, the methylprednisolone group was seen to suffer a higher rate of infection and wound healing complication, but this did not reach statistical significance [32].

NASCIS III responded to the results of NASCIS II by studying the effects of methylprednisolone administered within 8 h of injury for a total duration of either 24 or 48 h. NASCIS III randomized 499 patients with acute spinal cord injury but included an additional study arm to address the use of tirilazad mesylate, a lipid peroxidase inhibitor with fewer systemic side effects than corticosteroids. Patients were again assessed for neurological function on admission, at 6 weeks and 6 months. Patients receiving the 48-h course of methylprednisolone faired the best with respect to statistically significant improvement in neurological function. These patients also experienced increased rates of severe pneumonia and sepsis as compared to the remaining groups. Patients in the 24-h group and the tirilazad mesylate group faired similarly with no statistically significant difference if outcomes or complications [34].

Cranial nerve injury is also a common complication following TBI and similarly secondary inflammatory changes occur in peripheral and cranial nerves after primary traumatic injury. The overall incidence of cranial nerve injuries following TBI ranges between 5 and 23 %, but decreases to 0.3 % in patients with only mild head trauma [35, 36]. The most common cranial nerves affected include the olfactory, facial, and abducens nerves [36, 37]. Cranial nerve injury is associated with skull base fractures and cerebral contusions but may also arise without evidence of CT abnormalities [36].

Treatment of this heterogeneous group of injuries has been controversial. The management of cranial nerve neuropathies is often conservative and traditionally included observation. Most cranial nerves were noted to recover without medical or surgical intervention. Despite having high rates of spontaneous improvement ranging between 50 and 82 %, steroids and surgical decompression have been advocated to reduce secondary compression from neuronal swelling especially in cases of traumatic optic and facial nerve neuropathies [37, 38].

Anderson et al. proposed the use of high-dose steroids for the treatment of traumatic optic neuropathy after the observation of its potential efficacy in TBI [39]. In 1990 Spoor et al. reported improvements in 22 cases of traumatic optic neuropathy after steroid administration [40]. Cook et al. performed a meta-analysis of the management of traumatic optic neuropathy and found treatment with steroids and optic nerve decompression to be superior to observation [41]. Since then steroids and decompression have been at the forefront of treatment for treatment of traumatic optic neuropathy although steroids do not seem to provide any added benefit to surgical decompression [42].

Steroids have also been shown to be beneficial in the treatment of Bell's palsy and therefore extrapolated for the treatment of traumatic facial neuropathy [43]. A recent systematic review found an overall recovery rate of 67 % with the administration of steroids but was similar to the 66 % seen with observation alone [44]. Subgroup analysis also suggests surgical intervention may not increase rates of improvement compared to the natural history in which up to 80 % of patients may see improvement [44].

Given the significant morbidity of steroid use in critically ill patients, the recent CNS guidelines studied the three NASCIS reports in depth [45]. With regard to NASCIS I, obvious negative impacts were appreciated in morbidity and mortality, leading to early closure of the study. This raises concerns for the high dose of steroids over a prolonged period.

Critical review of NASCIS II reveals that while 487 patients were randomized in the planned window of less than 12 h, only patients treated by the 8-h mark were analyzed, effectively reducing the study population to only 196 patients. Conclusions from the final follow-up are based on only 135 patients. The imposition of a post hoc treatment window is not addressed. Independent analysis of patients treated from 8 to 12 h revealed

negative impact on neurological recovery. While complication rates of steroid treatment were reported as statistically similar, the study was not appropriately powered to avoid type II error. Several studies have been completed, using patients with SCI prior to 1990 that did not receive steroid therapy as historical controls. These have found that patients suffering blunt or penetrating SCI fair worse when treated with steroids [46, 47]. Similar evaluation of complication rates found pneumonia, length of intensive care admission and duration of mechanical ventilation to be significantly higher in patients treated with steroid therapy compared to historical control patients not receiving steroid treatment [48].

Review of the NASCIS III use of methylprednisolone in doses similar to NASCIS II for duration of 24 or 48 h revealed class I evidence for negative results. No improvement in neurological function was seen in motor or sensory function with administration of methylprednisolone for 48 h, or therapy with tirilazad. Post hoc analysis was suggestive of early motor function improvement in the 48 h group only if the medication was administered within 3 h of injury, but this was no longer significant by the 1 year follow-up assessment. The 48 h steroid therapy group also incurred increased rates of severe pneumonia and sepsis than the 24 h group. These were reported as statistically insignificant, however like NASCIS II, the study was not powered appropriately to avoid type II error [45].

In a prospective randomized double-blind clinical trial comparing NASCIS dosages of methylprednisolone to placebo for the treatment of acute SCI, Matsumoto et al. reported increased rates of pulmonary and gastrointestinal complications in the treatment group [49]. These results contributed to the recent change in the 2013 AANS/CNS guidelines for the treatment of SCI. The new guidelines site Class I, II, and III evidence that high-dose steroids are associated with harmful side effects including death; therefore, steroids are discouraged for the treatment of acute spinal cord injury [45]. Although strong evidence exists within the spinal cord injury literature, to the best of our knowledge no such evidence exists to support an increase in complications from methylprednisolone administration in TBI.

The CRASH trial provides Level 1 evidence against the use of steroids in TBI as it appears to increase mortality. Although there is heterogeneity within the NASCIS literature regarding the efficacy of steroids in SCI, the additional complications associated with high-dose corticosteroids may not be worth the risk. At the present time, there is insufficient evidence to support the use of steroids in TBI or SCI but there may be a potential role in traumatic cranial neuropathies.

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Interventional Radiology in the Civilian Neurotrauma Setting

10

Richard M. Young and Jeffrey C. Mai

Anatomic Overview

Anatomic Structure of the Artery

Arterial vessels are comprised of three main layers: (1) tunica intima, (2) tunica media, and (3) tunica adventitia [1–12]. The tunica intima is the most inner and thinnest layer, consists of a simple squamous endothelial cells linked by a thin subendothelial layer of connective tissue and elastic bands known as the internal elastic lamina. The tunica media is the thickest component of the artery which contains the most elastic fibers and connective tissues. Within this layer there are circumferential smooth muscles to allow for expansion and contraction of the vessel in response to the demands of the body. Lastly, the outer most layer, the tunica adventitia consists of a loose connective tissue and contains the nerves with small capillaries to support the artery itself. When arterial vessels transitions from extracranial to intracranial, the tunica media thins to approximately 1/4 of its original size while the tunica adventitia also decreases in thickness as it enters the skull [13]. This anatomic change makes the vessel more vulnerable to shear forces, either from blunt or penetrating trauma.

Great Vessels of the Aortic Arch

The aortic arch bifurcates into three distinct branches: (1) Brachiocephalic or innominate artery (2) Left common carotid artery and (3) Left subclavian artery. There are multiple variations in this aortic arch anatomy, some of the most common ones are described as such, where (a) the brachiocephalic trunk and left common carotid may have a common origin, (b) the left common carotid may be a branch of the brachiocephalic, (c) the left vertebral artery may originate between the left common carotid artery and left subclavian artery and (d) the right subclavian artery arises from the arch itself as the most distal branch, after the left subclavian artery [14].

Segments of the Carotid Artery

There are a few definitions when discussing about the different segments of the internal carotid artery. Monson et al. published in 1969, describing 24 patients who had undergone surgical exploration of extracranial neck vessels and associated it with three zones of the neck along with consequences of having such injuries in the different zones. These zones were arbitrarily designated as Zone 1—below the clavicle and

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sternal notch, Zone 2—between the angle of the jaw and clavicle and Zone 3—above the angle of the jaw [11]. The description of the zones using external anatomical landmarks was more useful in planning for surgical approaches along with determining the morbidity and mortality of having injury in the zones. Gibo et al. in 1981 [15], described the carotid artery from a microsurgical point-of-view. The current and more widely used nomenclature for the segments of the carotid artery was proposed by Bouthillier et al. in 1996 that encompasses a total of seven internal carotid artery segments: C1-Cartoid, C2-Petrous, C3-Lacerum, C4-Cavernous, C5-Clinoidal, C6-Ophthalmic, C7-Communicating [16].

Segments of the Vertebral Artery

Similar to the segments of the carotid artery, the vertebral artery can also be subdivided to help with anatomic localization in discussion. There are four segments: V1 is the origin of the vertebral artery to the entrance of the transverse process, usually C6, V2 is the segment that spans within the cervical transverse processes from C6 to C2. V3 is the extracranial segment between the transverse process of C2 and before it enters through the foramen magnum. V4 is the intracranial portion beginning at the atlantooccipital membrane and terminating at the junction of the basilar artery [17].

Imaging Modalities for Diagnosis

There are many different imaging modalities that have the ability to evaluate for carotid and vertebral artery injuries. When there is sufficient suspicion for such injuries, a head and neck angiogram should be obtained. Risk factors include high energy injuries to the head and neck with either a Leforte II or III fracture, subluxation of the cervical spine, fractures of the cervical spine extending into the transverse foramen, basilar skull fractures, diffuse axonal injury, and anoxic brain injury with associated showering of strokes [7]. To quantify the severity of vessel injury, the Biffl classification [18] has been commonly used to describe the grade of injury to the vessel (Table 10.1).

Table 10.1 Biffl Classification—Vessel Injury Index

Grade	Description
1	Mild intimal injury or irregular intima
2	Dissection with raised intimal flap/intramural hematoma with luminal narrowing >25 %/ intraluminal thrombosis
3	Pseudoaneurysm
4	Vessel occlusion/thrombosis
5	Vessel transection

Biffl et al. [18]

Ultrasound

Prior to popularization of the CT scan with the utilization of CT angiography (CTA), ultrasound imaging was an option for noninvasive imaging to detect carotid dissections in the neck and has a 86 % sensitivity [19] in detecting internal carotid artery injuries. Earlier studies advocated for this method and in one study, ultrasound was determined to be as good as arteriography with the added benefit of being faster and less expensive, but it was only ideal for Zone II injuries [20]. From experience, there are limitations with the ultrasound: patient size, body habitus, operator availability, and difficulty around bony structures such as the skullbase [3, 19]. Given these limitations, ultrasonography has had a limited role in primary assessment of vascular trauma; however, some contend that it may be useful as a noninvasive follow-up imaging modality in patients to evaluate the rate of healing [21].

CT Angiography

CT angiography (CTA) has become the primary initial imaging technique for evaluating head and neck vessel injuries. Earlier CT angiography had a sensitivity between 50 and 68 % [22, 23] however, with technological advances the sensitivity and specificity has improved to 90 and

100 %, respectively [24]. Advocates for CT over digital subtraction angiography (DSA or catheter-based angiography) argue that the major advantage is having the availability of CT scanners 24/7 in most of the hospitals in the US whereas having an angiography suite and an interventionalist on-call limits its utility. Furthermore, improved multidetector CT scanner and workstations that can postprocess the 2D and 3D data have been extremely useful in detecting dissections [6, 8, 25]. However, CTA may be suboptimal in patients with dental implants or severe atherosclerotic disease, improper bolus or timing of contrast, and motion artifact, which can affect the quality of image [6]. The requisite contrast bolus may also be undesirable in those patients with borderline renal function. Proponents for the use of CTA argue for diagnostic purposes, that CTA is less invasive and time-consuming when compared to DSA, and may allow for faster surgical intervention if warranted [26]. In general, the use of DSA can be reserved for definitive treatment or when diagnosis is equivocal in a case with a negative CTA despite having persistent clinical concerns [6].

MRI/MR Angiography

Utilization of MRI with MR angiography (MRA) is another noninvasive method to evaluate for possible vessel injury. The advantages in using MRI/MRA for investigating possible neck vessel injury includes the ability to assess adjacent soft tissue injuries such as, ligamentous injuries, spine disc ruptures, and spinal cord injuries. When assessing the head, it can evaluate for diffuse axonal injury or detect early signs of a stroke. Levy et al. reported from their investigation that MRA for carotid artery dissection had a sensitivity of 95 % and specificity of 99 % [27], however they mentioned that this can be limited by the bony anatomy of the skullbase and/or metal artifacts such as dental implants. The use of contrast in MRA can be avoided in those individuals with impaired creatinine clearance, albeit with lower sensitivity for detecting dissections. As with any MRI, the disadvantages of its use depends on the medical stability of the patient (due to a longer duration in the MR scanner when compared to CT), difficulties of a ventilated patient, metal implant, aneurysm clip, pacemaker, etc. Despite these disadvantages, patients with transient ischemic attack or stroke symptoms with a normal CT should undergo a stroke protocol MRI. If the imaging shows scattered emboli, a heightened index of suspicion should lead the team to reassess the vessels of the neck.

Digital Subtraction Angiography (DSA)

Digital subtraction angiography (DSA) is still considered the gold standard in evaluating for head and neck vessel dissections [3, 6, 7, 28]. Compared to the prior three imaging modalities, it is an invasive procedure with associated procedural risks such as, pseudoaneurysm in the groin, iatrogenic vessel injury/dissection, stroke, cerebral hemorrhagic, and surrounding tissue injury. The literature has reported combined procedural risks of 0.5–15 % [29]. Despite the procedural risks, DSA information has the highest sensitivity and treatment can be implemented immediately, if required. In many instances, the patient's overall stability is a priority before transporting a patient to the angiosuite [30]. Given these limitations, along with the labor-intensive nature of catheter-based angiography studies, CTA has remained the first-line vascular imaging treatment of choice for trauma patients.

The Signs and Symptoms—What to Look Out for

Head and neck vessel injury or dissection without any signs of external injury during the initial trauma surveys occurs in approximately 50 % of all cases [31]. There is often a *silent period* [4, 32] where the patient remains asymptomatic from their injuries, however as the disease progresses, acute symptoms may appear within a four hour window, which we have seen, or they may appear in a delayed fashion by remaining *silent* for as long as 75 days [3]. It is important for trauma surgeons,

emergency room physicians, neurosurgeons, and neurologist alike to consider head and neck vessel injuries when there is a sudden onset of symptoms that occur in patients with a remote trauma history. Delayed stroke-like symptoms or severe neck pain in a delayed fashion following trauma mandates immediate vascular imaging.

In the initial trauma scans, often the first head CT may be negative for stroke of hemorrhage, however associated chest injuries, skull base fractures [4] or other signs of external injury such as bruising around the neck, a broken collar bone, or skin abrasions may be an indicator to a possible vascular injury in the neck. Surrounding tissues of the neck may be tender to touch, and auscultation of the carotids with the stethoscope during the examination is very important when evaluating for a bruit to detect early signs of carotid injury [11]. The development of a delayed Horner's syndrome also mandates further imaging. The presence of increasing headaches, nausea/vomiting, hemiparesis, facial paralysis, visual disturbances, and aphasia may be signs of anterior circulation stroke. Both the Denver criteria [33] and Memphis criteria [23] are two commonly used screening tools used in blunt trauma situations to help guide further evaluation of the head and neck vessels (Table 10.2).

Similarly, vertebral artery injuries may also generate neurological deficits related to the posterior circulation. These may include headaches, dizziness, nausea, vomiting, blurry vision, loss of central vision, hemiparesis/paralysis, and even coma or death, particularly with brainstem strokes seen in severe vertebral artery injuries.

As mentioned in Table 8.1, the Biffl classification is used to stratify the severity of injury to vessels in the neck. In a follow-up publication by Biffl et al. in 2002, they were able to demonstrate the percentage of strokes associated with the different grades of injury [22] (Table 10.3).

Table 10.2 Screening criteria for vascular injury for the head and neck

Denver criteria [33]	Memphis criteria [23]
Signs/symptoms • Arterial hemorrhage or expanding hematoma • Cervical bruit • Focal neurological deficit • Neurological exam inconsistent with head CT findings • Stroke on follow-up head CT	• Cervical spine fracture • Neurological exam not explained by brain imaging • Horner's syndrome • LeForte II or III fracture pattern • Basilar skull fracture with involvement of the carotid canal • Neck soft tissue injury (seatbelt sign or hanging or hematoma)
Risk factors • LeForte II or III fracture pattern • Cervical spine fracture • Basilar skull fracture with involvement of the carotid canal • Diffuse axonal injury with GCS <6 • Near hanging with anoxic brain injury	

CT computed tomography scan, *GCS* Glasgow coma scale

Table 10.3 Stroke Rate via Biffl Classification

Grade	Stroke rate by grade	
	Carotid artery injury (%)	Vertebral artery injury (%)
1	8	6
2	14	38
3	26	27
4	50	28
5	100	N/A

Biffl et al. [22]

Treatments Options for Vessel Injury

The management of traumatic carotid or vertebral artery injuries varies widely amongst specialists. Dissection of the carotid artery is the most commonly seen injury resulting from blunt or whiplash injury [4], however other injuries such as a pseudoaneurysm can also occur (Fig. 10.1).

Although more rare than carotid injuries, vertebral artery injuries also require careful consideration. It has been estimated that vertebral artery injuries occurs between 0.20 and 0.77 % of trauma cases [34]. Earlier studies from the 1970s demonstrated mortality rates of 20–40 % [35], and that 70 % of the patients have ischemic

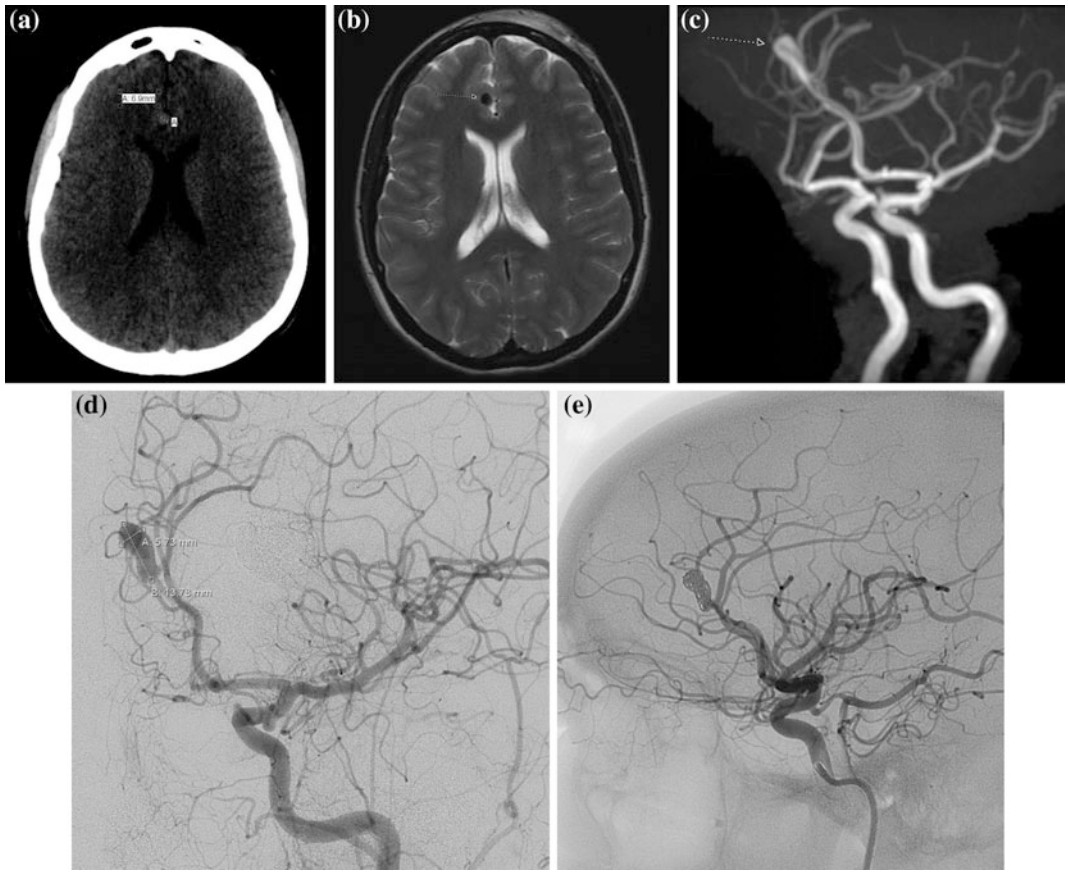

Fig. 10.1 Motor vehicle crash causing a traumatic intracranial pseudoaneurysm from shear of the anterior cerebral artery (ACA) against the falx: 32 year old woman who presented as a restrained driver in a motor vehicle crash. **a** Routine workup in the emergency department disclosed a 7 mm hyperdense right frontal lesion adjacent to the falx. **b** MR imaging subsequent to the CT demonstrated an associated flow void with confirmation of an unruptured traumatic pseudoaneurysm of the ACA on MR angiography (**c**). This right distal A2 segment of the anterior cerebral artery pseudoaneurysm measured 13.8 mm × 5.7 mm (**d**) and was treated uneventfully with coil embolization (**e**)

strokes from vertebral artery injuries [6, 7]. Recently this number has fallen as low as 7 % [36], likely due to early imaging detection and aggressive treatments. Nevertheless, Burlew and Biffl noted that regardless of the grade of injury to the vertebral arteries, there is a stroke risk of approximately 20 % [37].

Conservative, surgical, and endovascular management are the different methods we have to treat patients with vessel injury in the trauma population. First, conservative medical management should be considered prior to any intervention. In the event that an intervention is needed, the surgical methods have proven over time to be effective. Endovascular therapy, compared to surgery is in its infancy, and there have been promising results with decreased morbidity and mortality reported in the literature.

The Conservative Approach—Maximizing Medical Therapy

Medical therapy using either antiplatelet or anticoagulation medications [3, 7, 32] is the

first-line treatment in many but not all head and neck vascular injuries. When using anticoagulation such as a heparin drip, heparin should not be bloused and the prothrombin time (PTT) goal should be between 60–80 barring any contraindications from a trauma standpoint. In situations where heparin induced thrombocytopenia may be an issue, weight-based enoxaparin or fondaparinux could be substituted. The goal of anticoagulation would be to prevent further embolic strokes [38]. In the event of contradictions to heparin and/or other anticoagulants, antiplatelet agents can be used especially when anticoagulants are contraindicated in high-risk bleeding patients from either intracranial or major solid organ injuries [21].

If the patient's symptoms stabilize or improve, a full course of anticoagulation (for example, oral warfarin or subcutaneous therapeutic enoxaparin) for a minimum of 6 weeks with follow-up imaging is indicated. Once the imaging shows that the dissection has improved, the patient may be switched to an antiplatelet agents for the remainder of the treatment. This may be either full-dose aspirin or clopidogrel. Upon complete resolution of the dissection, usually at the 6 month follow-up, further anticoagulant or antiplatelet agents may not be discontinued.

The Surgical Approach—Proven Over Time

A surgical intervention for primary repair of carotid artery dissections is rare, and when it does occur, it is usually associated with other injuries (a neck hematoma, sharp dissection of the carotid artery, or propagating thrombosis within the carotid artery). For dissections that affect the intimal layer of the vessel, surgical techniques not limited to a thrombectomy, arteriorrhaphy, end-to-end anastomosis, EC-IC bypass, grafting of prosthesis, and in the most severe cases ligation of the carotid artery may be required [3, 10, 11, 39]. In rare instances, surgical exploration may be warranted if arteriography shows damage to the carotid artery that cannot be repaired from an endovascular perspective [39] or when vascular reconstruction is required in an unstable patient with/without active bleeding [30].

Surgical intervention for the vertebral artery is difficult owing to its relatively deep location in the neck, the narrow caliber of the vessel, and the partial bony course of the vessel in the cervical spine. The redundancy or frequent anastamosis with other surrounding vessels of the vertebral arteries is particularly useful; in the event that injury has occurred to the vertebral artery, it is possible for one of the arteries to be ligated, clipped, or packed with bone wax in the trauma setting [36] without severe neurological deficits. Nevertheless, if the injured vertebral artery is dominant in configuration and there is insufficient collateral supply from the anterior circulation (internal carotid arteries), unilateral sacrifice of the vertebral artery can lead to devastating consequences.

The Endovascular Approach—First-Line Alternative to Conservative Treatment

Endovascular approaches to vascular injuries have markedly expanded and matured over the past two decades. Timing, whether for a diagnosis study or intervention, should be carefully considered in an unstable trauma patient. With an acutely injured ICA, some advocate waiting 48–72 h prior to any catheterization due to the risk of additional stroke from catheter manipulation [40]. It is our opinion that with recent advancements in catheter technology, if the patient is in stable condition, the risk of causing a stroke from catheter manipulation would be similar to a standard diagnostic procedure. Earlier endovascular intervention would help decrease the morbidity especially in a polytrauma situation where other interventions are required.

Initial evaluation of the head and neck vessels using DSA as the modality of choice, can give information that MRA and CTA cannot. In particular, DSA can assess the degree of collateral flow from the contralateral side in the anterior circulation (ICAs) and if the posterior circulation

is supplied by the anterior circulation via a feta posterior communicating artery; it can also help determine the magnitude of flow between these two vascular intracranial territories. Such information is useful in determining whether a symptomatic injured vessel should be treated by open surgical repair, endovascular stenting, or if the vessel can be sacrificed. For example, a patient with a vertebral artery dissection with recurrent posterior circulation strokes despite maximal medical therapy can be a candidate for endovascular sacrifice if there is collateral flow to the basilar and posterior circulation from the contralateral vertebral artery or a fetal artery supplying from the anterior circulation.

Often times when distal flow is compromised from the vascular injuries, seen in a significant dissection, a stent will likely be required to reestablish the true lumen and to prevent additional strokes [41]. Rodriguez et al. reported two cases where treatment of carotid dissection with stents resulted in favorable outcomes without any stenosis at the site of injury [42]. Additionally, Coldwell et al. showed that pseudoaneurysm formation from a blunt injury to the carotid can be safely treated with stenting followed by anticoagulation, however close follow-up at 2 and 6 month intervals were necessary [43]. Although not currently FDA approved, flow diverters have been used off-label, in order to treat severe intracranial dissections with associated pseudoaneurysms [44]. Patients treated with stenting or flow diverters will ultimately require full anticoagulation and/or antiplatelet agents [21] for some duration of time, keeping in mind that up to 30 % of the population may be non-/partial-responders to clopidogrel [45]. It is our practice to keep patients with stents or flow diverters on dual antiplatelet therapy (aspirin 325 mg and clopidogrel 75 mg daily) for at least 3–6 months, and thereafter aspirin daily indefinitely.

It is important to mention other vascular formations arising from traumas can also been detected and treated by a neurointerventionalist. For example, arteriovenous fistulas (AVFs) and carotid cavernous fistulas (CCFs) can develop in a delayed fashion in such patients [46].

Finally, the formation of traumatic intracranial aneurysms should be kept in mind in trauma patients. Such aneurysms harbor an approximation of 50 % chance of rupture within the first week following injury [8]. As in ruptured or incidentally found cerebral aneurysms, similar techniques are used in treatment for traumatic cerebral aneurysms [28]. Traumatic pseudoaneurysms tend to arise in a location where typical intracranial aneurysms are not normally formed (see example in Fig. 10.1). Unfortunately, the only way to differentiate between these two types of aneurysms is through histopathologic studies [8]. Nevertheless, treatment should be implemented either with coils alone or deploying stents in conjunction with coil embolization. Kanasagra et al. reported a 61 % interventional treatment rate after examining 100 total arterial lesions resulting from trauma, with an associated 3.9 % complication rate [28].

In the event that the traumatic aneurysm cannot be treated from an endovascular perspective, open cerebrovascular surgery can be performed. But as newer technology is developed, the subset patients requiring surgical intervention is diminishing. It is known that surgery for ruptured aneurysms has an upfront increase in morbidity/mortality compared to endovascular surgery [47]; in trauma patients the risks would likely be even higher.

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Vertebral Artery Injuries in Penetrating Neck and Cervical Spine Trauma

11

Ralph Rahme and John F. Hamilton

Arterial injuries occur in 15–25 % of penetrating neck trauma. However, the majority of these (up to 80 %) involve the carotid arteries [22]. Given their smaller size and deeper location, often surrounded by bone, penetrating vertebral artery (VA) injuries are rare, with an incidence ranging from 1 % in gunshot wounds to 7.4 % in stab wounds to the neck [11, 27]. VA injuries tend to be particularly prevalent in penetrating trauma to the upper cervical spine, i.e., the craniocervical junction and atlantoaxial space [5, 23]. Given their associated risks of hemorrhage and cerebral ischemia, arterial injuries can negatively affect impact outcomes after penetrating neck trauma and, thus, should be promptly recognized and treated. While carotid artery injuries tend to be particularly devastating, leading to stroke and death in as many as 15 and 22 % of patients, respectively, VA injuries may also result in significant morbidity and mortality and are frequently associated with cervical spine injuries, given their close proximity to the spine [22]. The most common trauma mechanisms responsible for penetrating VA injuries seem to vary depending on the setting, with gunshot and blast injuries predominating in military combat, while stab and gunshot injuries being most common in civilian trauma [1, 7, 10, 15, 28].

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Anatomy of the VA (Fig. 11.1) [4, 17]

The VA usually arises from the posterosuperior aspect of the subclavian artery, of which it constitutes the first major branch. It ascends in the lower neck for a short distance, then enters the foramen transversarium of C6 (although, in 7 % of cases, it may enter C7, C5, or even C4). It continues to ascend within and between the foramina transversaria of the cervical spine, forming a wide lateral loop between C2 and C1. It then exits the foramen transversarium of C1 and turns medially behind the lateral mass of C1 and the atlanto-occipital joint, courses on a shallow groove on the superior aspect of the posterior arch of C1, before it pierces the posterior atlanto-occipital membrane and underlying foramen magnum dura. Intradurally, the VA ascends on the anterolateral aspect of the cervicomedullary junction, where it gives rise to the posterior inferior cerebellar artery (PICA), then joins the contralateral VA to form the basilar trunk, anterior to the pontomedullary junction. The anterior spinal artery (ASA) occasionally arises from the distal VA, just proximal to the vertebrobasilar junction. Likewise, the artery of the cervical enlargement, a

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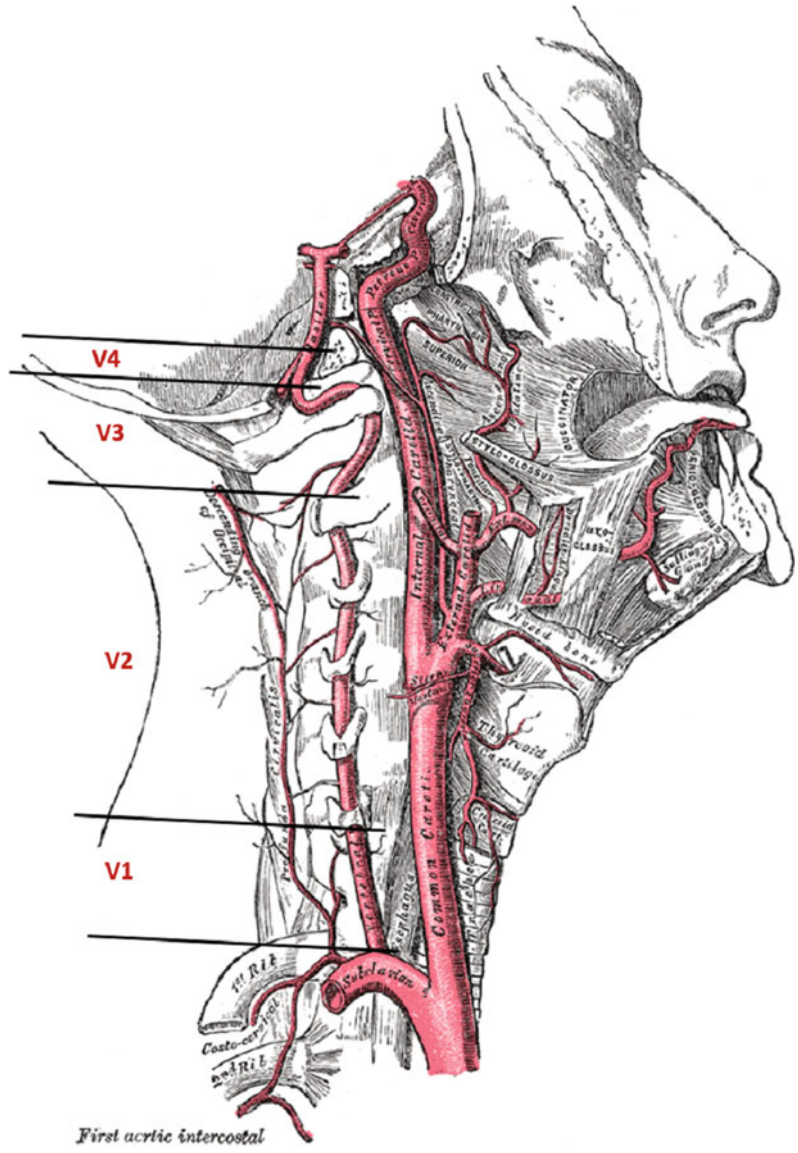

Fig. 11.1 Anatomy of the vertebral artery [modified from: Gray H, Lewis WH. Anatomy of the human body (20th ed). Philadelphia, PA: Lea & Febiger 1918]

large radiculomedullary artery to the cervical spinal cord, may arise from the cervical VA.

The VA is anatomically and angiographically divided into 4 segments:

- V1 (ostial segment), from its origin to its entry into the foramen transversarium of C6;
- V2 (foraminal segment), from its entry into the foramen transversarium of C6 to its exit from the foramen transversarium of C2;
- V3 (suboccipital segment), from its exit from the foramen transversarium of C2 to its dural entry;
- V4 (intradural segment), from its entry into the dura to the vertebrobasilar junction.

V2 is the longest segment, which is surrounded and protected by bone throughout most of its course. Therefore, although relatively less vulnerable to injury than other VA segments, it remains the most difficult to access surgically. Throughout their course, the V2 and V3 segments of the VA are surrounded by a dense vertebral venous plexus and give rise to muscular branches that anastomose with those of other major cervical arteries, including the ascending and deep

cervical arteries (branches of the thyrocervical and costocervical trunks of the subclavian artery, respectively), and the ascending pharyngeal and occipital arteries (branches of the external carotid artery (ECA)). The V3 segment also often gives rise to the posterior meningeal artery, which vascularizes the dura of the foramen magnum and posterior fossa.

Given that a robust collateral circulation usually exists in the vertebrobasilar system, including a contralateral vertebral artery and 2 posterior communicating arteries (PComAs) that can potentially backfill from the internal carotid arteries (ICAs), acute occlusion of 1 VA is usually well tolerated by the vast majority of people, and the rate of cerebral ischemic complications in this setting is very low, in the range of 2–3 % [14]. The latter typically occur in people with a hypoplastic contralateral VA and small or hypoplastic PComAs. Likewise, partial injuries to 1 VA (e.g., dissection) with preservation of anterograde flow carries a potential risk of posterior circulation stroke secondary to thrombus formation at the site of injury and distal propagation or embolization into the vertebrobasilar system.

Zones of the Neck (Fig. 11.2)

From a penetrating trauma perspective, the neck has been traditionally divided into 3 anatomic zones, each with its specific vascular and visceral contents and relative ease of surgical accessibility. The location of the entry wound with respect to these anatomic zones is often used by trauma surgeons to guide acute management [21, 22].

- Zone I extends from the sternal notch and clavicles inferiorly to the cricoid cartilage superiorly.
- Zone II extends from the cricoid cartilage inferiorly to the angle of the mandible superiorly.
- Zone III extends from the angle of the mandible inferiorly to the base of the skull superiorly.

In their course toward the skull, the VAs cross all 3 zones of the neck and, thus, can be virtually injured in penetrating trauma to any of these zones. In contrast to zone II, zones I and III are difficult to expose surgically (because of the sternum/clavicle head and mandible, respectively) and, thus, endovascular techniques are often preferred when managing unstable vascular injuries in those zones.

Table 11.1 Denver classification system

Grade I: arterial dissection with less than 25 % luminal narrowing
Grade II: arterial dissection with more than 25 % luminal narrowing
Grade III: pseudoaneurysm
Grade IV: occlusion
Grade V: transection

Patterns of VA Injury

The Denver classification system (Table 11.1) is often used to characterize blunt traumatic cerebrovascular injuries [3]. Although originally devised for blunt trauma, this classification system can also be easily applied to penetrating cerebrovascular injuries. In the setting of penetrating trauma, transection (grade V) and pseudoaneurysm formation (grade III) are particularly common injury patterns and may result in active hemorrhage (external bleeding, expanding neck hematoma, extravasation on CTA or angiography) or vertebral arteriovenous fistula (vertebral venous plexus or internal jugular vein). In one of the largest reported series from South Africa, the authors examined 92 penetrating VA injuries sustained in the civilian setting over a period of 16 years [15]. Among 88 patients who underwent angiography, they identified 39 VA

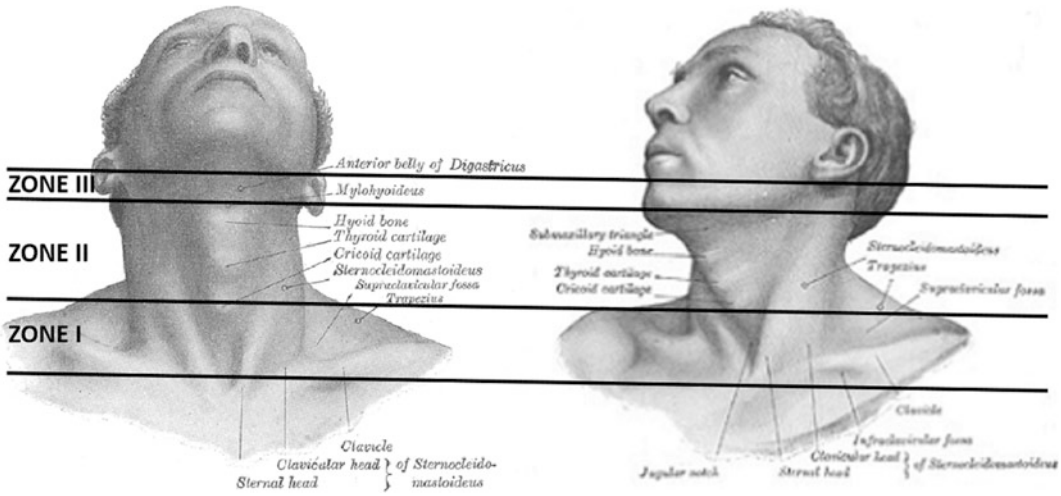

Fig. 11.2 Zones of the neck [modified from: Gray H, Lewis WH. Anatomy of the human body (20th ed). Philadelphia, PA: Lea & Febiger 1918]

occlusions, 36 pseudoaneurysms, 11 AVFs, and only 2 intimal injuries. Likewise, in a recent US military study of 11 penetrating VA injuries sustained in Iraq and Afghanistan over a period of 10 years, there were 5 pseudoaneurysms, 4 occlusions, 1 AVF, and 1 dissection [7].

Associated Injuries

Associated injuries are common in the setting of penetrating neck trauma and are more likely to affect patient outcome than the VA injury itself [7, 12, 15, 28]. Bony injuries, including cervical spine and facial fractures, are observed in 10–70 % and are more common in the military setting, given the higher incidence of gunshot and blast injuries [7]. Likewise, spinal cord and nerve injuries (cranial nerves, brachial plexus) occur in 20–30 %, and are more common in combat-related trauma. Vascular injuries, both arterial (carotid vessels, axillary/brachial artery) and venous (vertebral venous plexus, internal jugular vein) are seen in approximately 15 %. Finally, aerodigestive tract injuries (esophagus, pharynx, larynx, trachea) affect roughly 10 % of patients.

Principles of Management

Initial management of patients with penetrating neck trauma follows the Advanced Trauma Life Support (ATLS) guidelines and largely depends on whether signs of active bleeding or hemodynamic instability are encountered in the primary survey [21].

Unstable Patients

Patients presenting with active hemorrhage from the neck (external bleeding or expanding hematoma) or hemodynamic instability should undergo emergent surgical exploration (for all zones, particularly zone II) and/or emergent angiography (for zones I and III) to identify and repair the injured vessel [21]. If a VA injury is encountered, reasonable efforts should be made to preserve the continuity of the vessel whenever possible. However, given the small caliber of the VA, the often complex pattern of injury, and the limited surgical access to its V2 segment, reconstructive surgical strategies (i.e., primary repair) are seldom successful and vessel sacrifice (i.e., surgical ligation)

often becomes necessary. Conversely, emergency endovascular treatment, when available, offers the possibility of vessel preservation via placement of a covered stent graft across the injured VA segment or via stent-assisted coil embolization of a pseudoaneurysm or AVF [1, 10, 28]. Thus, when a hemorrhagic VA injury is encountered intraoperatively, surgical packing or tamponade with bone wax or a Fogarty balloon catheter (if bleeding from within the foramen transversarium) can be attempted, since it may provide temporary control of bleeding and allow a more definitive, potentially reconstructive, endovascular procedure (Fig. 11.3). It should be kept in mind, however, that stent-based endovascular reconstruction mandates dual antiplatelet therapy for several months after the procedure, to reduce the risk of in-stent thrombosis and secondary vertebrobasilar embolic stroke. Therefore, the hemorrhagic risks associated with dual antiplatelet therapy in the setting of a penetrating neck injury should be carefully considered when making the decision to stent an acutely injured VA.

When an artery cannot be reconstructed, both proximal and distal vascular control is generally required and can be accomplished either via direct surgical ligation or via endovascular embolization using platinum coils and/or liquid embolic agents (NBCA, Onyx). Fortunately, the rate of cerebral ischemic complications following acute unilateral VA occlusion is very low, in the range of 2–3 % [14]. In the endovascular setting, this can be further reduced by performing a complete cerebral and cervical angiogram prior to embolization, including the contralateral VA, bilateral ICAs, and ECAs, and bilateral thyrocervical and costocervical trunks (or subclavian arteries), to fully assess the extent of cervical and intracranial collaterals. In some cases, a balloon occlusion test of the injured VA can be performed prior to embolization, to confirm the presence of an adequate intracranial collateral circulation [10]. Endovascular access to the distal VA stump can be achieved either anterogradely via the proximal VA (in incomplete transections or lacerations) or retrogradely via the contralateral VA. However, distal vascular control is not always necessary after VA injury. In fact, in many cases, poorly developed distal cervical collaterals to the injured VA result in marginal retrograde flow and ultimately thrombosis and occlusion of its distal stump. Thus, if no significant retrograde angiographic filling or active bleeding is encountered from the distal VA stump, distal control can be safely omitted (Fig. 11.3). In the unlikely event of vertebrobasilar ischemia developing after unilateral VA occlusion, consideration may be given to surgical revascularization (e.g., ECA-VA bypass) at a later time.

Stable Patients

Patients with penetrating neck trauma who are hemodynamically stable should undergo a thorough physical examination followed by a CTA of the neck to determine the wound tract or trajectory and rule out underlying vascular or aerodigestive tract injuries [21, 22]. In the past, all zone II injuries were routinely surgically explored, given the relatively straightforward surgical access to that part of the neck. However, due to the high negative exploration rate encountered with this strategy, there has been a major paradigm shift over the past two decades, moving from mandatory neck exploration of all zone II injuries toward selective operative management based on the findings of CTA. Multidetector CTA has been shown to be a highly sensitive (90–100 %) and specific (90–100 %) imaging modality for traumatic vascular and visceral injuries. However, when bone fragments or metallic foreign bodies overlie the VA, beam-hardening artifacts may result in suboptimal visualization of the vessel. Thus, when CTA is inconclusive or doubt persists regarding a possible VA injury despite a negative CTA (e.g., wound trajectory crosses VA), catheter angiography should be performed, as it remains the gold standard for vascular imaging.

The optimal management of hemodynamically stable penetrating VA injuries remains largely uncertain, given the rarity of these injuries, resultant paucity of the literature, marked only by a few retrospective case series of small sample

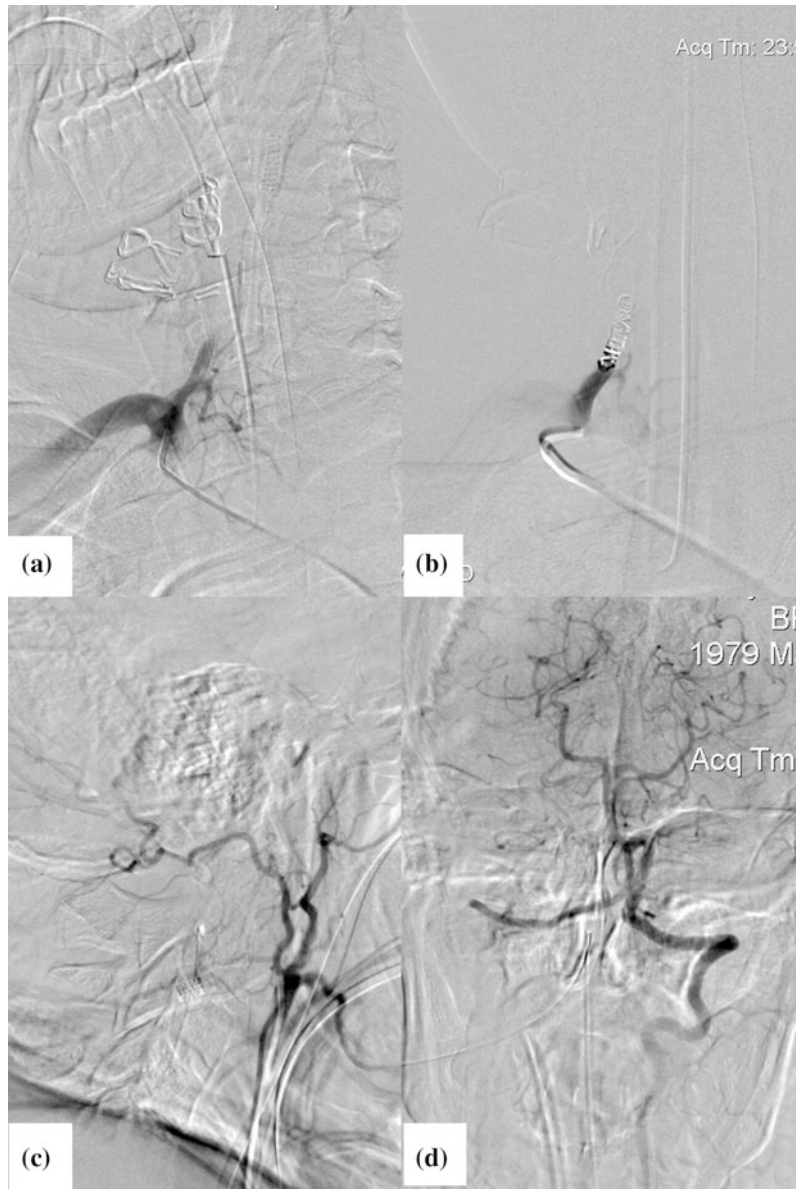

Fig. 11.3 A 34-year-old man sustained a stab injury to the neck (zone II) using a knife. He presented with profuse bleeding from the neck and hemodynamic instability. Emergent surgical exploration of the neck revealed active hemorrhage from transection of the V1 segment of the *right* VA. Surgical ligation was attempted, but was unsuccessful. The wound was packed allowing temporary hemostasis and the patient was transferred emergently to the neurointerventional suite. **a** *Right* subclavian artery injection demonstrates occlusion of the *right* VA in its V1 segment, likely as a result of surgical packing. There is no evidence of contrast extravasation or distal collateralization of the VA from the ascending and deep cervical arteries. **b** The proximal stump of the VA was occluded with coils to achieve permanent hemostasis. **c** *Right* external carotid artery injection shows no evidence of distal collateralization of the *right* VA. **d** *Left* VA injection reveals excellent flow in the basilar artery and retrograde filling of the V4 and distal V3 segments of the occluded right VA. Given that no opacification whatsoever of the distal VA stump was demonstrated, distal control was deemed unnecessary. The patient was subsequently taken back to the operating room and the packing was successfully removed, without any evidence of residual active hemorrhage. He had an uneventful post-operative course and remained neurologically intact

sizes [1, 7, 9, 10, 12, 15, 28], and their unknown natural history. Treatment of stable penetrating VA injuries usually varies with the type and severity of injury. In general, endovascular treatment is usually preferred over surgery, given its lower risk of complications, high technical success rate, and the possibility of vessel preservation [1, 10, 28].

Intimal Injury/Dissection (Denver Grades I and II)

The main risk of these injuries lies in their potential for thrombus formation and distal propagation or embolization into the vertebrobasilar circulation, which may result in life-threatening cerebellar, brainstem, or cerebral infarctions. To minimize this risk, patients with VA dissection have traditionally been managed with antithrombotic agents [7]. Compared with antiplatelet therapy (aspirin), anticoagulation with heparin and warfarin seems to carry a significantly higher rate of hemorrhagic complications, without clear superior efficacy [8]. Moreover, new data suggests that VA dissections with <50 % luminal narrowing are associated with a very low risk (<2 %) of posterior circulation stroke [20]. Therefore, the potential benefits of antithrombotic medications should be carefully weighed against their hemorrhagic risks in the setting of penetrating neck trauma. In our practice, VA dissections are usually treated with aspirin only and anticoagulation is seldom used, while antithrombotic therapy is withheld in patients with significant hemorrhagic risks. Though evidence of its superiority over aspirin is lacking, anticoagulation may be considered in patients with high-grade intimal injuries causing severe flow limitation, particularly those with an intraluminal thrombus. We reserve endovascular treatment (i.e., stent placement) for those rare cases of symptomatic vertebrobasilar insufficiency secondary to flow-limiting VA dissection with marginal distal collateral flow, and for cases that fail medical therapy. In the latter indication, a deconstructive endovascular procedure (unilateral VA sacrifice) may be considered when stent placement is not an option (e.g., technically unsuccessful procedure or contraindication to dual antiplatelet therapy).

Occlusion (Denver Grade IV)

Given the lack of anterograde flow, VA occlusions do not usually carry a prospective risk of distal embolization and, thus, do not require antithrombotic therapy [7, 15]. However, CTA may lack specificity to differentiate a true VA occlusion from a subocclusion (i.e., string sign). In cases of uncertainty, a catheter angiogram should be performed to make this distinction (Fig. 11.4). The latter is important because, in contrast to complete occlusions, subocclusive VA injuries carry a risk of posterior circulation stroke. As stated above, the vast majority of unilateral VA occlusions are well tolerated and do not result in cerebral ischemia. In contrast, most bilateral acute VA occlusions are symptomatic and often lead to brainstem infarction [6]. Approximately one third of traumatic VA occlusions tend to heal and recanalize on follow-up imaging [19]. If symptoms of vertebrobasilar insufficiency develop as a result of VA occlusion, consideration may be given to perfusion imaging and surgical revascularization (e.g., ECA-VA bypass).

Pseudoaneurysm (Denver Grade III)

Pseudoaneurysms lack an arterial wall and are contained by surrounding structures in the neck. Despite some well-documented cases of spontaneous resolution, VA pseudoaneurysms are associated with a significant hemorrhagic risk and, thus, usually require treatment [15]. Likewise, pseudoaneurysms can be a site for thrombus formation and distal embolization, thus resulting in posterior circulation stroke. Notwithstanding, small pseudoaneurysms in asymptomatic and clinically stable patients may be managed expectantly with serial angiography, and treated only if clinical worsening or radiographic progression occurs [1]. Endovascular

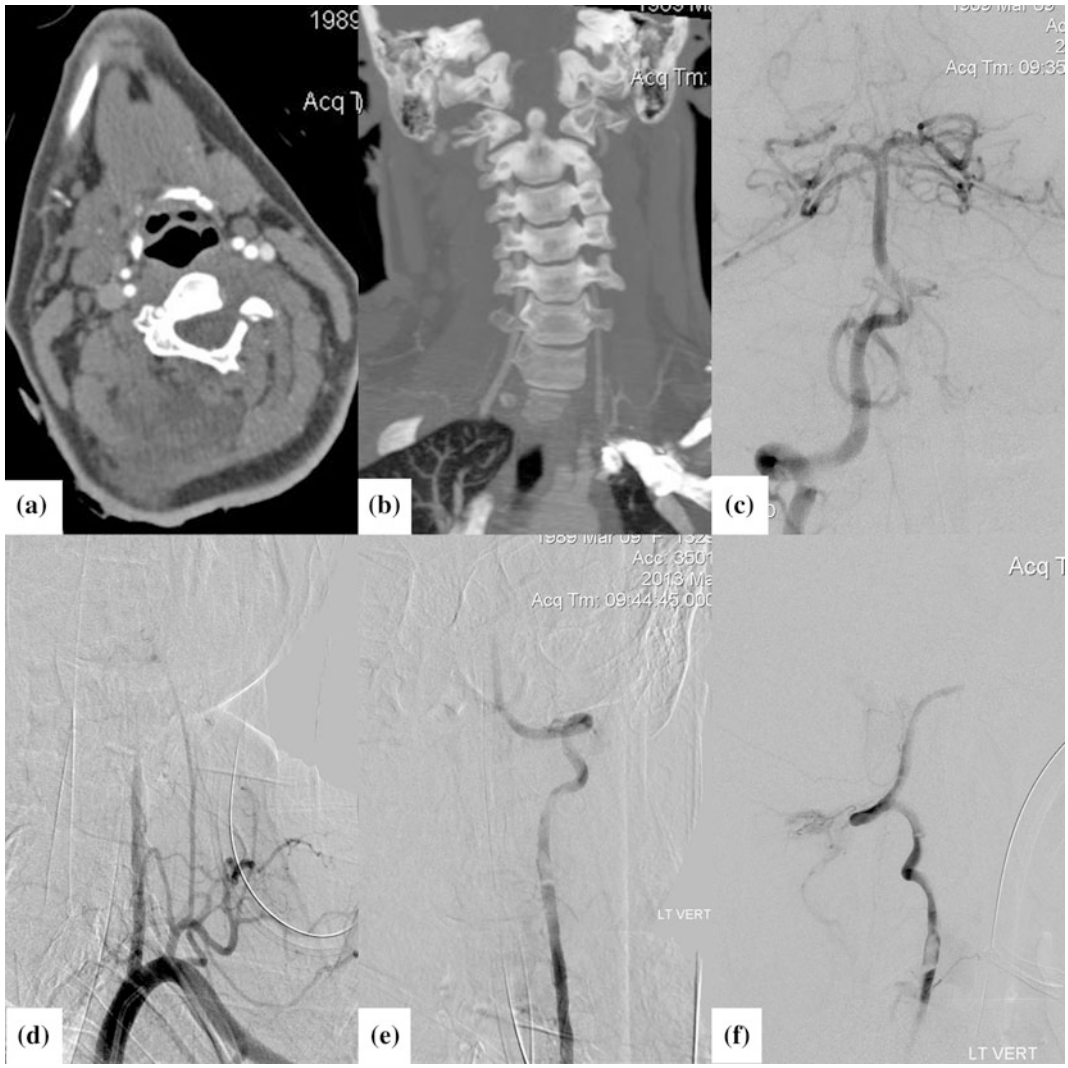

Fig. 11.4 A 24-year-old woman sustained a stab injury to the back of her neck using a knife. Although the entry wound was on the *right side*, she presented with a *left* Brown-Séquard syndrome. **a**, **b**, CTA of the neck demonstrates the oblique trajectory of the stab wound, which crosses the midline from *right* to *left*, traverses the *left side* of the spinal canal, and reaches the *left* foramen transversarium. As a result, there is evidence of injury to the *left* VA with seemingly complete occlusion in its V2 segment. Catheter angiography was performed to better characterize the VA injury. **c** *Right* VA injection reveals excellent flow in the basilar artery and retrograde filling of the V4 segment of the injured *left* VA, including the *left* PICA. **d–f**, *Left* subclavian artery injection shows, in contrast to CTA findings, that the left VA is in fact patent with very slow anterograde flow, secondary to subocclusive dissection of its V2 segment at the C3-4 level. The patient was anticoagulated with intravenous heparin followed by a 3-month course of oral warfarin. She did not experience any cerebral ischemic complications related to her VA injury and exhibited gradual neurological improvement from her incomplete SCI

techniques are usually preferred, given the possibility of vessel preservation. Reconstructive options include covered stent grafting or stent-assisted coil embolization, both of which mandate several weeks of dual antiplatelet therapy [7, 10]. However, in some cases, vessel reconstruction is not possible and endovascular occlusion (coils, balloons, liquid embolic agents) or even surgical ligation of the injured VA becomes necessary.

Arteriovenous Fistula (Denver Grade III or V)

Traumatic AVFs of the VA usually involve the vertebral venous plexus or, less commonly, the internal jugular vein. The natural history of vertebral AVFs is unknown [15]. Approximately 30 % of vertebral AVFs can be asymptomatic, discovered incidentally after auscultation of a neck bruit. However, symptomatic vertebrobasilar insufficiency and ischemia may occur as a result of arterial steal. Likewise, myelopathy can develop secondary to reflux of arterial blood into the perimedullary venous plexus and the ensuing spinal cord venous hypertension. Cervical radiculopathy secondary to nerve root compression by the engorged epidural veins has also been described [1, 10]. While high-flow and symptomatic AVFs require treatment, slow-flow AVFs in asymptomatic and clinically stable patients may be managed conservatively with serial angiography, and treated only if clinical worsening or radiographic progression occurs [1]. Closure of the AVF and preservation of the parent artery are the main goals of treatment, which can be achieved using endovascular techniques (covered stent grafting or stent-assisted coil embolization) but usually require several weeks of dual antiplatelet therapy following treatment [7, 10]. In cases where vessel preservation is impossible, parent vessel occlusion or fistula trapping using coils, balloons, or liquid embolic agents may be performed. Surgical ligation is usually reserved for cases that fail endovascular therapy.

Prognosis and Outcome

In general, outcomes after penetrating neck injury are more often determined by associated injuries than by the VA injury itself. In fact, neurological deficits in this setting are almost always due to associated direct spinal cord or nerve root damage, rather than VA-related ischemic injury. In the 1970s, VA trauma was associated with mortality rates of 20–40 %. This figure has now fallen to below 10 % (typically 5–7 %), probably as a result of improved prehospital care and resuscitation, improved operative techniques, and most importantly development of the endovascular field [15, 28].

Penetrating Cervical Spine Injuries

Penetrating injuries to the spine and spinal cord are usually caused by blast and gunshot injuries, both in the military and civilian settings. Non-missile penetrating spinal injuries are much less common. In fact, the damage caused by stab wounds to bony and soft tissue structures is rarely severe enough to cause significant spinal injuries. Likewise, the incidence of stab-related spinal cord injuries (SCIs) is very low, given that bony elements often deflect sharp weapons away from the spinal canal. When they occur, stab-related SCIs are usually incomplete, with a partial cord injury being most common (Fig. 11.4), [13, 16, 26].

Gunshot injuries traversing the spinal canal are associated with a complete SCI in approximately 70 % of cases. Moreover, in about 30 % of cases, a bullet fragment is retained in the spinal canal. Nonetheless, SCI may occur in the absence of spinal canal penetration by the missile. In fact, in addition to direct tissue damage, gunshot wounds can lead to shock wave and cavitation injuries, both of which may result in remote tissue damage. This is particularly true for high-velocity gunshot injuries sustained in the military setting, while less commonly seen with low-velocity civilian gunshot wounds [2, 26]. In contrast, spinal column injuries caused by gunshot wounds are rarely biomechanically unstable (<1 %) and, thus, field immobilization of the cervical spine with a rigid cervical collar is sometimes appropriately omitted to avoid delays in care, particularly when more serious and potentially life-threatening injuries in the setting of penetrating neck trauma require direct close monitoring (e.g., expanding neck hematoma, airway compromise) [2, 13, 26]. More recent evidence, however, suggests that the rate of cervical spine instability requiring surgical fusion or halo immobilization following civilian gunshot wounds may be as high as 30 % when there is

evidence of concomitant SCI [2]. These authors recommend intervention (surgery or halo) when there is evidence of either a 3-column injury or a 2-column injury with pedicle involvement [2]. Biomechanically unstable spine injuries (and SCIs) are much more common with blast injury, such as in the military setting, where a complex interaction of penetrating, blunt, and concussive trauma occurs [7, 18].

Management decisions for penetrating spine trauma are frequently based solely on clinical and CT findings, given that MRI is often contraindicated in this setting due to the presence of retained metal foreign bodies. Strong magnetic fields may cause displacement or heating of metal fragments, with potential for neurological deterioration. While some authors have suggested that MRI can be performed with minimal risk to the patient [2], the editors of this work suggest great caution for several reasons. Although it is true that the majority of projectiles from civilian firearms are a combination of lead and copper, many bimetallic (steel and copper) jacketed rifle and pistol bullets are readily commercially available. In addition, much of the ammunition for sporting shotguns is made from steel shot to prevent environmental toxicity when fired over water. Finally, the editors' experience in combat settings where steel is commonly used in artillery and mortar rounds and improvised explosive devices coincides with the unfortunate reality that these weapons may be used in our cities in the near future and certainly impact imaging decisions in such terrorist events. If MRI is considered, the possibility that ferrous fragments may be present and their proximity to neural and vascular structures should be taken into account, and the patient must be informed of the potential risks.

Medical management of patients with penetrating spine injuries is limited to external cervical immobilization (rigid collar) when indicated and hemodynamic support (maintenance of mean arterial pressures above 80 mm Hg) when there is associated SCI. Prophylactic antibiotics are controversial and may lead to selection of multidrug-resistant bacteria [2]. In general, the indications for surgery are rare. Apart from spinal instability requiring fusion, those include:

- spinal cord impingement (e.g., bone fragments, epidural hematoma, foreign body) requiring surgical decompression,
- persistent cerebrospinal fluid fistula (despite maximal conservative treatment, including skin closure and lumbar drainage) requiring surgical repair, and
- infection requiring surgical debridement [2].

Prophylactic removal of retained bullet fragments from the cervical spinal canal is usually not recommended, since it has not been shown to enhance functional recovery or reduce infections, and may be associated with complications [2, 24–26]. In rare instances, retained bullet fragments have been associated with late neurological decline, as late as 15 years following the injury, presumably secondary to scarring. In such cases, bullet removal and excision of reactive fibrous tissue can be attempted [2, 26]. In contrast, retained sharp foreign bodies in stab wounds should be removed early to prevent infection and delayed neurological worsening [27].

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Clearing the Cervical Spine in Blunt Trauma

12

Margaret M. Griffen

Cervical spine injury in the trauma patient is a devastating injury and occurs in 2–6.6 % of patients [1, 2]. Most injuries are diagnosed at the time of injury evaluation but the less than 1 % of injuries not found have generated the greatest amount of concern and controversy. Management of the patient with a cervical spine injury involves the coordinated care of the trauma team and spine specialist. This chapter's focus is not the diagnosis or management of the patient with a cervical spine injury. The main focus of this chapter is to discuss the clinical evaluation, imaging modalities and potential options for removal of the cervical collar in those patients without an identified injury. Patients without cervical spine injury require an organized plan for clearance of the cervical spine and removal of the cervical collar. Recent literature support the early removal of the cervical collar because of skin breakdown, the impact on intracranial pressure (ICP), ventilator days, ICU length of stay and hospital length of stay, as well as, pneumonia and delirium rates. The physical condition of the patient and their other injuries impact the available options for clearing the cervical spine. Through the years some of the controversies surrounding the clinical exam, imaging and clearance options for the C spine have been settled but many still exist.

Clinical Evaluation

In the alert and cooperative patient standard criteria has been evaluated and verified to provide an appropriate method to clear the C spine and remove the collar without imaging. In 1998 Hoffman et al. proposed a clinical evaluation tool for the awake trauma patient without posterior midline neck pain, neurologic deficit, altered mental status and/or a distracting injury [3]. If the physical examination was negative then the cervical collar (C collar) could be removed without imaging. This same group validated their findings with a much larger sample size in 2000 involving 34,000 patients [4]. In 2001 Stiell et al. published the Canadian C spine rules which again identified a safe strategy for clinical evaluation alone for clearing the cervical spine [5]. Twenty-five clinical variables were incorporated and the final rules require an answer to three main questions; are there any high-risk factors that mandate imaging, any low-risk factors that allow for safe assessment of range of motion and is the patient able to actively rotate their neck. The answers to these questions determine the need for imaging or not. Although many trauma centers today do not have a standard protocol for evaluation and clearance of the cervical spine, most agree that a clinical exam in an appropriate

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patient will allow removal of the C collar without imaging [6]. The Eastern Association for the Surgery of Trauma (EAST) Practice Management Guidelines (PMG) for cervical spine were updated in 2009 and state that in the awake trauma patient with blunt mechanism the C collar may be removed without imaging if the patient has no neck pain, no neurologic deficit and full range of motion [7].

Imaging

For all blunt trauma patients not meeting clinical clearance criteria an imaging study is needed to screen for cervical spine injury. Patients needing imaging of the cervical spine include those with neck pain, altered mental status, neurologic deficit, and/or a distracting injury. The diagnosis of a distracting injury is subjective and has been the focus of several research projects attempting to determine its true impact on clinical exam. In 2012 Rose et al. looked at 1000 patients deemed to have distracting injury and documented their neck exams [8]. It was found that even with a "distracting injury" a negative clinical examination had a 99 % negative predictive value. Distracting injury does continue to be an indication for imaging.

The highest quality imaging study would be the one with the least risk to the patient and the greatest ability to identify an injury. Prior to the development of computed tomography (CT) scanning, plain radiographic evaluation of the C spine was standard of care in the blunt trauma patient. As early as 1993 concern for the accuracy of plain radiographs to diagnose cervical spine injury was being questioned [9]. During the early 2000s several researchers compared the use of plain radiographs with CT scan for evaluation of the cervical spine [10, 11]. The consistent result was that plain 3-view or 5-view imaging of the cervical spine missed between 30 and 40 % of cervical spine injuries. The gold standard screening modality in the adult blunt trauma patient is CT scan from the occiput through the first thoracic vertebrae. The EAST PMG guideline in 2009 was revised and states that CT scan is the screening modality of choice in this patient population.

Screening CT Scan Is Positive

Patients with blunt trauma and positive findings on CT scan of the cervical spine should have spine consultation and a treatment plan as appropriate.

Screening CT Scan Is Negative

The best way to avoid any unplanned event is to have an organized plan of attack for a particular situation as evidence will allow. The plan for a patient with negative screening C spine CT scan will be determined based on patient condition. However, the use of a standard protocol for any trauma center will maintain consistency and avoid potentially dangerous practice patterns. The various patient populations will now be presented and the potential best practice pattern proposed.

The Alert Patient

The alert patient with neck pain who requires imaging for possible cervical spine injury must then have an organized treatment plan for the cervical spine when the CT scan is negative. The first major decision is does the collar stay on or not. The practice of a clinical exam after resolution of any mental status change or distracting injury for the determination of continued neck pain is alluded to throughout the literature. Como et al. discuss clearing patient cervical spine and removing the collar once the patient has resolved their mental status concerns and a reliable exam can be completed [12]. Using the clinical examination at a later time in the hospitalization for clearing the C spine and removing the collar after having had a negative CT scan is a safe practice.

The alert patient with continued neck pain and/or neurologic deficit after negative CT scan

imaging will remain in the collar and further imaging may be necessary. Flexion and extension films can provide a dynamic evaluation of the cervical spine and assess potential instability of the ligaments. The timing of flexion and extension films impacts the quality of the films toward completing the evaluation and clearing the C spine. In the acute setting there has been concern with use of flexion and extension films because of muscle spasm and an inability to have the patient adequately flex or extend the required 30 degrees. The patient body habitus may also impact the success of the films to imaging the C7–T1 junction. Two recent studies demonstrated great limitations to flexion and extension films in the acute phase of care. McCracken in 2012 did a retrospective review of their team's standard practice at the time of flexion-extension films in patients with a negative CT scan and continued neck pain. The overall rate of adequate films was 19.8 % and no useful data was gathered by completing flexion-extension films in the acute setting [13]. This team reviewed 1000 flexion and extension films and found 80 % to be inadequate to assess the cervical spine. The authors do not recommend the use of flexion and extension films in the acute phase of care to supply any additional information that would allow for clearance of the C spine and removal of the collar. There is some support for use of flexion and extension films in a later phase of recovery when muscle spasms have resolved to improve the ability to get adequate films. Khan et al. in 2011 reviewed the use of flexion and extension films in the acute setting and had similar conclusions to the above studies but did recommend the continuation of the cervical collar for patients with a negative CT and neck pain. Follow-up in clinic 7–10 days later with clinical exam should be completed and if neck pain persists flexion and extension films in this more chronic stage is warranted [14].

Magnetic resonance imaging (MRI) has also been used in this patient population for clearing the C spine. Although not a dynamic study to evaluate the cervical spine MRI can identify ligamentous injury, soft tissue injury, spinal cord contusion and disc herniation better then CT scan. Several studies have suggested the use of MRI in this patient population will allow for earlier clearance of the cervical spine and collar removal.

The final option in this group of awake patients is continuation of the collar and reevaluation in an outpatient setting for resolution of pain and collar removal versus continued pain and further imaging. The potential for losing patients to follow-up is always a concern.

The Obtunded Patient

The patient population that continues to be of the greatest debate is the obtunded or altered patient who has a physical exam that cannot be trusted. Many questions have arisen and some have answers rooted in evidence-based medicine but others continue to remain sources of controversy. A review of the most recent data to support the best evidence-based recommendations for clearing the cervical spine and removing the collar in the obtunded patient is provided. Data supports that with a negative CT scan it is unlikely that any ligamentous injury present is unstable and patients are stable in the cervical collar and may be mobilized as needed.

Four main options exist for managing the cervical spine and cervical collar in the obtunded blunt trauma patient. The use of flexion-extension films, the continuation of the cervical collar and no further imaging acutely, the use of MRI for clearance of the cervical spine or the removal of the C collar after negative CT scan and no evidence of neurologic deficit are all discussed in the literature. Flexion and extension films, although a dynamic study cannot be completed with patient participation and requires a healthcare provider to perform the flexion and extension of the neck. The inability to determine if the patient has pain or that potential harm is being done rules out this option as a viable plan for clearing the C collar in the obtunded patient. The use of dynamic flexion and extension cervical films to clear the neck in the obtunded trauma patient is not recommended.

Continuation of the cervical collar and no further imaging is an option for care. Concern for skin breakdown from prolonged use of the cervical collar has been studied for many years. The overall incidence has been shown to be 6.8 % in 2006 which is considerable lower than prior reports which were as high as 20–50 % [15–17]. This likely supports better ICU care and the attention to the risk of this potential complication. With the much lower risk for skin breakdown the continuation of the cervical collar for potential ligamentous injury can be safely recommended. The determination of length of time for the cervical collar has not been reviewed or studied and a recommendation cannot be made. Continuation of the cervical collar with a negative CT scan has been suggested to effect ICP levels, ventilator days and ICU length of stay. Because of these potential issues and the patient care impact a course for removing the collar in the obtunded patient is pursued.

All agree CT scan is highly sensitive for bony abnormalities in the cervical spine and the ligament and soft tissue are at risk for poor evaluation with CT alone. MRI evaluation of the cervical spine in the obtunded patient has been proposed as a diagnostic option to clear the cervical spine and allow the collar to be removed. It has been suggested that due to potential loss of sensitivity the MRI should be completed within 3 days of admission to avoid healing prior to diagnosis, but evidence-based support is lacking. Although the definition of the "obtunded" patient has varied between studies, several authors have recommended the routine use of MRI for evaluation of the cervical spine following negative CT scan in order to clear the C spine and remove the C collar. Positive findings on MRI range from 5 to 11 % in this patient population. Some findings were not felt to be clinically significant but change in treatment included 6 weeks of cervical collar use or operative intervention [18–20]. Muchow et al. in 2008 completed a meta-analysis of 5 level 1 diagnostic protocols related to the use of MRI in patient with negative CT scan and completed a statistical analysis. They concluded MRI should be the gold standard for clearing the C spine in clinically suspicious or unevaluatable patients as it had a negative predictive value of 100 % [21]. The authors do, however, discuss several limitations of the data analyzed because of patient inclusion variability. Since many of the patients in this category are critically ill the risks of transport, lack of nursing observation, patient positioning and time in MRI from a safety perspective has to be factored into the utility of the diagnostic study. The use of MRI has also increased cost of hospitalization.

The final option discussed in the literature is removing the cervical spine solely based on CT scan evaluation. Improvement in technology and imaging with multi-detector CT (MDCT) scans has resulted in less potential to miss a significant cervical spine injury [12, 22]. Recent studies have suggested MDCT scans have a negative predictive value for unstable cervical spine injury of 99–100 %. Chew et al. reviewed 1000 patients with CT scan and magnetic resonance imaging (MRI) for evaluation of the obtunded patient with blunt trauma and a negative CT scan of the cervical spine [23]. They found 125 "ligamentous" injuries on MRI however 82 % of this patient group had their collars removed within 17 days. By most treatment recommendations 17 days is not complete treatment for a "ligamentous" injury and suggests the patients were without risk for further injury. With this new data, recommendations from these authors have been, when the patient is neurologically intact and has a negative MDCT the collar may be removed without further imaging. Khanna et al. in 2014 reviewed 17,000 patients with GCS < 13, no neurologic deficit and negative CT of the cervical spine [24]. Of these 17,000 patients 521 had both CT scan and MRI evaluation of the cervical spine. Although 81 % had ligamentous or soft tissue injury on MRI no patient had their treatment plan changed based on MRI findings. In this patient population MRI was felt to add no information to the clinical management of the patient and not be of value. The Eastern Association for the Surgery of Trauma (EAST) in 2015 provided a conditional recommendation based upon a review of the current literature for removal of the cervical collar and

clearance of the C spine after negative CT scan alone in the obtunded patient [7].

Pediatric Patients

The pediatric population is unique and often the evidence-based support in the adult population is extrapolated to children. With concerns for radiation exposure in the pediatric population and the variation of their anatomic structures alternative pathways for children should exist for cervical spine evaluation and clearance. The incidence of cervical spine injury in children is lower than the adult population [25]. Review of the literature available allows for some basic recommendations for evaluation and clearing the cervical spine in the pediatric population but further data is needed.

Beginning with the patient physical exam variations exist between adults and children. The very young child may be difficult to examine due to stage of development. However the clearing of the cervical spine with physical exam alone has been evaluated. A percentage of the patients in the original NEXUS trial were children and it was felt to perform well [26]. Leonard et al. retrospectively reviewed their pediatric population combining components of the NEXUS criteria and the Canadian C spine rules and identified 8 factors that were sensitive for cervical spine injury [27]. Studies also discuss limiting this clinical evaluation and clearance to children over age 9. In general there is evidence to support the application of clinical clearance based on physical exam in the pediatric population. Creating a standard guideline to follow will ensure consistency and limit failure.

In general children with neck pain, neurologic deficit and those not able to be fully evaluated would qualify for an imaging study. In a child needing imaging to evaluate the cervical spine determining the type of radiograph is discussed. In the pediatric population the use of cross-table lateral films in many studies has been sensitive for identifying any significant injury. However, other studies have missed rates between 20 and 25 % with cross-table lateral alone. The addition of the anterior-posterior (AP) view of the cervical spine has been shown to be 87 % sensitive in children less than 8 years of age [28]. The use of the open mouth odontoid view is not felt to be necessary. Use of MDCT in adults has been established but the data in children is not and the radiation exposure risk is real. Use of MDCT in children should be limited to those with severe injury patterns or evidence on exam or plain radiographs of injury to the cervical spine. Age of the patient may influence use of MDCT as the cervical spine anatomy starts to change in many children beginning around age 8 and certainly by age 14 the cervical spine is anatomically similar to an adult. Again, the plan for a standard practice for evaluation and imaging in this unique trauma population will result in the consistent application of the evidence to avoid pitfalls in diagnosis.

Conclusion

The main conclusions for clearing the cervical spine and removing the collar in the adult trauma patient after blunt trauma are:

Physical exam alone can be used in the appropriate patient population.

In the awake patient with indication for imaging, MDCT is completed and if negative, clearing the collar can be accomplished through:

1) Repeat physical exam once a reliable exam can be completed and no pain or neurologic deficit exists
2) MRI of the cervical spine
3) Flexion and extension films in a delayed fashion and confirmation they are adequate.

In the obtunded patient initial imaging with MDCT is completed and the C spine may be cleared through:

1) If the patient is moving all 4 extremities and the attending radiologist has read the CT scan as negative the collar may be removed
2) MRI of the cervical spine
3) Continued cervical collar for 6 weeks with concern for stable ligamentous injury

The best plan for any program is to have an organized consistent process for the evaluation and clearance of the cervical spine based on the best evidence available and adjusted as improved quality of evidence is produced.

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Initial Evaluation and Management

13

Nilesh Vyas and Haralamos Gatos

Introduction

Multi-system trauma constitutes a major global problem affecting millions of people annually inflicting a substantial financial impact on healthcare systems. Traumatic injury remains the major cause of preventable deaths in patients under 40 years. In addition to significant mortality and morbidity rates, there is a considerable socio-economic burden on society to care for these patients with long-term disabilities. Quality of life with a goal of return to pre-trauma levels of functional status is of course the long and short-term goals of care.

Rapid simultaneous assessment and resuscitation permitting a complete physical examination are the principles of initial management of major trauma. Time is a critical challenge to the resuscitation team because 60 % of the polytrauma patients that die do so within the first hour of hospitalization due to loss of airway, excessive blood loss, or from major injury to the central nervous system.

The most significant milestone in the management of major trauma management is the first Advanced Trauma Life Support (ATLS) course in 1978. Since then, enormous efforts have been conducted to save as many patients as possible, especially during the "golden" or first hour after trauma. Nevertheless, most preventable trauma deaths occur early in hospitalization. Prior to surgical intervention one needs to establish direct control of obvious external bleeding, appropriate immobilization, and assurance of adequate airway and breathing. Internal bleeding within the skull, chest, abdomen, or pelvis requires rapid transport to a definitive care facility. Most potentially preventable deaths occur due to airway obstruction, hemopneumothorax, intracranial hemorrhage, intracavitary bleeding, and resultant coagulopathy [1].

Basic tenets of trauma management include assurance of an adequate airway, adequate breathing and primary survey while simultaneously resuscitating and determining key supportive interventions to stabilize the patient.

Overall Approach to the Unstable Patient

In order to achieve the prevention of potential deaths due to major trauma a multifactor and multidisciplinary approach is required. The primary goals of care are to stabilize the patient and prevent secondary injury. The trauma team

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achieves this by optimizing oxygenation, ventilation, and circulatory support. Identifying deranged vital signs and patients that are nearing physiological exhaustion is crucial during the initial assessment to act promptly for the safety of the patient.

The objective of triage is to prioritize patients with a high likelihood of early clinical deterioration. Triage of trauma patients considers vital signs and pre-hospital clinical course mechanism of injury, patient age, and known or suspected comorbid conditions. Findings that lead to an accelerated workup include multiple injuries, extremes of age, evidence of severe neurological injury, unstable vital signs, and preexisting cardiac or pulmonary disease.

Primary Survey

The primary trauma survey and following the "ABCs" of trauma serve to identify and immediately treat life-threatening injuries in a logical and systematic, sequential fashion. The primary survey is summarized in ATLS by ABCDE. ABCDE refers to airway, breathing, circulation, disability, and exposure. Frequent reassessment of "ABCs" during care is of great importance. Deforming and destructive injuries can be obvious but may distract the trauma provider. However, a systematic workup must be promptly conducted so that occult, potentially more critical injuries can be treated optimally. Any information obtained may prove crucial including preexisting medical conditions and medications, which may influence the decisions made during resuscitation.

Airway

Definitive airway control with endotracheal intubation is the goal standard, but obviously not indicated for all patients. The first priority is the airway because absence of a secure airway can kill the patient in minutes and therefore is frequently addressed by emergency medical services (EMS) personnel before arrival in the trauma bay of the hospital. The rapid assessment of signs of airway compromise consists of asking the patient a simple question. The absence of a response, or the presence of stridor or coughing can indicate inadequate airway management. The team must exclude airway obstruction by checking for foreign bodies, secretions, blood, vomitus, or fractures. Relief of obstruction with suction or jaw thrust maneuver frequently permits spontaneous ventilation.

All patients with polytrauma are assumed to have cervical spine injury (CSI) until proven otherwise, because there is a 4–20 % cervical spine injury prevalence. Therefore, all assessments and procedures must take care of the cervical spine by immobilization (rigid cervical collar) until subsequent investigations definitively exclude cervical spine injury. This should always be in a provider's mind while assessing and managing a patient's airway.

Definitive airway management with endotracheal intubation is required if there is (1) inadequate ventilation or oxygenation, (2) impending airway obstruction secondary to injury, (3) decreased level of consciousness (GCS <8). Early intubation must be considered in severe multisystem injury and hemodynamic instability, facial burns, inhalation injuries, and when the patient is dangerously aggressive.

Correct endotracheal tube position must be confirmed with end-tidal carbon dioxide and oxygenation measurements in addition to chest radiography. Special precautions may be needed if the resuscitation team suspects difficult airway management.

Breathing

Once the airway is checked or secured the assessment of breathing and ventilation is of next greatest priority. Life-threatening injuries that must be ruled out are tension pneumothorax, open pneumothorax, massive hemothorax, flail chest, and cardiac tamponade. Thoracic injuries are responsible for 25 % of all trauma deaths. In unstable patients, the diagnosis of tension pneumothorax is made clinically and may not require radiographic verification. In these circumstances,

the patient should be treated with needle decompression followed by chest tube insertion. One must be aware of the occult pneumothorax that is evolving rapidly after endotracheal intubation and rarely can even be fatal. Thoracic trauma in addition to causing respiratory collapse can also cause hemodynamic instability due to a massive hemothorax often from lacerated intercostal arteries but also from injury to the heart, lungs, or great vessels.

Circulation

Shock is a state of oxygen delivery insufficient to sustain normal tissue and cellular function. Hemorrhagic shock is the most common cause of traumatic shock. Other types of shock include cardiogenic (myocardial infarction, dysrhythmias), obstructive (tension pneumothorax, cardiac tamponade, pulmonary embolus), and distributive (septic shock, anaphylaxis, neurogenic shock). The lethal triad of the multi-injured patient is hypothermia, coagulopathy, and acidosis. All of these can result from prolonged and irreversible shock.

A decrease in core body temperature increases mortality of patients in hemorrhagic shock. Coagulation factors involved in hemostatic pathways and platelet activity are adversely affected during hypothermia [2]. Hypoperfused tissue that receives rapid restoration of normal blood flow can be secondarily injured by reperfusion injury. This should not prevent the rapid and full restoration of normal perfusion however. The adequate correction of traumatic coagulopathy is essential to increase the survival rate of trauma patients.

Restoration of intravascular volume and normalization of blood pressure ensures adequate organ perfusion. Systemic arterial hypotension has become the most widely used identification for potential shock, but it may not indicate the actual state of tissue oxygen perfusion. Multi-injured patient with a normal SBP may not always have adequate perfusion systemically.

Significant volume of blood loss can occur from several sites. Obvious external sites of bleeding must be controlled immediately. Scalp or other severe lacerations can cause excessive blood loss and should be treated with external pressure during resuscitation and, if this is not sufficient to control the bleeding, sutures should be considered. If available, a simple Weitlaner retractor applied to the laceration often provides quick attenuation of blood loss. Fractured long bones are dealt with by reduction and traction in order to decrease ongoing blood loss, as well as relieve pain, prevent further injury, and restore blood flow to potentially compressed vessels.

Bleeding wounds with obvious vessel injuries should be treated with pressure dressings, until a surgeon can definitively control them in the operating room. Specialized agents added to advanced, hemostatic dressings such as kaolin or chitosan can aid in controlling bleeding in addition to direct pressure. The use of tourniquets is appropriate but should be used judiciously because they can worsen ischemia and damage adjacent or distal structures.

Blood loss of 10–20 % of total blood volume can be treated with intravenous fluid administration and should be reversed rapidly. Blood loss of 20–40 % must be treated with blood transfusion. Blood loss of greater than 40 % is frequently due to ongoing bleeding and in addition to transfusion should be treated surgically as soon as possible to control the source of the blood loss.

Intra venous access is of paramount importance to maintaining adequate circulation and should be obtained simultaneously with the primary survey. Ideal intravenous access includes two large bore cannulas placed in the upper extremities. Subclavian or internal jugular venous access should be considered as the next alternative.

Systolic blood pressure (SBP) must be restored to normal levels by rapid intravenous infusions of an isotonic crystalloid solution (normal saline, lactated ringers). Colloid solution (albumin) is not recommended in the trauma

setting. Elevation of SBP prior to achieving adequate hemostasis may be harmful.

Disability

A rapid neurological assessment using GCS and examination of pupils is of critical importance. Traumatic brain injury (TBI) is common in polytrauma patients and is a common cause of long-term disability and even death. Early identification of TBI and appropriate interventions can minimize these negative outcomes. Cervical spine injury (CSI) is also common and assessment of extremity motor and sensory function is important. Particularly in patients who need early treatment for an unstable airway, a very quick assessment of the patient's neurological exam prior to sedation can help prioritize the need for intracranial injury management. Decreased level of consciousness may have numerous etiologies including but not limited to poor oxygenation, metabolic disturbances, intoxication, and brain injury. Focal neurological injuries are more likely to indicate brain, spine, or nerve injury.

Exposure—Environment

Clothes are removed taking care to avoid hypothermia by use of external warming and warm intravenous fluids. The trauma provider must exclude dorsal injuries by "logrolling" the patient to ensure stability of possible thoracolumbar spine or total spine precautions. Exposure of the patient facilitates the transition to the secondary survey and assessment of other injuries to the patient.

Monitoring

Continuous monitoring of pulse, blood pressure, and respiratory rate is necessary and indispensible even in hospitals that are not trauma centers. Monitoring if possible should include temperature, pulse oximetry, end-tidal carbon dioxide, and occasionally an arterial line for blood pressure.

If there is no suspicion of urethral injury, urinary catheter placement demonstrating sufficient urine output indicates adequate end-organ tissue perfusion. In all intubated patients, when skull base and facial fractures are ruled out, an orogastric tube should be inserted in order to avoid aspiration.

Assessment and Secondary Survey

Secondary survey and continuing resuscitation requires complete physical examination and focuses on directing further diagnostic studies.

Reassessment is essential, and can identify previously missed injuries. In polytrauma patients a definitively secured airway, SBP > 100, and Pulse rate < 100 per minute are crucial in order to leave the trauma bay for further investigations and treatments.

Samples of blood for cross matching for transfusion should be obtained. CBC, BMP, and tox screen. Arterial blood gas can help determinate acid–base deficits imbalances.

Any hemodynamic instability or hypoxemia must be immediately recognized, requiring rapid re-assessment. The differential diagnosis must suspect associated thoracic, abdominal, spinal, and long bone injuries.

Traumatic Brain Injury

Current TBI management focuses on prevention of primary injury and avoidance of secondary injury. The cornerstones of modern TBI treatment start with optimizing the "ABCs" of trauma care in both the acute and subacute time frames. A single episode of hypotension dramatically increases the risk for unfavorable outcome [3]. Brain Trauma Foundation guidelines recommend to strictly avoid hypotension, systolic less BP than 90 mm Hg.

Surgical evacuation of mass lesions causing neurological deficit in emergent fashion is also

required for focal lesions such as depressed skull fractures, epidural hematomas, subdural hematomas, or large intraparenchymal hematomas. For this reason, non-contrast head computed tomography (HCT) remains the optimal imaging modality for suspected TBI and should be performed in all appropriate patients as soon as the patient is stable to travel from the trauma bay to the radiology department. Treatments for TBI beyond surgery typically involve management of elevated intracranial pressure (ICP) and maintaining a cerebral perfusion pressure (CPP) of 60 mm Hg. Prior recommendations for CPP goals of up to 80 mm Hg may exacerbate both cerebral and pulmonary edema.

ICP monitoring is indicated for any patient with an acutely abnormal head CT and a GCS of 8 or less. This may also include patients requiring prolonged sedation for non-cranial surgical procedures or sedation for adequate ventilation. The gold standard for monitoring remains intraventricular catheter placement with the ability to monitor ICP and drain CSF as well, which can be a powerful method to decrease recalcitrant elevated ICP. Alternative ICP monitors use intraparenchymal fiberoptic or strain-gauge technology without the additional advantage of draining CSF. A target ICP of less than 20 mm Hg in combination with the CPP goal of 60 mm Hg is recommended. Sustained ICP greater than 25 mm Hg should prompt escalation of treatments to lower ICP either medical or surgical.

New multimodality monitoring techniques include brain tissue oxygen monitoring and parenchymal microdialysis. These new monitors can provide great volumes of data but are not at this point either the standard of care or proven to improve patient outcomes [4, 5].

First line treatments for elevated ICP include optimizing venous drainage with a loose fitting cervical collar and a straight cervical spine position with the head of the bed elevated 30° in the intensive care unit bed. Second line treatments for elevated ICP focus on hyperosmolar treatments with either hypertonic saline (more common) or mannitol (less common). Hyperventilation, although transiently effective, increases cerebral ischemia and therefore should be reserved exclusively for brief periods only during clinical evidence of herniation syndromes and as a bridge to surgical decompression. Third line treatments for refractory ICP management include barbiturate coma, therapeutic hypothermia, and even decompressive craniectomy. While barbiturate coma and hypothermia have long been used in improving outcomes and are the mainstay of complex ICP management in trauma patients, decompressive craniectomy remains controversial. The DECRA trial results have been used by some neurosurgeons as a reason to avoid decompressive craniectomy. This may be true for diffuse bilateral posttraumatic brain edema but does not apply to focal lesions or unilateral disease: circumstances which may be amenable to significant improvement with surgical decompression (Table 13.1).

The purpose of the initial survey in trauma concerning TBI is to diagnose and arrange evacuation of mass intracranial lesion and treat cerebral edema. Cerebral ischemia is the single

Table 13.1 Glasgow Coma Scale

Eye opening	Points	Verbal response	Points	Motor response	Points
Spontaneous	4	Oriented	5	Obeys commands	6
To voice	3	Confused	4	Purposeful movement	5
To pain	2	Inappropriate words	3	Withdraws	4
None	1	Incomprehensible	2	Flexion	3
		None	1	Extension	2
				None	1

most important factor that influences the outcome after TBI. Early monitoring aids the trauma provider in targeting therapy for cerebral edema and perfusion and minimizing secondary injury to the traumatized brain.

Summary

The initial care of the severely injured, polytrauma patient must focus the multidisciplinary trauma team on the methodical approach to evaluate and stabilize the patient. Following the ABCs outlined by the ATLS protocol provides this framework. This is the foundation for ensuring that any trauma patient achieves the optimal chance at improved outcomes, including patients with traumatic brain injury and other neurological compromise.

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Transport of the Neurotrauma Patient

14

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Introduction

Traumatic brain injury (TBI) is a common problem in both civilian and military settings. In 2010, the Centers for Disease Control and Prevention estimated that it resulted in 2.5 million emergency department visits in the United States (US) of which over 283,000 people required hospitalization [1]. Those who serve in the U.S. military are also at significant risk for TBI. Data from 2000 to 2011 indicate that 4.2 % service members were diagnosed with TBI [2]. While the initial injury can be devastating, additional physiologic insults are well known to potentiate the initial injury and lead to worse outcomes. These 'second hits' have historically included hypoxia and hypotension and, to a lesser extent, hyper- or hypoventilation and hyperthermia. New evidence suggests that the hypobaric environment encountered during aeromedical transport can itself result in increased inflammation, cerebral edema, and alterations in the cerebral metabolic rate [3]. Other environmental factors which have been less studied but may also play a role include vibration and temperature shifts [4]. First responders and medical transport teams are instrumental in limiting these physiologic second hits and minimizing subsequent injury regardless of the distance to be traveled. While patient movement may be absolutely mandatory, transport should be approached as a high-risk procedure: patient selection and preprocedural planning are paramount to minimizing transport related complications [5].

Mode of Prehospital Transport and Receiving Location

Aeromedical prehospital transport has been identified in two studies as a predictor of better outcomes in TBI transported to Level I and II trauma centers [6, 7]. Those patients most likely to benefit from prehospital air transport were hypotensive patients and those with a lower Glasgow Coma Score (GCS) [7]. These improved outcomes have been attributed to shorter transport times as well as to the higher levels of training and experience with air transport teams. More skilled teams who typically staff helicopter transport platforms may result in an improved outcome by their ability to safely perform prehospital interventions [8]. Careful selection of receiving facility is also paramount, with the recognized need to bypass a closer facility in order to reach a location with optimal resources.

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These capabilities should include 24-hour Computerized Tomography (CT) scanning capability, a 24-hour operating room, prompt neurosurgical care, and the ability to place intracranial pressure (ICP) monitors [9]. A New York study by Härtl et al. demonstrated as much as a 50 % increase in mortality of severe TBI patients when they were not taken directly to a trauma center with these appropriate resources [10]. This mortality difference must be weighed against the longer transport time and take into account resources available during transport.

PreTransport Considerations

Prior to transport, life-threatening concerns must be evaluated and stabilized when possible. Ideally, airway should be secured, oxygenation and ventilation should be optimized, hemorrhage controlled, coagulopathy characterized and treatment initiated, contamination limited and fractures stabilized. Obviously these will vary depending on the timing of their transport in relation to the care that has been received.

Despite conflicting data regarding field intubations and outcomes in severe TBI patients, field endotracheal intubation by a qualified team with subsequent O2 saturation and ETCO2 monitoring should be considered, especially with anticipated long transport times, in order to avoid hypoxia, fluctuations in PaCo2 and to protect from aspiration [11–16]. It should be understood that intubation with laryngoscopy itself may cause numerous complications to include temporary hypoxia, bradycardia, hypotension, or an increase in ICP, all of which may increase mortality [17]. Similarly, extubation should be avoided immediately prior to transport as intra-transport intubations are challenging and are more difficult to confirm.

The risk of cervical spine injury increases up to sevenfold in the presence of TBI, so cervical spine protection should be strongly considered [18]. After observing a series of occipital pressure ulcers across the continuum of care, the Department of Defense adopted the Miami J/Occian Back based on studies that demonstrated a reduced risk of pressure ulcers [19].

Following severe TBI there is significant cerebral edema. Several factors contribute to this edema, to include blood brain barrier leak (causing vasogenic edema), ischemia and inflammatory-ionic dysfunction (causing cellular edema), and loss of autoregulation (leading to vascular engorgement) [20]. Cerebral edema is exacerbated by hypoxia and hypotension. Cerebral edema begins to develop almost immediately post-TBI but may reach a peak level of edema by day 3–5. In rodent studies, this maximum swelling has been noted sooner at 48 h [21]. Anticipating this impending increase in edema may impact decisions regarding the timing of patient transport, theoretically avoiding transport during the window of peak edema. Currently, the DoD has elected to transport patients with severe TBI to a higher level of care as soon as is feasible, pending further data.

US Air Force and Army both use specialized transport teams for the interfacility movement of critically ill or injured patients and burn casualties. The critical care air transport teams (CCATT) undergo specific training in the movement of the neurotrauma patient. This approach has been used historically by pediatric hospital transport teams. Orr et al. demonstrated that using specialized pediatric transport teams from the Children's Hospital of Pittsburgh during interhospital transport resulted in increased survival: 23 % versus 9 % (specialized vs. nonspecialized teams). Unplanned events were more common with nonspecialized teams (61 % vs. 1.5 %) [22].

Pretransport checklists have become an integral part of interhospital and intrahospital transports by dedicated teams [23]. Checklists, dedicated oversight, and a focused training program have been shown to decrease serious unexpected events during intrahospital transport of emergency patients from 9 to 5 % [24]. CCATT checklists (see Tables 14.1 and 14.2) and training scenarios target potential complications, and the allowance standard includes supplies needed to treat these complications.

Table 14.1 Prehospital transport checklist

Airway secure/controlled
Chest, need for needle decompression
Hemorrhage, external, controlled/adjuncts (TXA, blood products)
C- Collar/spine precautions need
Splinting
Monitoring (O2 Sat, ETCO2)
Medications (Sedation, pain, seizure, RSI, and ICP elevation)

Table 14.2 Long-range aeromedical transport checklist

Airway secure
ETT cuff location/cuff pressure
Mechanical ventilation concerns (altitude compensation and sufficient oxygen stores)
Spine protection (collar and vacuum spine board)
CXR review for pneumothorax, pneumonia, and chest tube placement
Oral-gastric tube placement (increased risk ileus/aspiration)
Monitoring (ETCO2, EKG, Pulse Oximetry, and ICP)
Laboratory review (Lactate, PaCo2, and O2)
Medication considerations (Antibiotics, seizure prophylaxis, pain meds, sedation meds, hypertonic saline, DDAVP, and oral care)
ICP elevation treatment algorithm
Temperature regulation plan
Blood product need assessment
Medical records/images obtained
Fit to fly determination? (Oxygenation, ICP, and infection)
Positioning concerns (Head first, HOB elevated, and infection control)

Stressors of Flight

While ground transport by itself can introduce risk, aeromedical evacuation (AE) of the acute neurotrauma patient introduces additional complexity. The air transport environment is physiologically hostile to patients in a number of ways. Environmental stressors include hypobarism, hypoxemia, gravitational and acceleration forces, noise, vibration, and decreased humidity. Depending on the distance to be traveled, the austerity of the transport environment can also have a profound effect on ability to diagnose and treat the deteriorating patient. Each of these environmental stressors can potentially exacerbate TBI and must be ameliorated.

Goodman et al. demonstrated that mice exposed to hypoxic hypobarism 3 h after mild TBI had increased levels of inflammatory cytokine IL-6 and neuron specific enolase. Inflammatory biomarkers were not elevated if the hypoxic hypobarism was delayed until 24 h post injury. The authors concluded that early, but not delayed, exposure of post-TBI patients to high altitude was associated with increased neuroinflammation [25]. Skovira et al. demonstrated in rats that non-hypoxic hypobaric exposure even up to 7 days after TBI was associated with worsened cognitive deficits, hippocampal neuronal loss, and microglial/astrocyte activation in comparison to injured controls (no hypobaria) [26]. In addition, they found that exposure to 100 % FiO2 during hypobaria was associated with further spatial memory deficits. In clinical practice, all patients with TBI-regardless of severity should be monitored for oxyhemoglobin saturation during transport to avoid either hypoxia or hyperoxia. Johannigman et al. have demonstrated that autonomous control of the FiO2 may be most effective, and have demonstrated less significant hypoxia when the computer controls the FiO2 [27]. Limited conclusions can be drawn from the combination of these studies, and additional research is needed to further characterize the optimum timing of AE in relation to neuroinflammation and limiting the 'second hit' caused by hypobarism with or without hypoxia. Early transport to reach a more capable intensive care unit (ICU), improved neurotrauma monitoring and neurotrauma intervention may ultimately place the patient at lower risks.

Johannigman et al. provide recommendations for limiting many of the stressors experienced

during medical transport [4]. Helicopters and military cargo planes are commonly used for patient transport, and vibration and noise is unavoidable. Vibration can cause significant patient discomfort and so to limit this effect, patients' beds should be padded and placed in the middle of the air frame away from the fuselage to decrease the impact of vibration. Noise should be limited for both the patient and staff by use of hearing protection. At high altitudes, dry air can lead to dehydration and so excess fluids may be needed and eye lubrication (in addition to removal of contact lenses) and a heat and moisture exchanger (HME) for the ventilator should be used. Temperature regulation can also be challenging as cargo aircraft and helicopters are often below 55 °F, and so warming blankets should be available [4]. AE takeoff and landing are the phases of flight that cause the greatest changes of ICP, due to acceleration and deceleration forces. Acceleration during takeoff produces the more abrupt and dramatic shifts. For this reason, patients should be loaded on the aircraft head first with the head of bed at 30° elevation [4].

The AE environment can also constrain patient monitoring. The noise of the AE environment makes audible alarms difficult if not impossible to hear. Patients are not always able to be loaded directly in the line of sight of a team member. Monitors should be mounted such that critical information is most visible, and a heightened awareness of monitor display is necessary. Improved visual interfaces with equipment and smart monitoring may, in the future, aid in earlier recognition of a deteriorating patient.

Neurocritical Care During Transport

Extensive evidence exists for the importance of avoiding hypoxia in TBI. A prospective observational study by Chi et al. demonstrated prehospital hypoxia in 28 % of TBI patients, with mortality significantly increased in those patients (37 % mortality vs. 20 %, OR 2.66) in the face of similar injury severity scores between the two groups [28]. Of the survivors, the Disability Rating Scale and length of stay (LOS) were significantly higher when secondary insults had occurred (hypoxia and/or hypotension).

Two effective means of reducing hypoxia in a ventilated patient are increasing the FiO2 or the positive-end-expiratory-pressure (PEEP). Traditional thinking was that higher levels of PEEP should be avoided: increasing the PEEP would lead to increased thoracic venous pressure which would in turn decrease venous return resulting in an increase in ICP and a decrease in cerebral perfusion pressure (CPP). Huynh et al. looked retrospectively at this hypothesis in severe head injury patients with ICP monitors and found the opposite to be true: an increase in PEEP was associated with a decrease in ICP and an increase in CPP [29]. Notwithstanding this evidence, Barnes et al. found underutilization of PEEP in long range AE by CCATT in almost 50 % of patients [30]. As PEEP is an effective means of treating pulmonary injury after trauma and given the above data, appropriate use of PEEP is recommended during the transport of critically ill patients.

Historically, mild hyperventilation was used as a means of lowering ICP due to cerebral vasoconstriction. This practice has largely been abandoned except in acute situations of herniation due to a resultant decrease in cerebral blood flow resulting in increased morbidity and mortality [31, 32]. Jeremitsky et al. found 80 % of their severe TBI patients experienced hypocapnia at least once (defined at PCO2 < 30) and this was associated with an increased ICU LOS as well as overall LOS [33]. Davis et al. demonstrated that end-tidal carbon dioxide (ETCO2) monitoring led to a significant reduction (5.6 % vs. 13.4 %) of severe inadvertent hyperventilation (PCO2 < 25) during transport of head injury patients [34]. These studies and others have led to the recommendation for ETCO2 monitoring by capnography during transport [35–38].

Along with hypoxia, the most well-studied 'second hit' is hypotension. Jeremitsky et al. reported that 68 % of their severe blunt TBI patients (GCS $\leq$ 8) experienced a hypotensive episode (MAP < 70) and this was independently associated with increased morbidity (length of

stay, discharge to rehab rather than home) and mortality [33]. Chestnut et al. also looked at hypotension in severe head injury patients (GCS $\leq$ 8) and found a high prevalence (34.6 %) and an associated doubling in mortality (55 % vs. 27 %). Furthermore, the combination of hypotension and hypoxia at admission resulted in a 65 % mortality [39]. From this evidence, regular blood pressure monitoring (every 5 min) and invasive blood pressure monitoring when available are highly recommended prior to and during transport.

There is mounting data regarding the importance of temperature control in TBI patients. While controlled hypothermia in severe TBI was shown earlier in smaller trials to be beneficial, [40, 41] the more recent data favors maintenance of normothermia [33, 42]. Jones et al. found hyperthermia to be one of the three most important predictors of mortality in severe TBI patients (along with hypotension and hypoxemia) [43]. Hyperthermia is thought to be detrimental in several ways. It is associated with ICP elevation [44] and found to be an independent risk factor for posttraumatic vasospasm [45]. As transport environmental temperatures may be difficult to monitor and control, regular monitoring and maintenance of patient normothermia are important to prevent further ischemia, inflammation, edema, and secondary injury. This can usually be adequately accomplished during transport with external warming and cooling techniques; invasive and noninvasive targeted temperature management systems are being used more frequently in neuro ICUs.

Current guidelines for the management of severe brain injury recommend ICP monitoring in all patients with severe TBI (GCS $\leq$ 8) and evidence of intracranial pathology on CT scan [9, 46]. Further, any patient with severe head injury without CT evidence of intracranial pathology but with any two of the following: age older than 40 years, any hypotensive episodes with Systolic Blood Pressure (SBP) < 90, or abnormal motor posturing (unilateral or bilateral) should have ICP monitoring in place [46]. Hospital monitoring of the neurosurgical patient involves turning off sedation for neurologic checks frequently. This is more challenging in austere transport environments that are hyperstimulating with both noise and vibration which may independently exacerbate ICP. As a result, it is necessary to keep these patients more deeply sedated and minimize neuro checks; thus additional methods for monitoring are often needed. During long transports, ventricular drains may be preferred over intraparenchymal fiberoptic catheters as ventriculostomies allow therapeutic CSF drainage in addition to ICP monitoring. However, ventricular drain collection systems must be handled correctly to avoid inadvertent CSF drainage. Transport teams must be trained with and feel comfortable using and troubleshooting these devices. As an example, occlusion of the air filter (with moisture) has resulted in inadvertent pressurization of the system and increased ICP readings. A prevention strategy includes maintaining the systems upright (do not lay down). Those patients with an ICP intraparenchymal monitor may require calibration and an inflight monitor specific to the manufacturer of the catheter.

Prior to transport, hard copies of all documentation and imaging should be obtained and transported with the patient. This is especially important if the electronic medical record system becomes nonfunctional or the patient is diverted to an unintended location while en route.

Neurocritical Care Standard Bundles

Seizures are a well known complication of TBI. Prior to empiric prophylaxis with anti-epileptics, seizures affected an estimated 5000–30,000 head injury patients a year in the United States. Temkin et al. in 1990 conducted a landmark randomized, double-blinded study of severe TBI patients which assigned to seizure prophylaxis with phenytoin compared to no prophylaxis. Phenytoin significantly decreased the risk of seizure during the first week after injury (3.6 % vs. 14.2 %) [47]. This and other studies have led to the current recommendation of a loading phenytoin dose followed

by 7 days of phenytoin prophylaxis. Levetiracetam has essentially replaced phenytoin due to its ease of administration.

Stress ulcer prophylaxis (proton pump inhibitors or histamine-2-receptor antagonists) is used in high-risk patients (i.e., in ventilated or coagulopathic) who are not undergoing enteral feeding [48]. In patients without progression of intracranial pathology on CT or other contraindications to anticoagulation (coagulopathy and active bleeding), enoxaparin (30 mg subcutaneously twice daily) should be started for this high-risk population [49]. In patients without abdominal pathology, nutrition should be started as soon as possible. This has been safely accomplished during 10 h transports by USAF CCATT using an oral gastric tube decompression and placement of a feeding tube distal to the ligament of Treitz to prevent aspiration during transport. Patients receiving enteric nutrition must be monitored closely due to the increased incidence of ileus in TBI as well as the known intestinal gaseous expansion at altitude (Boyle's Law).

Hyperglycemia has also been shown to exacerbate secondary brain injury and is an independent predictor of outcome [50–53]. In addition, tight glucose control (80–110 mg/dL) is associated with worse outcomes versus loose control (120–150 mg/dL) [54]. From this body of evidence, control of blood sugar (120–150 mg/dL) is recommended and frequent checks during transport should be performed.

Complications and Management Considerations During Transport

Transport of the trauma patient over long distances requires an absolute awareness of the numerous potential neuro and trauma specific clinical complications which may develop. The goal CPP (MAP-ICP) is currently recognized to be > 60 mm Hg [9]. In treating low CPP, the first step should be normalization of blood pressure. In severe TBI, SBP should always be above 90 mm Hg [46] or above 100 mm Hg [9] and with some evidence supporting a goal greater than 110 mm Hg [55] using isotonic to hypertonic fluid resuscitation (to maintain normovolemia) and vasoactive agents when necessary. A treatment algorithm for the management of elevated ICP should be followed, see Table 14.3.

Table 14.3 Increased ICP treatment algorithm (Maintain ICP < 20–25)

1. Head of bed elevation > 30 degrees
2. Head midline positioning
3. C- Collar tightness limited
4. PaCo2 titrated to 35–40
5. Treat hypoxia; maintain saturation $\geq$ 95 %
6. Treat hypotension, maintain CPP > 60
7. Treat potential pain
8. Sedation; limit external stimuli
9. Evacuation of CSF if ventriculostomy present
10. Consider hyperosmolar therapy
11. Head CT imaging once available
12. Consider subclinical seizure activity

In hemorrhagic shock or in severe bleeding associated with a coagulopathy, a more aggressive and balanced approach to blood product resuscitation should be implemented [56]. Targeting a 1:1:1 ratio of PRBC:plasma:platelets decreases hemorrhagic shock mortality [57]. Flight teams increasingly carry blood and blood products to obtain this survival advantage [58].

Pain and discomfort should be controlled with short-acting sedatives and analgesics to avoid increases in ICP caused by agitation. If sedation is thought to be inadequate in the face of increased ICP, a sedation bolus should be administered.

Combat- or trauma-related central nervous system injuries have an overall infection rate of 5–10 % with an associated high morbidity and mortality [59]. This infection rate increases to 26 % with a cerebrospinal fluid leakage from the nose, ear, or wound [60]. Initial field care should consist of bandaging all open wounds with sterile dressing and administration of antibiotics. The Prevention of Combat-Related Infection Guidelines Panel recommends treating penetrating brain and spine injuries as well as those with ventriculostomy drains with cefazolin 2 g every

6–8 h or alternatively with vancomycin 1 g IV every 12 h and ciprofloxacin 400 mg every 8–12 h with redosing after large volume resuscitation for a minimum of 48 h (and longer for CSF leaks) [59].

Intubated TBI patients have a high risk for the development of pneumonia. Standard prevention protocols and AE strategies should be followed when possible to include oral care, HOB elevation, use of an HME, metered nebulizer treatments, subglottic drainage, and maintenance of adequate endotracheal tube (ETT) cuff pressures.

Central diabetes insipidus (DI) has been shown to be more frequent after MVA and those who have sustained moderate/severe TBI [61]. The major symptoms include polyuria, polydipsia, and nocturia, due to the defect in concentrating urine. During transport, monitoring of urine output is critical for early recognition. If electrolyte assessment is not possible, treatment may be required and based on clinical suspicion alone. Treatment is primarily aimed at fluid replacement and decreasing urine output, usually by increasing the activity of antidiuretic hormone. Preflight preparation with a supply of desmopressin (i.e., DDAVP) and extra crystalloid fluids is imperative to successful treatment.

Pneumothorax is common after blunt trauma. Although a stable small pneumothorax, especially an occult pneumothorax seen on CT scan, is unlikely to create a problem in ground transport, aeromedical transport will result in trapped gas expansion. One should consider chest decompression before flight or be prepared for inflight chest decompression should instability develop. Ascent from sea level to 7500 ft can result in an 18.3 % increase in the size of trapped gas [62].

Gas-filled devices should be used with caution as they will expand and cause increased pressure on the patient. These devices should be monitored closely. Some commercial flight teams have insisted on filling the ETT balloon with water to avoid the gas expansion concerns but this in fact increases the risk of mucosal pressure necrosis [63]. ETT balloons and air splints should be filled with air and recalibrated with a manometer before, during and after ascent and descent. Air within IV bags and bottles has been shown to pressurize and lead to inadvertent line disconnection or expanding air pockets in the tubing. All non-vented air collections must be monitored with changes in cabin pressure. While there is general concern about air transport of patients with intracranial air, a recent small series reported no neurologic events in twenty-one patients transported from the Middle East to Germany with volumes of pneumocephalus from 0.6 to 43 mls [64]. All equipment brought aboard on aircraft should have a flight worthiness certification to ensure that the equipment does not interfere with the avionics of the aircraft. In addition they should be certified to perform at the ranges of altitude expected and ideally be altitude compensated (important with ventilators to ensure appropriate tidal volumes).

Summary

Transport of the TBI patient is an often unavoidable high-risk procedure that requires careful consideration and meticulous attention to detail in limiting further injury. While the most well-known secondary insults are hypotension and hypoxia, additional risk factors for potentiating worse outcomes include hyper- and hypocarbia, hypo- and hyperthermia, ICP elevations, and hypobaric exposure. The addition of aeromedical environmental challenges including hypoxemia, hypobarism, gravitational and acceleration forces, noise, vibration, and decreased humidity creates a hostile environment for casualties. Field responders and transport teams are essential in limiting these additional physiologic and environmental insults. Preparation for transport including airway and spine protection, careful selection of accepting facility, medications (oxygen, sedatives, analgesics, and crystalloid fluids), appropriate monitoring (oxygen saturation probes, end-tidal CO2 capnography, invasive blood pressure monitoring, and ICP monitors when indicated), and thorough training of transport teams is critical in mitigating the risk of TBI patient transport. Further research is needed into

the appropriate timing of transport in severe TBI, especially in regard to aeromedical evacuation.

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Part III
The Operating Room/Damage Control

Multiple Surgical Teams in the O. R. at Once—Priority of Effort and Who Takes the Lead?

15

Neal D. Mehan, Matthew A. Bank, Jamie S. Ullman and Raj K. Narayan

Introduction

Patients with high-velocity injuries are at increased risk for trauma to multiple organs. Such patients require rapid assessment, resuscitation, and sometimes invasive intervention. The atmosphere in the trauma bay during the initial management after presentation can often be chaotic, but it is critical to maintain order so that the various teams can work together efficiently. Such coordination can be challenging due to the stressful nature of this situation. In order to consistently assure the best possible outcome for these patients a team-based approach with close coordination and frequent communication between the trauma, neurosurgery and other appropriate teams is essential. Major extracranial injuries in patients with severe TBI are common and have been reported to have an incidence of up to 23–41 % of patients [1]. However, the need for the simultaneous surgical treatment of intracranial and extracranial injuries is relatively rare [2]. It is crucial in these select operative cases that coordination begins in the trauma bay and extends into the operating room.

Roles and Responsibilities in Initial Evaluation

The roles and responsibilities of the various teams involved in the care of trauma patients are fairly well established and are reviewed by the American College of Surgeons during the trauma center verification process [3]. The Trauma Surgery team conducts the initial resuscitation. Level 1 or level 2 trauma centers should also have a Neurosurgery team readily available to participate in the assessment of the patient if necessary. There may be institutional peculiarities that should be understood and compensated for. The current standard for level 1 and 2 trauma centers verification by the American College of Surgeons Committee on Trauma requires neurosurgeons to be physically present in the emergency department within 30 min [4]. This time frame has been chosen so that the neurosurgeon is able to participate in critical decision-making during the earliest part of the patient's hospital course.

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Priorities in the Initial Resuscitation

The priorities for the initial resuscitation are similar for all trauma patients and a full account is described in the Advanced Trauma Life Support (ATLS) manual [5]. The initial evaluation and management is done promptly with an emphasis on an orderly completion of primary and secondary surveys, along with any indicated imaging studies. Intravenous fluid administration should be started in most cases, although in cases of hemodynamic instability due to penetrating injury, studies have argued against full resuscitation back to a normal blood pressure until the source of hemorrhage has been controlled [6]. This strategy is termed hypotensive resuscitation. Theoretically this decreases the rate of bleeding from uncontrolled penetrating injuries and avoids "popping the clot" until definitive control can be established in the operating room. However, other randomized studies have brought this thinking into question [7]. It seems fairly clear that in the patient with a significant intracranial injury, sustained hypotension can cause secondary injury due to hypoperfusion. The Guidelines for the Management of Severe Traumatic Brain Injury recommend that hypotension (systolic blood pressure less than 90) be avoided [8]. In the setting of the multi-trauma patient with signs of significant intracranial injury, hemodynamic instability should be rapidly treated by fluid and blood product replacement. This resuscitation should begin on presentation to the trauma bay and continue into the operating room. In other words, hypotensive resuscitation strategies should be avoided in patients with severe TBI. Furthermore, hypotonic IV fluids should never be used for the resuscitation of patients with TBI for fear of exacerbating brain edema. Hypertonic saline is a reasonable resuscitative fluid to use in this setting.

Preoperative Priorities and Decision-Making

In the hemodynamically unstable multi-trauma patient, the prioritization of operative control of thoraco-abdominal hemorrhage versus CT scanning for intracranial injuries was often a contentious issue in the past. However, with the speed of more modern CT scanners, these images can be obtained within a few short minutes and this is rarely an issue. The decision to forgo CT imaging and bring the patient directly to the operating room can miss critical intracranial injuries. If imaging is not available for any reason, this decision is more difficult and the trauma team leader must decide on the approach using his or her best judgment. As stated earlier, resuscitation generally takes priority over intracranial interventions.

Response to Resuscitation

One of the most important factors in decision-making in a hypotensive trauma patient is the response to resuscitation. Trauma patients who present with hypotension can usually be divided into three broad groups based on their response to initial resuscitation. In the first group, the hypotension does not respond well to resuscitation. Such non-responders should be taken directly to the operating room for hemorrhage control. In the second group, hypotension responds to initial resuscitation only to recur while the patient is still being evaluated in the trauma bay. These "transient responders" likely have ongoing hemorrhagic injuries. At the first sign of these patients beginning to become less responsive to resuscitation, imaging must be aborted and the patient taken directly to the operating room for hemorrhage control. In the last group, hypotension rapidly corrects with the initial resuscitation. Even with clear indications for laparotomy/thoracotomy, patients who quickly respond to resuscitation are generally able to undergo CT scanning before the surgery. A summary of the decision-making process is shown in Fig. 15.1.

The initial Glasgow coma score (GCS) score can be added to the decision-making process as an indicator of the severity of intracranial injury. Using the response to resuscitation and initial GCS score, mature trauma systems have been able to safely select patients for preoperative CT

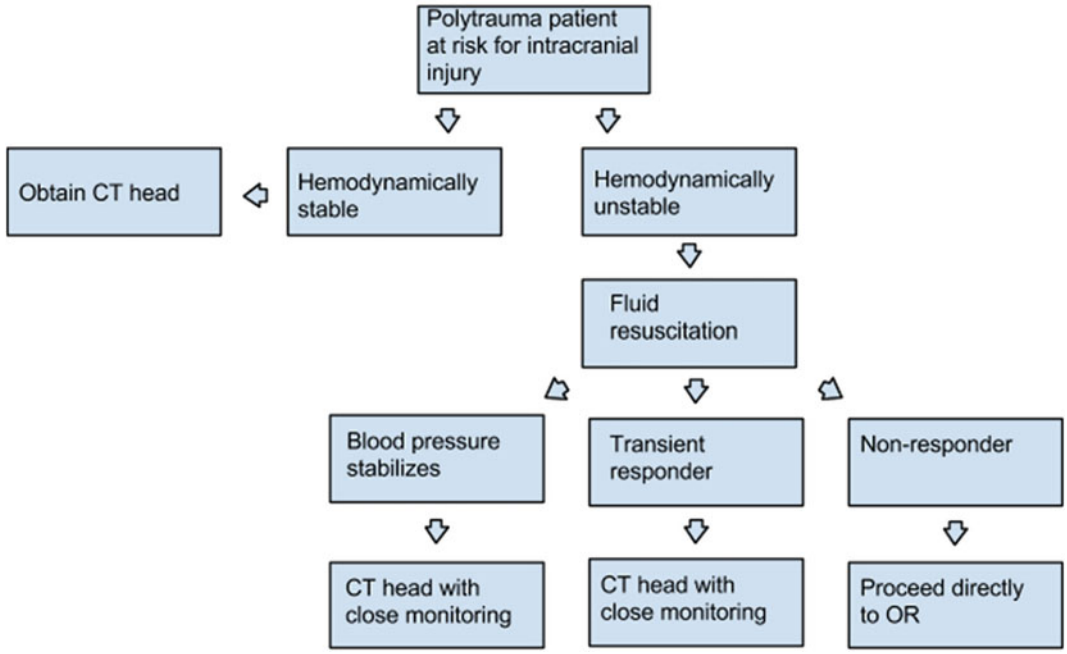

Fig. 15.1 Management of polytrauma patient at risk for intracranial injury

scanning even when an immediate laparotomy is indicated [9]. This requires very careful coordination among the trauma team members, neurosurgery, radiology, and the operating room.

An important caveat to remember is that initial GCS scores may be low in patients without intracranial mass lesions due to hemorrhagic shock and cerebral hypoperfusion. Additionally, the GCS score does not take lateralizing findings into account. Examples of lateralizing findings include a unilaterally dilated pupil, motor posturing, or hemiplegia. Lateralizing findings on neurological exam have been shown to be associated with a higher likelihood of the need for craniotomy [10]. A quick neurological exam is part of the primary and secondary surveys during the initial management of all trauma patients. Any lateralizing finding argues more strongly in favor of a CT scan of the head.

Retrospective reviews and case reports have shown that the Focused Assessment Sonography for Trauma (FAST) exam can be used to prioritize multiple simultaneous operative injuries [11]. In hypotensive blunt trauma patients who respond to initial resuscitation, using scoring systems for the evaluation of intra-abdominal free fluid as seen by ultrasound can help with prioritization of preoperative imaging studies versus foregoing investigations for intracranial injury and proceeding directly to the operating room. Huang et al. applied a scoring system based on the amount of free fluid seen on FAST exam to prioritize immediate laparotomy versus CT scan before laparotomy in multi-trauma patients. There were no deaths due to a delay of laparotomy when patients underwent preoperative CT scans of the head [12].

Ultimately the trauma team leader, in close collaboration with the neurosurgeon, must take into account all of the above factors to make a reasonable judgment on the priority of immediate OR versus preoperative CT of the head. Retrospective reviews have shown that in hypotensive trauma patients, the need for urgent laparotomy/thoracotomy for hemorrhage control is ten times higher than the need for urgent craniotomy [13].

Priority of Procedure

As stated earlier, in the hypotensive patient with signs of active hemorrhage, immediate operative control of ongoing bleeding is indicated. In this case, a laparotomy and/or thoracotomy must be performed before any intracranial procedures. Once the thoracic and/or abdominal hemorrhage is controlled, any indicated cranial procedure can be started during the same trip to the OR. Close communication between the general surgical, neurosurgical, and anesthesia teams is essential to respond to the rapidly changing physiology of major trauma patients in the operating room.

A polytrauma patient may present with head injury and an extremity injury needing surgical repair. It has been demonstrated that patients with closed femur injury who undergo early repair of the femoral fractures receive more fluids and have worse neurological outcomes [14]. The worse outcomes are thought to be caused by hypoxia or hypotension during early surgery leading to increased secondary brain injury. However, a delay in surgery can lead to increased rates of pulmonary complications including pneumonia and acute respiratory distress syndrome [15]. It is recommended that priority of treatment goes to management of the head injury. Orthopedic injuries should be treated as soon as is safely possible. In all such cases, care must be taken to avoid hypotension and ICP surges during the orthopedic procedure. It is recommended that the neurosurgeon specifically discuss these issues with the Anesthesia and Orthopedic team prior to clearing the patient for surgery.

Spine Immobilization

Cervical spine immobilization is critical for all trauma patients. Cervical spine instability can result from either a spine fracture or ligamentous injury. This instability may lead to misalignment or subluxation of the spine, which can cause compression of the spinal cord or nerves. This may lead to permanent neurologic injury, which can be prevented by use of proper precautions. The cervical spine is the most mobile portion of the spine and cervical collars are used to maintain alignment and prevent subluxation. Avoiding hyperextension or hyperflexion should be a priority especially during intubation. Often airway obstruction can be cleared using a jaw thrust or chin lift maneuver. Endotracheal intubation can be performed in a neutral position and if necessary, a cricothyroidotomy can be performed. The thoracic and lumbar spine are also susceptible to instability and injury and so log rolling precautions should be used when moving the patient to prevent possible further injury. A high quality CT of the cervical spine read as normal by a qualified reader makes it extremely unlikely that there is a significant instability [16].

Positioning in the Operating Room

The proper positioning of the patient in the operating room is necessary to allow each team to have adequate access to the patient. In rare cases a patient may require a craniotomy simultaneously with a laparotomy or a thoracotomy. In these situations, it is important to position the patient so that the neurosurgery team has access to the head. In addition, the patient position must allow the anesthesia team to have access to the airway and intravascular lines. Fortunately, the supine position used for most laparotomies is also compatible with the position used for a trauma craniotomy. The lateral position if needed for a thoracotomy may be more challenging. It is crucial that the neurosurgical, trauma, and anesthesia teams discuss positioning issues prior to the sterile prep and drape of the patient. In a single-center survey of 29 general surgeons and 12 neurosurgeons, Hernandez found that 82 % of general surgeons and 100 % of neurosurgeons found a “hybrid” craniotomy/laparotomy position acceptable for simultaneous procedures [17]. Maintaining a neutral neck position is necessary if spinal instability has not been ruled out.

Intracranial Pressure Monitoring

As described in the Severe TBI Guidelines, intracranial pressure (ICP) should be monitored in all salvageable patients with GCS score of 3–8 after resuscitation. This is especially so in patients with an abnormal CT head. An abnormal CT head includes hematomas, contusions, cerebral edema, herniation, sulcal effacement, or compressed basal cisterns. If the CT head is normal in a comatose patient, the likelihood of raised ICP is low, unless two or more of the following features are present: age over 40 years, unilateral or bilateral motor posturing, or a systolic blood pressure under 90 mm Hg [18]. In a minority of cases, if a CT-head could not be obtained preoperatively, an intracranial pressure monitor can be placed in the operating room simultaneously with a thoracotomy or laparotomy. This scenario has become much less common as CT scanners have become faster and can almost always be obtained expeditiously before taking the patient to the OR.

ICP may be accurately monitored by either an intraparenchymal monitor or an external ventricular drain (EVD). Deciding upon which type of monitor to place is at the discretion of the neurosurgeon. There are advantages and disadvantages to each choice. A major advantage of EVD placement is that it can be used to treat high intracranial pressure by removing cerebrospinal fluid. An advantage of intraparenchymal monitors is that it be placed quickly through a small twist drill hole. A disadvantage of EVD is that it can become clotted or obstructed and ICP readings may be lost. Both ICP monitoring technologies have some associated risks including infection and hemorrhage. After ICP monitor placement, the monitoring of intraoperative ICP requires familiarity with the equipment by all personnel involved, especially the Anesthesiologists.

Increased Intracranial Pressure During Laparotomy or Thoracotomy

If the ICP goes over 20 mmHg during the laparotomy or thoracotomy and a preoperative CT of the head has not been done, the patient should be treated with either mannitol or hypertonic saline. A CT scan should then be obtained immediately after the thoracic or abdominal surgery has been completed. Placement of exploratory burr holes can be done in this scenario instead of obtaining a CT head. Which side to perform the burr holes on can be decided based on localizing signs such as contralateral hemiparesis or an ipsilateral blown pupil. Hemiparesis can occasionally be ipsilateral to a mass lesion due to Kernohan's notch phenomenon and a blown pupil can occur with ocular trauma [19]. Exploratory burr holes are placed in manner so that if a hematoma is discovered, the incision and craniotomy can be converted into a standard trauma craniotomy flap. However, exploratory burr holes are not as effective as one might think and although they may be considered as an option of last resort, they have mostly fallen out of favor and are hardly ever performed.

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Laparotomy for Refractory ICP

16

Craig Shriver and Amy Vertrees

The Monro-Kellie doctrine of intracranial pressure notes that as the cranial vault is fixed, and that the blood, CSF, and brain tissue exist in a volume equilibrium, therefore any change in one (blood, CSF, brain tissue) would have to be compensated for by an obligate reactive change in another [2]. This doctrine only considers the fixed nature of the cranium. The thoracic and abdominal compartments have volume limitations as well. Compartment syndrome in all compartments has been postulated to have similar causes: massive resuscitation and damage to capillaries leading to third-spacing of fluid and increase in intracompartment pressure that overwhelms compensatory mechanisms [2].

Abdominal compartment syndrome (ACS) has been well documented in recent years [2]. It is a complex phenomenon where the abdominal pressure rises, compressing the IVC and renal veins initially, resulting in decreased cardiac output, pulmonary dysfunction, acute renal failure, and mesenteric ischemia. If left unchecked, it will result in hemodynamic collapse and death. Studies of the ACS have noted a concomitant increased ICP [1, 3, 4]. This relationship has been seen in the trauma and non-trauma setting [4, 5]. Many disease processes result in increased intracranial pressure, specifically obesity, pseudotumor cerebri and insufflation associated with laparoscopic surgery [6]. Abdominal insufflation with laparoscopy has been shown to increase ICP to a maximum of 25 cm H_2O with the standard 15 mm Hg [6]. This is especially remarkable since 15 mm Hg is a routine insufflation setting for laparoscopy, and 25 cm H_2O exceeds the threshold for ICP that requires maximal intervention.

Over the last two decades, there has been a greater appreciation for the interrelationship between the cranial, thoracic and abdominal compartments. Building on the previous theories that pressure on the diaphragm causes increased intrathoracic pressure, it was presumed that elevations in the other compartments may impact the compensation mechanism of another. Bloomfield et al. acknowledged the potential of decompressive laparotomy (DL) for improving refractory ICP, and reported the first human case of decompressive laparotomy with the specific intention of reducing elevated ICP not responding to conventional treatment [3]. His patient was a 33 y/o male who fell off a ladder. There was no abdominal injury as indicated by a negative diagnostic peritoneal lavage. His ICP was maintained with paralysis, hyperventilation, sedation, mannitol, and ventricular CSF drainage, but on

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hospital day 6, his ICP increased to 35, his ventilation became more difficult with $PaCO_2$ of 45 mm Hg and a tense abdomen. Bladder pressure was not obtained. Decompressive laparotomy was performed and all of his physiologic parameters immediately improved, including ICP decreasing from 35 to 14. His intracranial pressure monitor was removed 24 h later. His abdomen was closed with retention sutures at postoperative day 10, and he was discharged to a rehabilitation facility with a near complete neurologic recovery.

Bloomfield et al. then investigated the pathophysiology of this suspected phenomenon of elevated IAP affecting ICP with a porcine model designed to create increased intraabdominal pressure with an inflated balloon [7]. Measurements were taken of the intraabdominal pressure, ICP, central venous pressure (CVP) and pleural pressure. Volume expansion was performed in some pigs prior to DL, and he noted an increase in cardiac output and cerebral perfusion pressures with that intervention, although volume expansion did increase the ICP prior to the decrease seen with laparotomy. He postulated that the increased intraabdominal pressure led to increased pleural pressure, causing increased central venous pressure, decreased cerebral venous outflow, and ultimately elevated ICP. He documented a normalization of ICP with surgical decompression.

The term "multiple compartment syndrome" was coined by Scalea et al. [1]. Since 2003, their group has published the majority of clinical data supporting this phenomenon [1, 4]. The incidence of multicompartment syndrome (MCS) was estimated as 2 % of TBI at their institution [1]. In their largest study including 102 patients with severe TBI, patients underwent DC alone and DC and DL [1]. They found that MCS patients had higher ISS, ICP, and IVF requirement, but no difference in mortality. They noted good results with both DC and DL in decreasing ICP, and that these can be used in sequence. They noted that DC was performed first unless IAH was present, in which case DL was performed first. They noted a significant decrease in ICP regardless of whether DC or DL was first. The MCS is thought to be a cycle from IVF and/or lung injury requiring fluid therapy to increase CPP. Fluid resuscitation used to increase CPP may lead to over-resuscitation and resulting visceral edema that leads to IAH. IAH leads to elevated CVP then ICP. There was a significant drop in CVP in survivors compared to nonsurvivors. ICP decrease was transient in those whose CVP did not decrease, supporting Bloomfield's theory of the role of CVP in DL [7]. Scalea et al. concluded that decompressive laparotomy, timed well, had the most success for improvement of neurologic function and prediction of survival was noted with decreased CVP after DL [1].

Others have also noted success with DL, but these studies are small, uncontrolled, and inconsistent in their results (Table 16.1) [1, 3, 4, 7–10]. Miglietta et al. noted that the refractory ICP was seen with only mildly abnormal abdominal pressures, but the resulting improvement in ICP after laparotomy was remarkable (9–10 mm Hg reduction in ICP), although one was immediate and the other delayed [8]. They noted the decrease in CVP, but no other measures were taken. Miglietta et al. noted (but did not reference) that previous experience with laparotomy with refractory ICP was only done once overt signs of ACS were evident, but they did not find significant improvements [8]. There is likely a time when irreversible damage may be done, and that intervention might be needed sooner rather than later.

The heterogeneity in the literature may be explained by looking at inconsistent variables and lack of controlled studies. Nagpal et al. explored a different measure, cerebral hypoxia, because they noted that cerebral ischemia could occur despite normal ICP and CPP. The patient in their case study had elevated ICP to 38, but was able to bring down the threshold to the accepted 20 mm Hg with mannitol, although the cerebral oxygenation as noted by the $PbtO_2$ was deficient [9]. Although Bloomfield hypothesized that JVD and cerebral congestion were the cause of the elevated ICP, Nagpal, and Migletti postulate that the lung function is also critical [7–9]. Nagpal notes that DL may have a beneficial effect on ICP, but more so on $PbtO_2$ (cerebral oxygenation) by improving pulmonary gas exchange and blood pressure [9]. Migletti noted

Table 16.1 Laparotomy effect on intracranial hypertension. ICP: Intracranial pressure, IAP: Intraabdominal pressure

Study	Patients (*n*)	DC as well?	Time to laparotomy	ICP change mmHg (average)	IAP mm Hg (average)	Survival	Neurologic follow up Glasgow Outcome Score
Bloomfield et al. [3]	1	N	6d	21 (35–14)	n/a	Y	Rehab
Bloomfield et al. [11] (Swine)	5 swine	N	Same day	16.6 (27.8–11.2)	25 above baseline	n/a	n/a
Miglietta et al. [8]	2	1 of 2	6d, 1d	30 (45–15)	30 mm Hg	Y	"Full recovery"
				30 (45-15)	28 mm Hg		
Joseph et al. [4]	17	Y	5.8d	12.5 (30–17.5)	27.5	65 %	Rehab
Scalea et al. [1]	24	Y	–	7	28.5	44 %	Heterogeneous sample
Nagpal et al. [9]	1	Y	4d	38	24	Y	Rehab
Dorfman et al. [10]	1	N	2d	30 (40–10)	32	Y	3

that DL reduces the positive pressure applied to the diaphragm, and this may shift the compliance curve of the lung. Improved compliance may allow improved buffering of volume and pressure changes from all compartments [8].

Efforts to decrease ACS with nonoperative measures to avoid decompressive laparotomy have been disappointing [11, 12]. Migletti found that paracentesis alone does not change the ICP significantly [8]. Continuous negative applied pressure (CNAP) to the abdominal wall failed to lower ICP in the absence of IAH. With IAH, there was improvement [11, 12].

In an effort to standardize the management of the patient with refractory ICP, Scalea et al. used their extensive experience to create an algorithm for management related to the multiple compartment syndrome [1, 4] (Fig. 16.1). The emphasis is on conventional management of initial elevated ICP as its primary management. Initial conventional interventions include maintaining and establishing airway, breathing and circulation. Achievement and maintenance of optimal physiology is used to prevent secondary injury. First tier recommendations (Table 16.2) should be continued until ineffective, then second tier, then consideration for heroic measures. Each of these measures should be checked and reinforced if there are deviations from the recommended management. Emphasis was placed on timing of interventions and continuing to reverse the process provoking the increased intracranial pressure. They emphasize awareness that many interventions may initially worsen the ICP. For example, fluid therapy to improve the mean arterial pressure (MAP) may lead to third space accumulation, worsening ICP and IAH.

Insertion of a Camino or interventricular catheter (IVC) ICP monitor allows pressure monitoring. Cerebral perfusion pressure (CPP) is maintained at over 60 mm Hg. Throughout management, there is a high index of suspicion for intracranial changes necessitating CT scan of the head and deviations from conventional treatments (for example, checking an arterial gas to ensure PaO_2 and $PaCO_2$ are in the desired range and head of bed is elevated).

Intra-abdominal pressure is measured to monitor IAH [13]. Bladder pressure is measured by foley catheter drainage, instilling 100 cc sterile saline into the foley catheter, and inserting a 16-gauge needle into the urine collection port, which is connected to a pressure monitoring system using sterile tubing. The pressure is zeroed at the symphysis pubis. Serial bladder pressures are measured every 2–4 h [4].

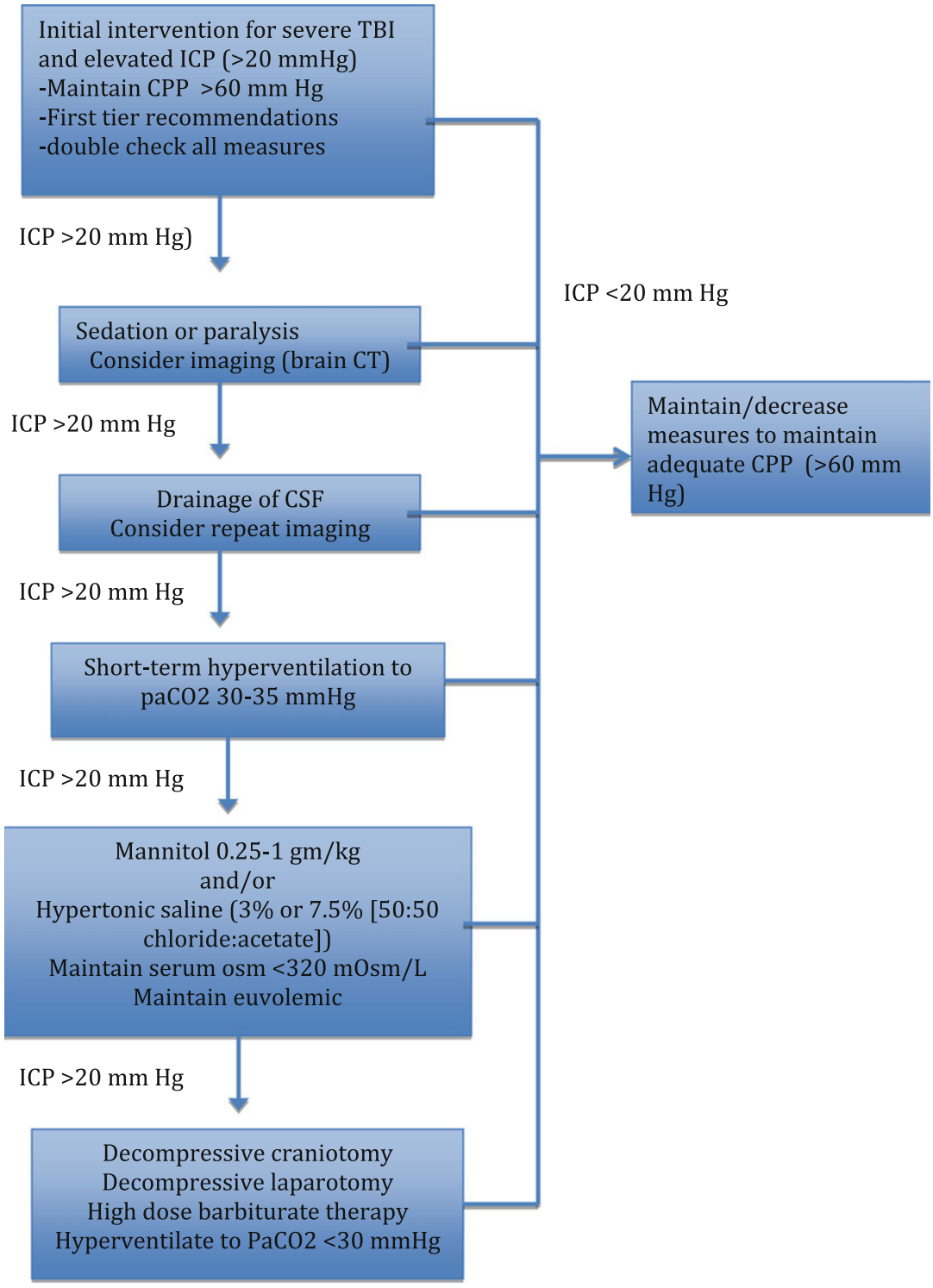

Fig. 16.1 Algorithm for management of intractable elevated intracranial pressure. All steps assume consideration for conventional measures and re-imaging as appropriate. Modified from Scalea et al.

Table 16.2 Available measures to decrease ICP and control secondary brain damage

First tier
Maintain airway, breathing, circulation
Elevate head of bed (HOB)
Optimize hemodynamics with systolic blood pressure > 90
Hematocrit 30–33 %
Serum sodium 140–145
Serum Osm < 320
Maintain euvolemia/minimize fluid overload
Maintain $PaCO_2$ at 35 mm Hg
Maintain normothermia
Optimal pain control and sedation
Reduce unnecessary noxious stimuli
Second tier
Drain cerebrospinal fluid
Increase sedation/paralysis
Short term hyperventilation to $paCO_2$ 30–35 mm Hg
Mannitol 0.25–1 g/kg
Hypertonic saline (3 or 7.5 % [50:50 chloride:acetate])
Heroic
Barbiturate coma
Therapeutic hypothermia
Decompressive craniotomy
Decompressive laparotomy

Decompression is considered with IAH of over 20 mm Hg [4]. This level of IAH is lower than advised for only ACS. Joseph et al. hypothesized that the ICP is the earliest symptom of ACS, and that other than the elevated ICP, there was not widespread organ dysfunction [4]. Intervening earlier seemed to improve outcome.

Similar to the results from decompressive laparotomy, outcomes from decompressive craniotomy have been mixed [1, 4]. It is not clear if this should be done first, or at all. Joseph et al. noted a trend towards worse survival with decompressive craniotomy and/or barbiturate coma, but neither was statistically significant [4].

As the patient progresses and improves, each intervention should be carefully removed as appropriate. Any deviation from expected results should prompt careful assessment of the current interventions and consideration of repeat imaging (CT scan), adequacy of ventilation, and assessment of lab values.

Conclusion

Several challenges still exist in the understanding of the MCS. The MCS is difficult to study given its infrequency and the difficulty in recognizing the syndrome outside of a high-volume center. Most current studies are small in number, highly variable, not randomized or even standardized. The brain has multiple regulatory mechanisms, and although ICP is one measurement, tissue oxygenation, free radical generation, and other confounding factors likely influence neuronal injury. Inconsistent outcomes of studies may reflect the unknown optimal timing of intervention to prevent irreversible damage. Unanswered questions remain, including understanding the prevention of MCS, proper timely diagnosis of the syndrome, which parameters to measure, when to perform DL, and if nonoperative measures could be successful to achieve decreased ICP.

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Associated Musculoskeletal Injuries 17

James R. Ficke and Brian J. Neuman

Introduction

Severe central neurologic or axial skeletal trauma is commonly associated with high-energy extremity injuries. In fact, the prevalence of injuries sustained along with spine injury in the polytrauma patient has been reported in the English-language literature to be as high as 10 %. Anderson et al. [1] reported that in patients with spinal cord injury, the most commonly associated fractures involved the radius, tibia, femur, humerus, fibula, and ulna. These were nearly all long-bone injuries, indicating more severe mechanisms of injury, and they often delayed patient mobilization and created challenges in nursing care and hygiene. Of these injuries, 48 % were caused by motor vehicle accidents, 41 % by falls, 6 % by recreational accidents or assaults, and 5 % by gunshot wounds. In other parts of the world, the prevalence may be even higher.

Archdeacon et al. [2] reported a high prevalence of spine injuries associated with acetabular fractures. In their review of 275 sequential acetabular fractures, concomitant spine fractures were seen in 12 % (54 fractures in 34 of 275 injured patients). Four percent of their patients sustained major thoracolumbar fractures (burst, flexion-distraction, or dislocation). When they occur concomitantly with severe pelvic trauma, spine injuries are closely related to higher rates of complications and death. Schoenfeld et al. [3] conducted an extensive review of the National Trauma Databank, which included 75,351 incidents of spine trauma. Patients had a mean age of 46 years, 64 % were male, and 9 % were black/African-American. Higher rates of complications (16 %) and death (6 %) were associated with older age, male sex, lower blood pressure on admission, and higher injury severity score. Nonwhite and black/African-American race were also associated with higher risk of death. Among trauma patients in Germany, Pape et al. [4] correlated the worst 10-year functional outcomes with limb amputations and severe spine fractures.

Polytrauma

Polytrauma is commonly seen in patients who sustain spine fractures with or without spinal cord injuries. The most common injuries associated with spine trauma are head injuries (17 %), lower limb fractures (5.9 %), upper limb fractures (4.4 %), chest injuries (2.9 %), pelvic fractures (2.5 %), and abdominal injuries (1.5 %) (Fig. 17.1) [5].

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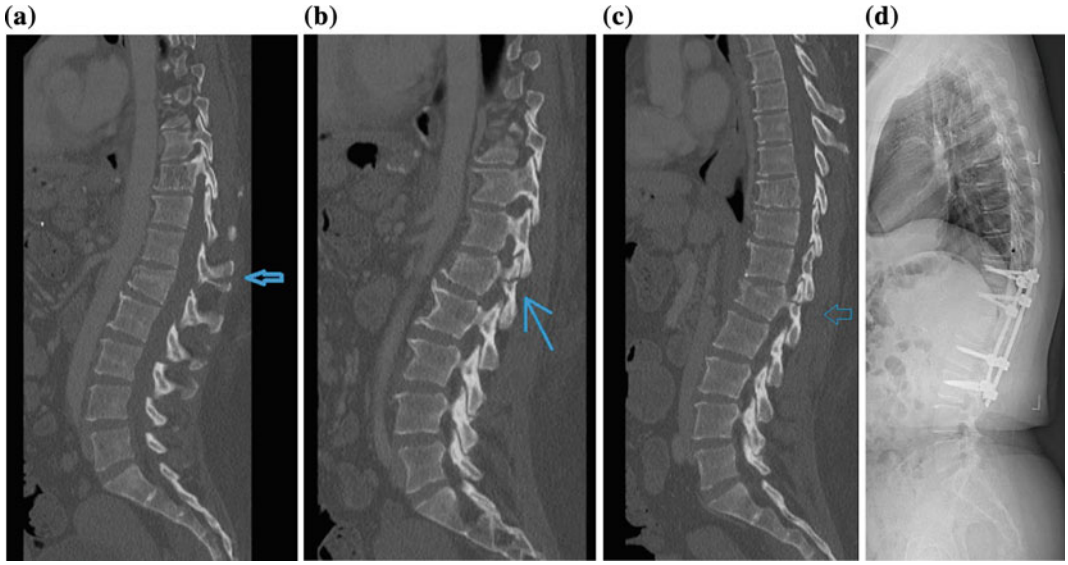

Fig. 17.1 **a–c** Preoperative CT scans of an unstable thoracic chance fracture, which is a flexion injury of the thoracic spine, demonstrated by the anterior vertebral body compression fracture with a transverse fracture through the posterior elements (*blue arrows*). **d** Postoperative radiograph showing treatment with posterior spinal instrumented fusion

The Injury Severity Score (ISS) is a tool that reflects all of the body's systems and helps assess the severity of each injury to determine its overall affect on the patient with polytrauma. ISS scores range from 0 to 75, with scores from each region of the body ranging from 0 (no injury) to 6 (unsurvivable). The ISS is calculated as the sum of the squared score from the three most severely injured body regions [6]. The ISS correlates linearly with mortality rates, morbidity rates, length of hospital stay, and other indicators of injury severity. Spine fractures contribute to the ISS, and treatment of these fractures in polytrauma patients is often complex, with associated injuries presenting obstacles to definitive surgical treatment. Therefore, coordination among multiple specialties is crucial in determining which injuries require immediate care and which can undergo delayed surgical treatment. In addition, polytrauma patients may be unresponsive, so injuries such as compartment syndromes, open fractures, joint injuries, and unstable pelvic injuries can be missed and treatment delayed.

Notable Associated Orthopaedic Injuries

Compartment Syndromes

When traumatized tissue swells, the swelling creates a functional constriction, and the blood pressure required to maintain perfusion is higher than for noninjured tissue. Soft tissue compartment syndromes can occur in trauma patients for several days after the initial trauma. In a patient with spine injury, perhaps with altered sensorium, the consequences of missing such a condition are grave. Whereas the diagnosis in a conscious patient is best made through serial clinical examinations, this is often not possible in unconscious or insensate patients [7]. The most common sites of compartment syndrome are the leg and forearm. When compartment syndrome is suspected because of aggressive fluid resuscitation, peripheral edema, or traumatic injury itself, the "five Ps" should be assessed: pain with passive

stretch, paresthesia, pallor, paralysis, and pulselessness. When these are not reliable, the diagnosis is made using compartment tissue pressures and determining a "delta P" (i.e., the difference between the tissue pressure and diastolic pressure) of less than 30 mm Hg indicating compartment syndrome [8]. In the event of compartment syndrome, early diagnosis, before irreversible tissue ischemia occurs, is imperative and represents a surgical emergency. Standard treatment involves compartment fasciotomy of all fascial compartments at and below the level of constriction.

Damage-Control Orthopaedics

The care of the multiply injured patient has improved substantially over the past several decades, as advances in rapid, life-saving surgery, as well as resuscitation techniques have led to higher survival rates. Damage-control orthopaedics refers to temporizing treatment through rapid debridement of open wounds, restoration of tissue perfusion, and limb circulation, stabilization of long bones, and, when possible, limb salvage using techniques not requiring extensive time and resources. Timing is critical, and with regard to orthopaedic injuries, stabilization through external fixation or judicious internal fixation can greatly facilitate both immediate survival and intermediate stabilization and intensive care management. These approaches should be considered whenever a patient is undergoing emergent control of major organ injuries, preferably simultaneously, with the goal of avoiding coagulopathy, acidosis, and hypothermia in the setting of evolving soft tissue injury, hemorrhage, or brain injury. The specific techniques are not within the scope of this text but should be discussed with the trauma team early and often.

Timing of Spine Surgery

The timing of surgery (early vs. late) for spine fractures is controversial. However, there is general consensus regarding several absolute indications for urgent surgical intervention.

The most agreed upon reason for early intervention is any progressive neurological deficit caused by spinal cord or root compression. Spinal dislocations associated with a neurological deficit or spinal kyphosis that compromises the overlying skin or patient positioning for non-spine procedures are also strong indications for urgent surgical intervention.

Multiple studies have evaluated the effects that early (<24 h) versus intermediate (24–72 h) versus late (>72 h) surgical spine intervention have on mortality rates, neurological outcomes, and non-neurological outcomes.

Multiple studies have shown that timing of spine surgery has little to no affect on overall mortality rates [9–12]. However, a subgroup analysis of one of these studies demonstrated that patients with an ISS greater than 25 have a higher risk of death when they undergo spine surgery less than 72 h after injury (12 %) than when they undergo surgery 72 or more hours after injury (2 %) [13]. Contrary to this, Schinkel et al. [14] reported higher mortality rates in patients who undergo late surgical intervention (17 %) versus early intervention (6.3 %). Conversely, Kerwin et al. [15] showed a higher mortality rate in patients who underwent spine surgery less than 48 h after injury. The most frequent cause of death was from acute respiratory distress syndrome. Controversy exists on the timing of spine surgery and its affects on mortality rates; therefore, it is important to evaluate each patient individually with a team approach to determine the optimal time for surgical stabilization (Fig. 17.2).

The effect of early decompression on neurological improvement is also controversial. Studies have compared early (<24 h) to late (>72 h) decompression and showed no significant difference in neurological recovery [13, 16–18]. However, these studies were conducted in small cohorts. Other studies have reported that patients who underwent early surgery had greater neurological improvement, particularly those patients with incomplete spinal cord injuries [19, 20]. To better evaluate the effects of timing of surgery on neurological recovery, Fehlings et al. [21] conducted a large, international, multicenter, prospective study of 313 patients. They

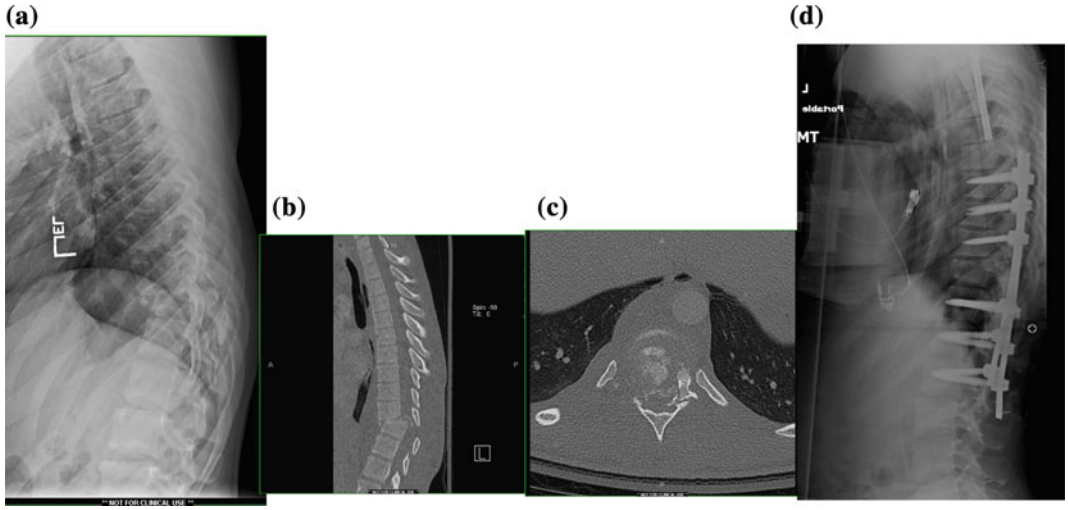

Fig. 17.2 Preoperative **a** radiographs and **b, c** CT scans showing a fracture dislocation of the thoracic spine after a motor vehicle collision. **d** Postoperative radiograph showing treatment with an open reduction with posterior spinal instrumented fusion

randomized patients to early or late surgery and showed that decompression within 24 h after injury was associated with neurological improvement of at least two American Spinal Injury Association (ASIA) grades at 6 months postoperatively. There was also a 2.8-fold higher chance of seeing an improvement of two ASIA grades in patients who underwent surgery early versus late. The mortality and complication rates were also similar between the early and late cohorts. Given these data, it appears that, when possible, early decompression (<24 h after injury) is safe and beneficial in regard to neurological recovery [21].

There are few data on the effects of early spine surgery (<24 h after injury) on the patient's hospital course. However, studies have shown that spine surgery within 72 h after injury is associated with shorter hospital stays, shorter stays in the intensive care unit (ICU), and less time mechanically ventilated [13, 14, 19, 22]. Frangen et al. [23] demonstrated that severely injured patients (ISS > 38) benefited greatly from undergoing surgery within 72 h, with the average ICU stay decreasing by 6 days and the average hospital stay decreasing by 52 days compared with patients who underwent surgery more than 72 h after injury. Although the data are limited on the effects that early surgery (<24 h after injury) has on the hospital course, surgery within 72 h appears to be beneficial.

Optimal timing for surgical stabilization of spinal column injuries and long-bone fractures in polytrauma patients is controversial. Any injury that is life- or limb-threatening must be addressed first. As described previously, early spine decompression and stabilization can reduce morbidity, shorten ICU and hospital stays, and potentially improve neurological outcomes. Similarly, studies have shown that early stabilization of long-bone fractures, particularly femur fractures, in patients with polytrauma is associated with lower complication rates and shorter ICU and hospital stays [24–26]. Therefore, it is accepted that early stabilization of unstable spine fractures, pelvic fractures, acetabular fractures, and femur fractures enables early mobilization of patients and reduces complications [25, 27–32]. This has not only been demonstrated in patients with isolated injuries, but also in those with polytrauma. With that said, definitive care of fractures soon after injury can expose the patient to a "secondary hit," which can cause a detrimental systemic inflammatory response. In severely injured patients, damage-control orthopaedics, with placement of provisional external fixation, is a

viable option to limit operative time and blood loss [33, 34]. Unstable spine fractures, however, cannot be treated with temporary fixation. Therefore, when assessing the polytrauma patient, it is important to (1) determine which fractures can be provisionally stabilized with a splint or external fixator, (2) stabilize those fractures, and (3) then treat the unstable fractures that can be managed only with definitive stabilization. It is important for the general trauma surgeon, orthopaedic trauma surgeon, and spine surgeon to be in close communication to methodically plan the order of each procedure so the surgery can be completed in a timely fashion, and so that each procedure does not hinder the performance of subsequent procedures.

Conclusion

Spine-related trauma is often associated with appendicular trauma, including fractures, vascular injury, compartment syndromes, and hemorrhage. Damage-control orthopaedics involves temporizing and stabilizing long-bone fractures prior to onset of the "secondary hit" phenomenon or systemic inflammatory response and should be considered in the immediate resuscitation phase along with other life- or limb-saving procedures. Spine fractures and long-bone injuries often lead to poor long-term outcomes; appropriate timing and adequate surgical fixation for spine and extremity fractures are critical components of favorable outcomes.

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Neuro Anesthetic Considerations

18

John Dunford

The severity of primary injury from neurotrauma is the major factor that determines the final neurological outcome. Secondary neurological injury caused by physiological effects that develop after the initial primary injury, contributes to the worsening of neurological outcome. Minimizing secondary neurological injury is the goal of the Anesthesiologist. Post injury hypotension, hypoxemia, hyercarbia, hypocarbia, hyperglycemia, hypoglycemia, and coagulopathy can all develop after neurological injury and contribute to final neurological outcome.

Traumatic brain injury is a contributing factor in 30.5 % of all injury related deaths in the United States, it occurs more often in young children, aged 0–4 years, adolescents aged 15–19 years, and elderly aged over age 65 [1–3]. Evidence based guidelines for both prehospital and perioperative management of patients with traumatic brain injury are published and updated. [4] Unfortunately, in spite of significant improvements in treatment of head injury in both the prehospital and hospital environment, the prognosis of patients with severe head injury still remains poor making prevention of head injury a high priority.

Primary traumatic neurological injury is the damage caused by the initial trauma from mechanical impact to the skull and brain tissue due to acceleration, deceleration, rotation, or penetration. This injury results in brain contusion, skull fracture, expanding intracranial hematoma, or diffuse axonal injury. The primary injury then initiates inflammatory processes with edema and excitotoxicity which result in further increases in intracranial pressure and decreased cerebral perfusion. [6–8] Secondary injury progresses after initial injury resulting in additional brain damage and worsened neurological outcome. The IMPACT study meta-analysis demonstrated that hypotension (Systolic pressure <90 mm Hg) and hypoxia (PaO_2 < 60 mm Hg) were associated with a worse prognosis. [8–10] The duration of intraoperative hypotension along with hypocapnea, hypercapnea, hyperglycemia, and hypoglycemia can all worsen secondary brain injury [8, 11–15] Coagulopathy is commonly associated with neurotrauma. Patients with severe combat-related trauma and isolated traumatic brain injury had worse coagulopathy than non-traumatic brain injury trauma [16]. Patients with traumatic brain injury with coagulopathy had worse outcomes than those with traumatic brain injury without coagulopathy [17–20]. Since secondary head injury is treatable, perioperative management with rapid evaluation, continuation of resuscitation, early neurosurgical intervention, intensive monitoring, and anesthetic planning all play a role in the treatment of neurotrauma.

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A resuscitation continuum begins at the point of injury, continues on to the operating room then to the intensive care unit. Specialized care in designated trauma centers has been demonstrated to improve outcome in patients with serious injury (Injury Severity Score > 15, Glasgow Coma Scale Score < 9) [21]. Patients taken directly to a trauma center have a lower mortality than those taken to another treatment facility first and then transferred to a level one trauma center [22] Stabilization and emergency transport requires trained emergency responders that have the skills necessary to treat hypoxia and hypotension. Proficiency in airway and both blood pressure and volume management are required in first responders. Targeted prehospital ventilation is associated with lower mortality after severe TBI [23]. Forward critical care resuscitation is an important component of trauma care in the military. The use of physician based emergency evacuation teams in the British military has resulted in improved survival in traumatic brain injury thought attributable to early expert emergency physician anesthesia and ventilation [24]. "Damage control" emergency trauma treatment takes it name from the US Navy term for emergency control of only systems required to prevent a damaged ship from sinking. This consists of rapid abbreviated surgery followed by resuscitation and aggressive correction of the "lethal triad" of coagulopathy, hypothermia, and acidosis. Damage control neurosurgery consists of stopping intracranial bleeding, evacuation of intracranial hematoma, early surgical debridement to limit wound contamination and possible decompressive craniotomy and surgical reduction of increased intracranial pressure [25].

Initial assessment and treatment in the emergency department needs to include evaluation of the airway with confirmation of proper placement of an endotracheal tube placed by the transport team [23]. The ability to ventilate along with assessment of both volume status and blood pressure is followed by a rapid assessment of neurological status. Mental status, Glasgow Coma Scale score and pupillary responses should be assessed. Evaluations for both cardiac and noncardiac causes of hypotension need to be considered especially frank bleeding, pneumothorax and pericardial tamponade. Consent, allergies, last meal, preexisting medical history, medications and laboratory assessment should be obtained as time permits. Resuscitation should continue on the way to the operating room.

Patients with traumatic brain injury will most often need endotracheal intubation. All traumatic brain injury patients should be considered to have a full stomach and possible cervical spine injury. A lower the Glasgow Coma Scale Score and a greater extent of facial fractures are associated with an increased chance of cervical spine injury. This is especially true with a GCS score less than 8 on presentation [26, 27]. The technique for tracheal intubation is determined by the urgency of the case, the expertise of the Anesthesiologist and the available airway resources. A rapid sequence intubation, with in line cervical stabilization, with the use of cricoid pressure in the most common technique. Use of video assisted laryngoscopy is becoming more commonplace and can provide a helpful alternative to direct laryngoscopy. Nasal intubation is usually avoided in patients with a coagulopathy, nasal or skull fractures. The ability to create a surgical airway should always be available.

Instrumentation of the airway is often greatly facilitated by the use of anesthesia induction agents and muscle relaxants. Selection of the best induction agent is based on level of consciousness, need for a muscle relaxant and hemodynamic stability. All of the induction drugs can be associated with significant hypotension and should be avoided in patients with significant hemodynamic stability. Midazolam and scopolamine, which are commonly used in trauma patients with significant hemodynamic instability, are often avoided in significant head injury due to their longevity and the lack of reversal agents. Flumazenil is often relatively contraindicated in head injury due to its ability to facilitate seizures [28].

Propofol is by far the most common drug used for anesthesia induction prior to intubation [29]. Etomidate and where available sodium thiopental can also be used. All of these agents decrease the systemic response to intubation, decrease cerebral metabolic rate for oxygen, and blunt the increase

in intracranial pressure that can be seen with laryngoscopy. Etomidate does provide improved hemodynamic stability when compared to propofol or sodium thiopental, however, its use is associated with adrenal insufficiency [30, 31]. Ketamine is associated with better hemodynamic stability but it is uncommonly used in neurosurgical trauma due to its longer half life, its association with increased cerebral blood flow, increased intracranial pressure and focal increases in cerebral metabolic rate. Outcome data contraindicating the use of ketamine in the neurosurgical patient has been questioned [32]. Neuromuscular blockade is commonly performed for laryngoscopy with either the depolarizing neuromuscular blocker succinylcholine or the non depolarizing neuromuscular blockers rocuronium or vercuronium [33]. Succinylcholine administration has been associated with an increase in intracranial pressure, however, the clinical significance seems to be marginal at best. The significance of hypoxia and hypercarbia from hypoventilation are more likely to result in worse clinical outcome then a small transient rise in intracranial pressure [34].

Intraoperative anesthetic management consists of the management of physiological parameters as established by the Brain Trauma Foundation and the Multidisciplinary Task Force for Advanced Bleeding following severe injury with appropriate anesthetic agents [35]. Hypotension should be avoided and a systolic blood pressure of greater than 90 mm Hg should be maintained. Hypoxia should be avoided. The PaO_2 should be kept greater than 60 mm Hg and the oxygen saturation should be kept greater than 90 %. Hyperventilation should be avoided unless being used to acutely decrease intracranial pressure. Mannitol should be used when acute treatment of increased intracranial pressure especially when signs of transtentorial herniation or progressive neurological deterioration are not attributable to extracranial causes. Hypertonic saline should be considered as a treatment modality in patients with increased intracranial pressure. Prophylactic hypothermia is not associated with decreased mortality. Moderate hypothermia (33–34 C) beginning within 8 h of traumatic brain injury for between 24 and 48 h could be considered as a treatment for refractory increased ICP with rewarming slower than 5 C per hour [35]. Hyperglycemia after traumatic brain injury is associated with worse outcomes. A target glucose range of between 80–180 mg/dl is reasonable [36–38].

Hyperthermia should be avoided. Intracranial pressure should be monitored in patients with severe traumatic brain injury and an abnormal CT scan or in patients with a normal CT scan if two of the following are present: Age greater than 40 years, motor posturing, or systolic pressure less than 90 mm Hg [4]. Cerebral spinal fluid drainage through and external ventricular drain can be used for refractory increased intracranial pressure if the basal cisterns are open, and there is minimal evidence of mass lesion or shift on imaging studies. If intracranial monitoring is in place, cerebral perfusion pressure should be maintained between 50 and 70 mm Hg. Increase in oxygen delivery should be performed if possible when brain tissue oxygen tension is less than 15 mm Hg or jugular venous saturation is less than 50 %. In patients with severe traumatic brain injury, high dose methylprednisolone is associated with increased mortality and contraindicated [39].

The anesthetic is performed with the knowledge of the pharmacodynamics and pharmacokinetics of the intravenous and volatile anesthetics used. Volatile agents (isoflurane, sevoflurane, desflurane) decrease cerebral metabolic rate while increasing cerebral blood flow. They uncouple autoregulation. However, at less than one MAC these affects are minimal and all three agents can be used at low doses in patients with traumatic brain injury [40]. IV anesthetic agents including propofol, etomidate, and thiopental decrease cerebral blood flow, cause cerebral vasoconstriction and decrease cerebral metabolic rate. All can be used in head injury. The FDA recommends against the use of a propofol infusion for the management of refractory intracranial hypertension due to the possibility of propofol infusion syndrome [41]. Etomidate is associated with a reduction in ICP and significant improvements in cerebral perfusion pressure with reductions in mean arterial

pressure. Adrenal suppression is associated with the use of etomidate [42]. Ketamine, unlike the other IV anesthetic agents, has a longer half life, increases cerebral blood flow and cerebral metabolic rate. In spite of this, it is being used in some centers for head injury due to its ability to maintain blood pressure [32, 43]. Nitrous oxide can increase cerebral metabolic rate and cause cerebral vasodilation with increased ICP. Transient myelopathy has been described in patients with B12 deficiency nitrous oxide. Data is lacking showing its use causes worsening outcome and institutions with a long history of administering nitrous oxide continue with its use [44–46]. Opioids provide excellent hemodynamic stability. Although many in vitro and animal models have demonstrated cerebral protection from anesthetic agents secondary to cerebral ischemia, clinical data to suggest any particular anesthetic agent provides improved clinical outcome in patients with head injury is lacking [47, 48].

Anesthetic management will include arterial catheterization for careful blood pressure monitoring as well as blood gas and chemistry analysis during surgery. Central venous access is indicated when required for resuscitation or for vasopressor administration. Timely placement of invasive monitors is important. Placement of access should not significantly delay emergent intracranial procedures. Monitors of cerebral oxygenation can be helpful especially if significant hemodynamic instability is expected or if hyperventilation is used to control intracranial pressure. Jugular venous oximetry, brain tissue oxygenation, and cerebral oximetry can be used for this purpose [49–53].

Hypotension should be avoided and the systolic blood pressure should be maintained at greater than 90 mm Hg while maintaining a cerebral perfusion pressure between 50 and 70 mm Hg. A mean arterial pressure of greater than or equal to 80 mm Hg should be targeted in patients with combined hemorrhagic shock and severe head injury. (GCS < 8) [35]. Hypotension occurring during the first 6 h after head injury has the highest prediction of poor neurological outcome at discharge [54]. Euvolemia, maintained with non glucose containing isotonic crystalloid solutions, should be maintained. Albumin has not shown to be preferred over crystalloid solutions [55]. 3 % hypertonic saline should be considered as a treatment modality in patients with significant increases in intracranial pressure either by bolus or continuous infusion, however it has not been associated with improved outcome over normal saline [35]. Hypertonic saline may be a more effective treatment for increased intracranial pressure management than mannitol [56]. Mannitol should be used only as a short-term acute therapy for increased intracranial pressure. Vasopressors are used to maintain mean arterial pressure and should be used early if blood pressure does not respond to volume treatment [35]. Phenylephrine, norepinephrine, dopamine, and occasionally vasopressin are used and are often institution specific. Current evidence does not support the use of one vasopressor over the others [57, 58]. Hypothermia at 33–35 °C with duration of greater than 48 h with rewarming lasting 24 h and cerebral perfusion pressure greater than 50 mm Hg may improve outcome. This is especially true for head injury patients with a Glasgow Coma Scale of between 4 and 7 [59–62].

The brain is susceptible to injury at low hemoglobin concentrations due to its high metabolic requirements. The current packed red cell transfusion strategies in neurological injury are not well defined and evidence for the best transfusion trigger is sparse [35, 63]. Hemoglobin levels of 5–6 g/dl alter cognitive function in health human volunteers producing subtle, reversible increases in reaction time and impaired immediate and delayed memory [64]. These cognitive dysfunctions are reversible by erythrocyte transfusion or alternately by the transfusion of oxygen. Patients with traumatic brain injury and mean even day hemoglobin of less than 9 g/L was associated with a threefold increase in hospital mortality [65].

A higher hemoglobin concentration might have the potential to increase oxygen delivery, resulting in a better outcome. However, this has not been translated in clinical practice and no consensus has been reached on appropriate transfusion thresholds in patients with head injury [63].

Hemoglobin thresholds for transfusion in critically ill patients have shown that restrictive transfusion strategies (hemoglobin thresholds between 7 and 9 g/dl) are as safe as liberal strategies (thresholds between 9 and 12 g/dl) [66]. A restrictive transfusion strategy was found to have a lower incidence of pneumonia, urinary tract infection, deep venous thrombosis, bacteremia and septic shock in severe head injury [67]. In 200 patients with traumatic brain injury, neither the administration of erythropoietin or maintaining hemoglobin concentration of greater than 10 g/dl resulted in improved neurological outcome at 6 months [67, 68]. The rate of favorable neurological outcome was similar in patients receiving blood at transfusion trigger of 7–10 g/dl [69]. A retrospective analysis of 139 traumatic brain injury patients suggested that increasing hematocrit above 28 % during the initial unstable operating room phase following severe traumatic brain injury was not associated with improved outcome as measured by extended Glasgow outcome scale at 6 months [70]. Erythrocyte transfusion increased the cerebral tissue oxygenation in anemic patients with severe TBI with a low baseline brain tissue oxygen ($PtiO_2$) levels. (<15 mm Hg) [71]. Similar results with transfusion resulted in an increase in brain tissue oxygen ($PtiO_2$), however no appreciable improvement on cerebral metabolism was measured by cerebral microdialysis. Lactate and pyruvate ratios and brain pH remained unchanged after transfusion of packed RBCs [71]. Therefore, a target hemoglobin of 7–9 g/dl is reasonable in transfusion goal. Patients with severe traumatic brain injury should be transfused to the same threshold as other critically ill patients [35].

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Decompressive Craniectomy for Severe TBI

19

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That military surgery does not differ from the surgery of civil life, is an assertion which is true in letter, but not in spirit. As a science, surgery, wherever practised, is one and indivisible; but as an art, it varies according to the peculiar nature of the injuries with which it has to deal, and with the circumstances in which it falls to be exercised.

—George HB Macleod.

Introduction

Unintentional injury is the leading cause of death in US patients aged 1–44 [2] and traumatic brain injury (TBI) is involved in approximately one-third of all injury deaths [3, 4]. According to the CDC there are more than 1.7 million new TBI cases each year; an estimated 275,000 are hospitalized, and 52,000 die [4, 5]. The current global TBI rate of 106 per 100,000 is increasing as developing countries expand and increase the use of motorized transportation [4, 6] While the rate of TBI is increasing, the number of TBI-related deaths has decreased in the US. In 2010 there were approximately 17.1 TBI-related deaths per 100,000 US population compared to 18.5 per 100,000 in 2001 [4]. TBI-related medical expenses place significant short and long-term burden on the US economy. In 2010, direct and indirect TBI-related costs were $76.5 billion dollars up from $60 billion in 2000 [3, 7, 8]. These numbers indicate the burden that TBI places only on the civilian population ignoring the military population.

There were over 320,300 diagnoses of TBI in deployed and non-deployed U.S. forces between 2000 and 2014. Of these diagnoses 2.4 % were either severe or penetrating TBI [9]. There was an increase in incidence of TBI from 10,958 cases in 2000 to a peak of 32,668 in 2011 [9]. It is difficult to evaluate TBI-related costs in the military. The only report known to date that calculates TBI-related hospital admissions of military personnel estimated it to be more than $41.9 million for fiscal year 1992 [10]. In 2008, RAND published an extensive report on the financial effects of major depression, PTSD, and TBI among OEF/OIF veterans. Based on per-case cost estimates for a single year (2005) mild TBI cost $25,571–$30,730 whereas moderate to severe TBI cost $252,251–$383,221. Using these estimates the total estimated one year cost for all deployment-related TBI cases occurring in 2005 ranged from $90.6 to $135.4 million dollars. Costs included treatment, rehabilitation, TBI-caused death, suicide, and productivity loss [11].

The diagnosis and management of TBI continues to evolve as recognition and surveillance of symptoms improve, emerging medical and

Notes on the surgery of the War in Crimea; With remarks on the Treatment of Gunshot Wounds [1].

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technologic advancements improve outcomes, and public support continues to fund research. This chapter will focus on the most recent information published regarding severe and penetrating TBI, and review the technical aspects of decompressive craniectomies.

Pathophysiology of Closed and Penetrating Head Injuries

Traumatic brain injury (TBI) is described as the alteration of normal brain function with micro- and macroscopic tissue destruction as a result of trauma. There are three types of TBI: closed, penetrating, and blast. TBI can be further characterized as acute or chronic, and mild, moderate, severe [12–15]. TBI can lead to temporary or permanent alteration of cognitive functions, slowing of psychosocial functions, and physical disability [16, 17]. The initial insult is termed the primary brain injury. Mechanisms that may prevent the initial injury include public policy initiatives, education, and protective equipment [3, 5]. The goal of medical and surgical intervention is to prevent the effects of secondary brain injury due to hypotension, hypoxia, cerebral edema, intracranial hypertension, and vasospasm [18, 19].

The pathophysiology of injury is dependent on the mechanism. In closed head injuries where the calvarium is not compromised, the primary injury results from acceleration/deceleration forces. These forces cause parenchymal contusions as the brain hits the inner table of the calvarium. Contrecoup injuries can be seen on the opposite side of the primary injury as the brain rebounds against the inner table [20]. The orbitofrontal and anterior temporal lobes are often affected [20]. In addition, the acceleration/deceleration forces place significant strain at tissue transition areas resulting in shearing injuries. The shearing forces lead to diffuse axonal injury (DAI) most often seen at the gray/white matter junction, corpus callosum, basal ganglia, and the brain stem [17, 20, 21].

The Iraq and Afghanistan wars have identified blast as a significant category of TBI [22]. There are similarities between blast and closed head trauma; however, blast TBI can have earlier cerebral edema and vasospasm suggesting a different pathophysiology [15, 23]. During an explosion the initial shock front, with high pressure, temperature, and supersonic speeds, is followed by a blast wind. The blast wind is capable of changing the medium in which it travels, which is distinct from sound waves [15]. As the wave propagates it causes tissue shearing due to the relative differences in tissue density, also known as spalling. This results in endothelial damage, increased permeability due to tight junction dysfunction, microglia infiltration, and a resultant inflammatory cascade leading to axonal damage and neuronal death [24, 25]. In addition, the blast wave damages hollow organs including the ears, eyes, and vestibular system [15, 20, 25]. Blast TBI can also result in penetrating injuries (secondary blast injury) and closed head injuries (tertiary blast injury) as a result of being thrown by the shock wave [25].

Penetrating brain injuries cause significant local tissue destruction dependent on the projectiles' kinetic energy, shape, trajectory, material composition, and characteristics of the intervening tissue [26, 27]. The initial tissue destruction as a result of the penetrating projectile is followed by a temporary cavitation due to the radially transmitted kinetic energy to the surrounding tissue. The cavity will collapse under negative pressure and this dynamic expansion and collapse can cause tissue damage 10–20 times the size of the projectile [26]. Projectiles can fragment upon impact with the calvarium resulting in comminuted skull fractures and multiple projectile paths resulting in more global tissue destruction. The tissue destruction leading to axonal loss, neuronal and glial death, and vasculature damage can be seen to gradually taper away from the projectiles path, likely related to the oscillating temporary cavity [28].

Current Guidelines

In 1995, the Brain Trauma Foundation (BTF) in collaboration with the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) reviewed the published literature to develop guidelines for the management of severe traumatic brain injury. It was most recently updated in 2007 [29]. In addition, the

BTF published another set of guidelines in 2006 for the surgical management of closed TBI [19]. In 2001 the International Brain Injury Association, in collaboration with the AANS and CNS, reviewed all published literature between 1966 and 2000 to publish a set of guidelines for the surgical management of penetrating brain injury [26]. Since then, there have been many publications from large civilian institutions and from the Iraq and Afghanistan wars that have added valuable knowledge to the growing body of literature. A review of the guidelines is beyond the scope of this chapter but is available for further review [18, 19, 26].

The primary indications for a decompressive craniectomy are severe TBI with refractory ICP to medical management and malignant cerebral edema secondary to a large hemispheric stroke [19, 26, 30–32]. Severe TBI can be associated with epidural, subdural, and traumatic parenchymal hematomas each with their own criteria for surgical evacuation. There are no comparative studies favoring craniotomy over craniectomy however craniectomy is usually reserved for patients with diffuse contusions, large extra-axial collections with significant mid line shift, and impending herniation [19]. In addition complex skull fractures can limit closure necessitating a craniectomy and delayed cranioplasty.

There are important clinical and radiographic factors that are considered prior to DC. Clinical factors associated with poor outcome in penetrating or closed head TBI include low GCS, age, bilateral fixed pupils, hemodynamic status, and coagulopathy [8, 33–39]. Radiographic findings of bihemispheric injury, ventricular or brain stem involvement also portend a worse prognosis in penetrating TBI [40–43]. While some have implemented aggressive surgical protocols for low GCS scores in closed TBI, others argue against decompression when the post-resuscitative GCS is 3–5 and there is no demonstrable hematoma on CT [39, 44]. The debate is ongoing and the presence of these factors does not exclude patients from surgery but are important prognosticators to be aware of when selecting patients for DC. In addition, resource limitations, regional capabilities, and time to definitive care can also influence the timing of decompression [45].

Outcomes

During World War I Harvey Cushing helped redefine the triage system and clearly documented the importance of early surgery, debridement, and aseptic technique to reduce the mortality rate of penetrating head injuries. Prior to WWI the mortality rate was greater than 50 % [46]. In 1918 Cushing published a 3 month case series of 219 surgically treated head injuries, 133 of which were penetrating. He saw a decrease in the mortality rate from 54.5 % in the first month to 28.8 % in the last month [47]. Surgeons would begin to publish their results and view the craniectomy as a physiologic procedure to combat the effects of cerebral edema rather than just a debridement technique for contaminated open head injuries [48, 49]. In 1971, Kjellberg and Prieto published a technical review of utilizing the bifrontal craniectomy for massive cerebral edema not controlled with full medical management [49]. Of 73 patients, there were only 13 survivors (18 %) and no survivors of penetrating brain injury. They concluded the operation should only be considered in the following scenarios: coma, fixed and dilated pupils, apnea, and/or decerebrate posturing [49]. The introduction of CT, MRI and novel techniques to measure intracranial pressure has been a valuable addition to the clinical indications for decompression. The question remains whether decompressive craniectomy for severe head injury improves overall functional outcomes or does it prolong survival with an increase in vegetative states.

Military Penetrating TBI

During the Vietnam War it was standard practice to extensively debride penetrating tracts and retrieve all retained fragments. This was influenced by the detailed observations and improving mortality rates from WWI. To further support the idea of aggressive debridement in 1971, Hammon published an analysis of 2187 penetrating brain injuries during the Vietnam War where he described his technique, “The tract of the missile was followed to its depth, the walls of

the tract debrided with suction, and all in driven debris removed." He reported a 9.74 % in hospital mortality rate and a 4.61 % rate of retained bone fragments identified on post-op plain skull films with a 0.63 % rate of postoperative meningitis [50].

The idea that retained bone fragments could cause intracerebral infections had already been questioned. In 1946, Maltby published results of 200 cranial war injuries between 1943 and 1945 reporting a 23 % infection rate, of which only 44.6 % of those infected had retained fragments. Compare that to the 55.4 % uninfected group with 47 % of those having retained fragments. Further review of penetrating injuries from the Vietnam era has demonstrated a lack of correlation between cerebral infections and retained bone fragments [51, 52].

During the Lebanese conflict from 1982–1985 practice shifted away from early and extensive debridement toward a surgical goal "to remove gross contamination with minimum manipulation of cerebral tissue" as described by Brandvold et al [51]. With a median follow-up time of 6.4 years, no patient with retained fragments developed a delayed intracranial infection and there was no relationship to the development of a delayed seizure disorder [51].

In 1990, Aarabi published a retrospective review of 435 patients sustaining projectile head injuries between 1981 and 1988 during the Iran–Iraq War. There was an overall mortality rate of 16.3 %. There was a significant correlation between increasing mortality with lower GCS scores on admission. Of patients presenting with GCS 13–15, 5.8 % had a poor outcome compared to 65.2 % of those presenting with a GCS score of 3–5. There was no correlation between outcome and site of injury or presence of retained bone or fragmentation [38].

Weisbrod et al. reviewed the long-term functional outcomes of 137 soldiers with penetrating brain injuries from OEF/OIF admitted to NNMC between 2003 and 2011. 65 % underwent unilateral craniectomy and 13.9 % underwent bilateral craniectomy. The entire cohort showed significant improvements in their GOS score through 2 years of follow up. There were 31 soldiers admitted to NNMC with a GCS score 3–5 and 32 % of those had a GOS ≥ 4 at 2 years. 74 % of soldiers presenting with a GCS score 9–11 and 100 % of soldiers presenting with a GCS score 12–15 had a GOS ≥ 4 at 2 years [53].

Bell et al. reviewed 408 patients presenting with severe head injuries between 2003 and 2008 during OIF/OEF and sought to identify the differences between those undergoing decompressive craniectomy and those managed nonoperatively. A total of 188 decompressive craniectomies were performed on 154 penetrating head injuries and 22 closed head injuries. There was a significant difference between the DC group and the nonoperative group in the initial GCS score (7.7 vs. 10.8, $p < 0.05$) and ISS (32.5 vs. 26.8, $p < 0.05$). The nonoperative group had higher GOS scores at all times points during follow-up compared to the craniectomy group but improvement was seen in both groups at all time points. At 2 years, 84 % of all patients had a GOS score >3. Patients with bilateral hemispheric involvement had the worse outcomes [45]. These outcomes pertain to those soldiers who survived their initial injury and were transported back to the United States for higher level care. It does not reflect those soldiers were died prior to transport or killed in action.

From the same cohort as Bell et al., Ecker et al. reviewed only those patients undergoing bilateral or bicompartmental decompression. 33 of 188 patients underwent bifrontal (58 %), bihemispheric (24 %), or supra- and infratentorial (18 %) decompression for blast penetrating (88 %) and gunshot wounds (12 %) to the head. The median initial GCS score was 5. After 1 year, 60 % had a GOS score ≥ 4, 10 % had a GOS of 3, and 30 % had a GOS score of 1–2. Bifrontal injuries had better outcomes than ventricular or subventricular injuries. In addition patients with cerebrovascular injuries had worse long-term outcomes [54].

Armonda et al. reviewed 57 patients with severe TBI for the presence of traumatic cerebral vasospasm. In a subgroup analysis, they evaluated the post-resuscitative GCS and the discharge GCS between patients undergoing hemicraniectomy, craniotomy, and those without surgical intervention.

They found that despite the hemicraniectomy group having statistically significant lower post-resuscitative GCS scores their discharge GCS scores did not differ significantly [23].

Civilian Penetrating TBI

In 1994 Levy et al. published their series of patients with penetrating craniocerebral injuries. Over a 6-year period, 190 patients were admitted with a GCS score of 3–5; 60 were managed operatively and 130 were managed nonoperatively. Operative management included superficial debridement, copious irrigation to remove superficial debris/fragments, and dural closure. Retrieval of deep-seated fragments was avoided. Only two patients of the operative cohort had a good outcome (GOS 4–5) and none in the nonoperative cohort had a good outcome. A predictive model of mortality was developed with a significant relationship between admission GCS and SAH and/or pupillary changes when responsive on admission. Another predictive model for morbidity was developed with a significant relationship between admission GCS score, bihemispheric injury with IVH and diffuse fragmentation. They concluded that patients presenting with GCS scores 3–5 with any of the findings above may not benefit from surgical intervention, but those with GCS scores 3–5 without fragmentation, SAH, IVH, bihemispheric injury, and responsive pupils should be followed more closely [55].

It was previously known that bihemispheric injuries portended a worse prognosis. In 1986 Kaufman et al. reported a worse prognosis with bihemispheric involvement, with only a 15 % survival rate compared to 64 % survival rate with unilateral hemisphere involvement [56]. Nagib et al. published their series of 55 patients with gunshot wounds to the head with a 50 % mortality rate overall and an 82 % mortality rate with bilateral hemispheric injuries. 23 patients presented with bihemispheric injuries and only 3 had satisfactory outcomes (GOS 3-4) [40].

Levy followed up with an additional study in 1999 evaluating outcomes in 294 patients presenting with GCS score of 6–15 during the same time period as the previous study. His predictive models of morbidity and mortality were confirmed in this study. 208 patients underwent surgical intervention and 86 were managed medically. There was a significant relationship between surgical intervention and survival with patients with admission GCS scores of 6–8. 24 % with admission GCS scores of 6–8 had a good outcome compared to 0 % who were managed nonoperatively. There was no relationship between surgical intervention and survival with admissions GCS scores of 9–15, but there was a relationship between intervention and morbidity with admission GCS scores of 12–15 [57].

A prospective study of 100 cranial gunshot wounds was published in 1990, which demonstrated no favorable outcomes for patients with post-resuscitation GCS score 3–5. However, surgical debridement included wide debridement of necrotic brain and bullet track, with retrieval of bone and missile fragments. A treatment algorithm was developed recommending no treatment for patients with post-resuscitation GCS 3–5 or GCS 6–8 with transventricular or multilobar injuries and absence of intracranial hematomas [39].

With dismal survival rates for patients presenting with GCS scores of 3–5 Joseph et al. implemented an aggressive resuscitation and surgical intervention protocol between 2007 and 2011 for patients with gun shot wounds to the head. The 5-year survival rate was 30.2 % (40/132). 107 patients presented with a GCS < 8. They noted an increase in survival with patients presenting with GCS scores 3–5 from 0 % in 2007 to 23 % in 2011. They did not report functional outcomes [44].

Closed TBI

There are many single center retrospective studies reporting mortality rates and functional outcomes with DC. The differences in outcomes can

be attributed to the heterogeneity of trauma, variability in surgical techniques and preferences, timing of surgery, and the inability to control for all factors such as age, sex, GCS, ISS, coagulopathy, sample size, ICP thresholds, ICP monitoring, and others. There are a few meta-analyses that have reviewed the past literature but none are able to definitively conclude that the use of decompressive craniectomy improves functional outcomes [33, 58, 59].

Recently reported series have published DC associated mortality rates ranging from 18 to 55 % [33, 35, 60–63]. However, those that survive have favorable functional outcomes on follow-up ranging from 37 to 82 % [33, 35, 60–63]. Improved outcomes have been correlated with younger age, early surgery, a larger change in ICP after decompression, and higher preoperative GCS scores. Aarabi et al. found that those admitted with a GCS score 6–15 were 10× more likely to have a good outcome compared to those with GCS scores 3–5 [35].

In 2001 Taylor et al. published a single center RCT that compared standard medical management to standard medical management and decompressive craniectomy in 27 children (median age 10 years) with severe TBI. The median admission GCS in the control group (n = 14) was 5 and the decompression group (n = 13) 6. The patients were randomized on admission and decompression occurred within a median of 19.2 h from injury. A bitemporal craniectomy without dural opening was performed in all patients. At 6 month follow–up, seven children (54 %) had a favorable outcome in the decompression group compared to two children (14 %) in the control group. They concluded that early decompression compared to medical management alone results in fewer episodes of intracranial hypertension and an improved functional outcome. These findings cannot be extrapolated to adults and one significant limitation of this study is the lack of dural opening [64].

In 2010, Chibbaro et al. reported a large prospective series of 147 patients undergoing early DC and early cranioplasty for severe TBI with a median preoperative GCS score 6. Bifrontal craniectomy was performed in 18/147 (12 %) and unilateral DC was performed in 129/147 (88 %). At a mean follow-up of 26 months, 89 (67 %) had a good recovery (GOS 4–5) and 19 (14 %) died. All cranioplasties were performed within 12 weeks. Younger age and earlier decompression had a more favorable outcome [34].

The DECRA trial (2011) was a multicenter, randomized control trial evaluating the functional outcome effects of bifrontotemporoparietal DC in adults under the age of 60 with severe TBI and refractory intracranial hypertension. 73 were assigned to the decompressive group and 82 were assigned to the control group. The median admission GCS did not differ significantly between groups (5 for the treatment group and 6 for the control group p = 0.31) but the treatment group did have more patients with nonreactive pupils (27 % vs. 12 % p = 0.04). Median time to surgery in the treatment group was 38 h after injury. There was a significant reduction in ICP after decompression compared to standard care and those undergoing decompression had less time on mechanical ventilation and shorter stays in the ICU. However, the treatment group had an unfavorable outcome in 51 patients (70 %) compared to 42 patients (51 %) in the control group (OR 2.21, CI 1.14–4.26, p = 0.02). Thus, contrary to their hypothesis patients undergoing decompressive craniectomy had worse outcomes at 6 months despite having improved ICP reduction. There are several limitations to this study that limit its applicability to general practice. The authors used an intent-to-treat analysis despite an 18 % crossover from the control group to the treatment group. Of 3478 patients evaluated for eligibility, only 155 were included thus narrowing the conclusions to only a small subset of patients with severe TBI. Finally, the protocol only evaluated one specific type of decompression surgery, bifrontotemporoparietal, which did not include sinus ligation and division of the falx [8].

It is difficult to generalize the strategies and outcomes of military TBI to civilian TBI due to the inherent differences in the mechanism of injury and post-injury resuscitation practices. It must be understood that the military literature typically reports younger healthier populations and earlier decompressions, often within hours of

the injury, in anticipation for air evacuation. Also, most soldiers are well trained in buddy aid and begin immediate resuscitation protocols as soon as the injury occurs [45].

In 2011 a comparison of isolated severe TBI during combat operations and civilian TBI was published by Dubose et al. Mechanism of injury, post-injury resuscitation and medical/surgical interventions, and mortality rates were compared from the military database (The Joint Theater Trauma Registry) to the civilian database (The National Trauma Databank). Between 2003 and 2007 there were a total of 604 military members with an isolated TBI, with 19.5 % penetrating injuries and 18.5 % blunt injuries. The rest were from explosive trauma and were excluded in the analysis. Compared to the NTBD between 2002 and 2006, there were 11,029 patients with isolated TBI, 92.8 % blunt TBI, and 7.2 % penetrating TBI. The military cohort was more likely to have an ICP monitor placed (13.8 % vs. 1.7 % $p < 0.001$) and more likely to undergo a neurosurgical operation (21.5 % vs. 7.2 % $p < 0.001$). While the military cohort more often presented with a GCS between 3–8 (26.9 % vs. 16.9 % $p < 0.001$) their mortality rate was 3x lower than the civilian cohort (7.7 % vs. 21 % $p < 0.001$) and when comparing penetrating injury mortality rates the military cohort was 10x lower than the civilian cohort (5.6 % vs. 47.9 % $p < 0.001$) [65].

General Background

Decompressive craniectomy refers to the removal of bone in order to expand the volume of the intracranial vault. This practice is based on the Monroe–Kellie theory, a fixed intracranial volume with three incompressible constituents (brain, CSF, blood). The goal of the decompression is to enlarge the intracranial volume to reduce intracranial pressure, minimize herniation, improve cerebral perfusion pressure, obtain hemostasis, and to evacuate any large extra-axial mass. Too small of a craniectomy can limit exposure, fail to achieve the previously stated goals, and can potentially lead to transcraniectomy herniation causing ischemia of the extravasating brain tissue [66].

More recently, the techniques for decompression have evolved from simple burr hole craniotomies and minimal subtemporal decompressions to large unilateral hemispheric or bifrontal craniectomies [46, 47, 67, 68]. When elevated ICPs are refractory to all medical maneuvers, a decompressive craniectomy can be employed as a salvage technique. Decompressive craniectomies can be unilateral, bilateral, bifrontal, or bihemispheric. Bifrontal is defined as bone removal up to the coronal suture and bihemispheric is defined as bone removal posterior to the coronal suture [54].

Setup and Positioning

Patients with severe traumatic brain injuries often have multiple systemic injuries. If the spine is unable to be cleared, this will have to be taken into consideration when preparing the patient for surgery. 3-point pin fixation may be used however for simplicity in an often chaotic environment a horseshoe head rest is typically used. Patients are placed supine on a standard operating table. Reverse trendelenburg, one of the first tiers for medical management of increased ICP, is used to help improve venous outflow. For unilateral craniectomies the patient's head is turned 15°–20° to the contralateral side, if there is no concern for C spine injury. A shoulder bump is placed under the ipsilateral shoulder to rotate the body in order to improve exposure and to prevent kinking of the contralateral jugular vein from over rotation. For bifrontal craniectomies the patient is left in neutral position The hair should be removed, per surgeon preference, with clippers [69] Preoperative antibiotics should be administered and for contaminated wounds longer duration should be considered, although there is no specific recommendation for type or duration [70]. Intradermal injection of a mixture of an anesthetic and epinephrine can help control bleeding and reduce postoperative pain [71].

Unilateral Hemispheric Craniectomy

A unilateral craniectomy (also known as a standard trauma craniectomy, frontotemporoparietal craniectomy, or trauma flap) begins with a reverse question mark incision beginning within 1 cm of the tragus to avoid the superficial temporal artery and facial nerve [72, 73]. Knowledge of the location of the STA, occipital, and posterior auricular artery is important in complex scalp lacerations so as not to devitalize the scalp [66]. The incision extends around the ear, posteriorly around the parietal boss toward the midline, and is then carried forward midline toward the supraorbital ridge [66]. If posterior extension is needed for adequate decompression a linear incision can be extended off the posterior aspect of the incision; although this may place the occipital artery at risk. Rani clips are used to control scalp bleeding. The pericranium is lifted off the skull and is reflected anteriorly with the temporalis muscle as a single myocutaneous flap. Fish hooks are used to hold the flap in place to maintain exposure. Additionally the temporalis can be dissected in a subfascial or interfascial plane to better preserve the frontotemporal branches of the facial nerve but this can be time consuming in an emergent situation [73–75]. Burr holes are then drilled at the pterion, above the temporal root of the zygoma, above the asterion, and then several are placed just off midline to avoid the superior sagittal sinus. A penfield 3 or similar dissector is used to reflect the underlying dura from the cranium. A craniotome is used to connect the holes, being careful not to strip the underlying dura. The craniectomy should be at least 14 cm in anteroposterior direction and 12 cm in superoinferior direction to ensure adequate exposure and to ensure maximal ICP reduction [35, 45, 76]. Once completed the bone is removed and rongeurs are used to remove the remaining squamosal portion of the temporal bone and greater wing of the sphenoid bone down to the floor of the middle cranial fossa. Failure to do so can result in inadequate decompression, continued brainstem compression, and/or transcraniectomy herniation [66, 77, 78]. Bone wax is used to block any visible mastoid air cells and to control bone bleed. If the frontal sinus is entered during the craniectomy it should be cranialized to prevent a postoperative CSF leak [79]. There are numerous techniques to open dura but typically it is opened in a "C-shape" fashion with or without stellate cuts depending on the amount of swelling [80–83]. Stellate cuts can allow greater decompression if there is still brain compression along the dural edges. Dural tack up sutures are used to prevent any epidural fluid collection beneath the craniectomy site, although this technique has been questioned since its first introduction in 1932 [84]. There is no level I evidence on dural closure technique or material however there is increased risk of infection with delayed CSF leaks so careful attention must be paid to wound closure [85, 86]. Dural closure can be accomplished with an autologous patch duraplasty (pericranium or tensor fascia lata) or with synthetic dural substitutes as an onlay or in a watertight fashion with running nurolon sutures [66, 86, 87]. After thorough inspection, hemostasis, debridement, and removal of any extra-axial mass, the myocutaneous flap is reapproximated and galeal sutures are placed followed by skin closure with nylon or staples.

The Kempe incision is a variation of the unilateral craniectomy incision. This involves a midline sagittal incision extending from widows peak to the inion and then a unilateral coronal incision from the vertex to the temporal root of zygoma [88]. Ragel et al. published a series of 90 craniectomies and noted instances of posterior wound breakdowns with the standard reverse question mark incision. They began to use the Kempe incision which spares the occipital and posterior auricular arterial blood supply in complex scalp wounds [66, 79].

Bifrontal Craniectomy

The bicoronal incision begins at the root of the zygoma, within 1 cm of the tragus. The coronal incision is carried to the contralateral temporal root of zygoma. How far the incision is posterior to the coronal suture will be determined by the extent of injury seen on CT scan. Kjellberg and Prieto described the craniotomy 1 cm posterior to the coronal suture. Once the incision is complete

and scalp bleeding is controlled, the scalp is reflected forward until the supraorbital ridge is identified. The temporalis muscles are reflected subperiosteally, anteroinferiorly with the scalp flap. The burr holes are placed at the pterion, above the root of the zygoma but below the superior temporal line within the squamosal portion of the temporal bone, and straddling the superior sagittal sinus in the coronal plane with the temporal burr holes [49, 60, 66]. While the frontal sinus can typically be avoided with even a large hemicraniectomy, on the occasion that a bifrontal craniectomy is required the frontal sinuses will invariably be violated. The requirement to remove the frontal bone to the frontal fossa floor in order to prevent the swelling brain from being injured is similar to the requirement with a unilateral hemicraniectomy to remove bone to the floor of the temporal fossa. Large, aggressive bony incisions for decompressive craniectomies are the rule, not the exception. Frontal sinus entry requires exenteration in the typical fashion. (See Frontal Sinus Injury Repair.) For emergent decompression a subtemporal window can be created at this time. The dura is carefully reflected off the bone with a dissector and the holes are connected with a craniotome. The craniectomy is carried forward to the supraorbital ridge, and to the middle cranial fossa floor by additional removal of the greater wing of the sphenoid bone and the squamosal portion of the temporal bone with rongeurs. The anterior extension of the superior sagittal sinus can be ligated with 2-0 nurolon sutures to allow for transection of the falx. This affords the frontal lobes further room for expansion [49, 60]. One variation is to perform bilateral frontal craniectomies, leaving a strip of bone over the superior sagittal sinus for protection [89]. The dural opening can be completed in several ways. As described by Kjellberg and Prieto, the dura is incised bilaterally along the craniectomy to connect along the supraorbital ridge where the anterior portion of the superior sagittal sinus is ligated. The dura is then reflected posteriorly to allow anterior expansion of the frontal lobes [49]. Harvested pericranium or a dural substitute can be placed as an onlay or sutured to the native dura in a watertight fashion [49, 60, 66, 86, 87]. The closure begins with galeal reapproximation typically with 2-0 vicryl sutures and then skin closure with nylon or staples.

Prior to closure of any craniectomy it is imperative to obtain meticulous hemostasis to prevent an unnecessary repeat surgery for an extra-axial hematoma. This can be achieved with bipolar cautery on the cortical surface and monopolar cautery on the skin. In addition to bipolar cautery, a number of hemostatic agents (gel foam, surgicel, surgiflo, surgical patties) in addition to finger pressure can achieve adequate hemostasis. At the surgeons discretion drains can be left behind and are typically subgaleal and extend posterior to the incision [90].

Complications

If patients survive the initial trauma and successfully undergo a decompressive craniectomy, there are still many complications that result due to the physiologic disruption in ICP, CBF, and CSF flow dynamics [78]. Immediate complications include continued swelling, transcraniectomy herniation, evolution of cerebral contusions, and extra-axial hematoma formation. Persistent edema and elevated ICP post decompression may be related to the size of the craniectomy and thus potentiate the possibility of transcraniectomy herniation. This can compress cortical vessels leading to new areas of infarction and rising ICPs. Postoperative CT scans may reveal new or persistent areas of hemorrhage. Residual hematomas may result from inadequate exposure or poor hemostasis on closure. Blossoming of parenchymal contusions is reported to occur 5–58 % postoperatively and is theorized to occur as a result of increased CBF and removal of the tamponade effect of the overlying calvarium [35, 60, 78, 91–93]. These contusions tend to occur on the same side as the craniectomy. Extra-axial hematomas, however, commonly occur on the contralateral side and are reported in 7.4–28 % of cases in recent series [92, 94]. These hematomas

tend to occur around fractures and may also be related to release of a tamponade effect [78, 92, 94].

Delayed CSF leaks, superficial and deep-seated infections, and subdural hygromas tend to occur days to weeks postoperatively. CSF leaks occur with poor wound apposition and healing, failure to cranialize encountered sinuses, failure to obliterate mastoid air cells, basilar skull fractures, and inadequate skull base reconstruction [66]. CSF leak is directly related to surgical site infections to include superficial skin infections, meningitis, and ventriculitis [85, 95, 96]. Wound infections vary depending on the mechanism of injury. The infection rate in civilian series of predominately closed TBI is 2–7 % [8, 35, 60, 76, 91, 92, 97]. The infection rate in military series in the post antibiotic era, which includes significantly more penetrating brain injuries, is 4–24.8 % [53, 70, 98–100]. Gram-positive organisms, mostly *Staphylococcus aureus,* cause most wound infections; however, in certain populations, especially military, Gram-negative organisms (*Escherichia coli*, *Acinetobacter, Enterococcus, Klebsiella*) are often seen [70, 85, 98, 99, 101]. Subdural hygromas, with a reported occurrence of 16–50 %, are typically ipsilateral and do not require any intervention [35, 76, 89, 90, 97]. Some authors describe performing serial percutaneous taps or other CSF diversion techniques but these may place the patient at increased risk for infection. These hygromas tend to resolve spontaneously in days to weeks. Occasionally definitive diversion with a ventriculoperitoneal or lumboperitoneal shunt will be required [89]. If the bone flap is still removed, CSF diversion for hygromas or LP punctures to rule out infection may lead to paradoxical herniation [102, 103].

Up to 50 % of patients with severe TBI will develop seizures and this rate may be even higher with penetrating brain injuries [104–106]. Routine prophylaxis against early onset seizure, described as within 7 days of injury, is recommended [18, 107]. Prophylaxis does not prevent against late onset seizure [18, 108–111].

Hydrocephalus may occur weeks to months after a decompressive craniectomy as a result of altered CSF flow dynamics or subarachnoid fibrosis [112, 113]. It has been reported to occur in up to 29 % in some series and may be related to the size of the craniectomy [8, 35, 60, 78, 94, 97, 112, 114].

The syndrome of the trephined has been well characterized in literature and may be as subtle as new cognitive slowing, depression, headaches, personality changes, visual disturbances to more apparent lethargy, obtundation, weakness, or hemiparesis. Additional work up is necessary to rule out other reasons for the symptoms. If the symptoms are related to the syndrome of the trephined they will resolve after cranioplasty [115–117].

Frontal Sinus Injury Repair

Frontal sinus injuries are frequently encountered in traumatic brain injuries and can lead to significant morbidity and cosmetic defects. These fractures are often complex and comminuted as the blunt forces are transmitted through the frontal, ethmoidal, and sphenoid sinuses often involving multiple craniofacial bones [118]. Craniofacial reconstructions are often handled in collaboration with OMFS, ENT, plastics, and neurosurgery. Isolated injuries to the frontal sinus without obvious disruption of the sinus walls may present more insidiously with headache, sinus pressure, rhinorrhea, meningitis, or abscess. When CSF leaks are present for more than seven days, there is an 8–10× increased risk in developing meningitis and the rate may be even higher in penetrating injuries [119, 120]. The rate of meningitis from penetrating head injuries returning from Operation Iraqi Freedom tripled, when there was an associated CSF leak [121]. The goal of surgery is to prevent or repair CSF leaks, cranialize the sinus, obliterate the nasofrontal duct, and achieve cosmesis [118, 120].

Frontal sinus injuries can be classified into three groups based on the involvement of the anterior table, posterior table, or both [118, 120, 122]. There is no class I evidence reporting the best operative management for frontal sinus injuries [120]. The timing (immediate vs.

delayed), method (open vs. endoscopic), and use of prophylactic antibiotics are still debated and much depends on institutional guidelines, surgeon preference, and injury characteristics. Surgery can be delayed or avoided if there is only anterior wall involvement and no gross cosmetic deformity or if only the posterior wall is disrupted and there is no obvious dural injury or CSF leak. However, in either case if the nasofrontal duct is compromised surgical intervention to either exenterate the sinus or cranialize the sinus should be considered to prevent mucocele formation [122]. If there is a subtle, persistent CSF leak determined by physical exam or other imaging modalities (radionuclide CSF flow study, CT myelography, or intrathecal fluorescein injection) a trial of observation with or without CSF flow diversion (EVD, LD or serial lumbar taps) can be used. When there is gross disruption of the anterior and posterior wall or a persistent CSF leak with concomitant CSF flow diversion surgical correction should be attempted. Surgical repair involves adequate exposure typically with a bicoronal incision in order to cranialize the entire sinus. The entire posterior table is removed with either high-speed drill, leksell and/or kerrison rongeurs to open the sinus to the intracranial cavity. It is extremely important to then remove all the mucosal lining within the cavity of the sinus down into the nasofrontal duct with a combination of high-speed drill, electrocautery, and curette scraping. The nasofrontal duct is then obliterated with a combination of bone chips, temporalis fascia, adipose tissue, and/or exogenous materials such as hydroxyapetite or methyl methacrylate [120]. Failure to remove all mucosal lining will result in mucocele formation and potential infection. If able to do so during exposure, a pericranial flap is created by incising near the coronal suture and bringing it forward so that it remains attached at the supraorbital ridge. This is laid back over the cranialized frontal sinus and on top of the anterior cranial fossa floor. If possible it is sutured to the ventral dural surface to prevent migration. If the anterior fossa floor is disrupted and requires titanium plating the pedicled graft can be sutured to the plates as a source of fixation. If the pericranium is damaged allo- or autograft dural substitutes can be used to partition the intracranial contents and the cranialized sinus. The goal is to prevent direct communication from the nasal and intracranial cavity leading to CSF fistulas and ascending infections [119, 120]. Post operatively CSF flow diversion with an EVD or lumbar drain can be used for several days to help the repair heal. There is no prospective data on the routine use of prophylactic antibiotics in CSF leaks. The use of antibiotics should be based on institutional guidelines and in consultation with infectious disease to prevent overuse and potential selection for drug-resistant bacteria [119].

Illustrative Cases

Case 1: (see Figs. 19.1, 19.2, 19.3, 19.4 and 19.5)

A 21-year-old male was involved in a T-bone collision while riding a motorcycle wearing a full face helmet. He was a GCS 3T on arrival to the hospital. His head injuries involved a left parieto-occipital contrecoup contusion and subtle bifrontal hypodensities and multiple orthopedic injuries. An EVD was placed and his intracranial pressures were managed medically for the first 5 days. Eventually the right parieto-occipital contusion and bifrontal hypodensities evolved causing 5 mm of left to right midline shift and medically refractory elevated ICPs > 20 mmHg. A wide bifrontal craniectomy was performed. He developed bilateral subdural hygromas 2 weeks after surgery that resolved spontaneously after 3 days of observation. He underwent a bifrontal cranioplasty 4 months after the craniectomy. He was discharged to neuro-rehab with a GCS 14. He has moderate cognitive changes and emotional lability consistent with his frontal lobe injury.

Case 2: (see Figs. 19.6, 19.7 and 19.8)

A 27-year-old male deployed overseas suffered a gunshot wound to the head from an unknown caliber weapon. He underwent an emergent cricothyroidostomy and was transferred to higher level care with an admission GCS score of 8T. Initial head CT demonstrated significant right

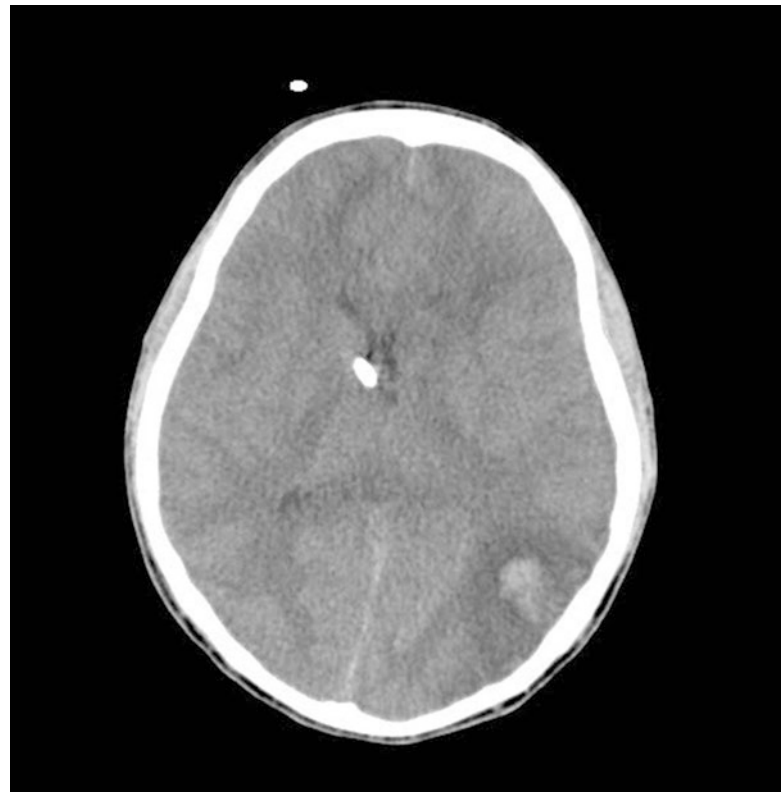

Fig. 19.1 Axial noncontrast head CT demonstrating a left parieto-occipital contrecoup contusion with surrounding hypodensity and subtle bifrontal hypodensities with 5 mm of left to right midline shift. There is a right frontal EVD in place

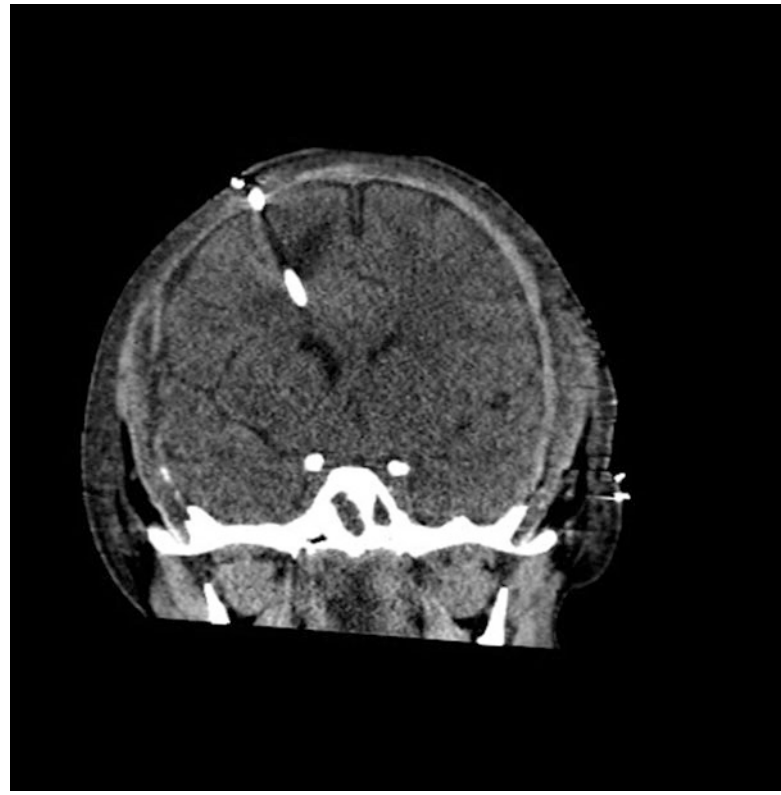

Fig. 19.2 Coronal head CT at the posterior border of the sphenoid sinus demonstrating a wide bifrontal craniectomy with extension to the middle cranial fossa floor

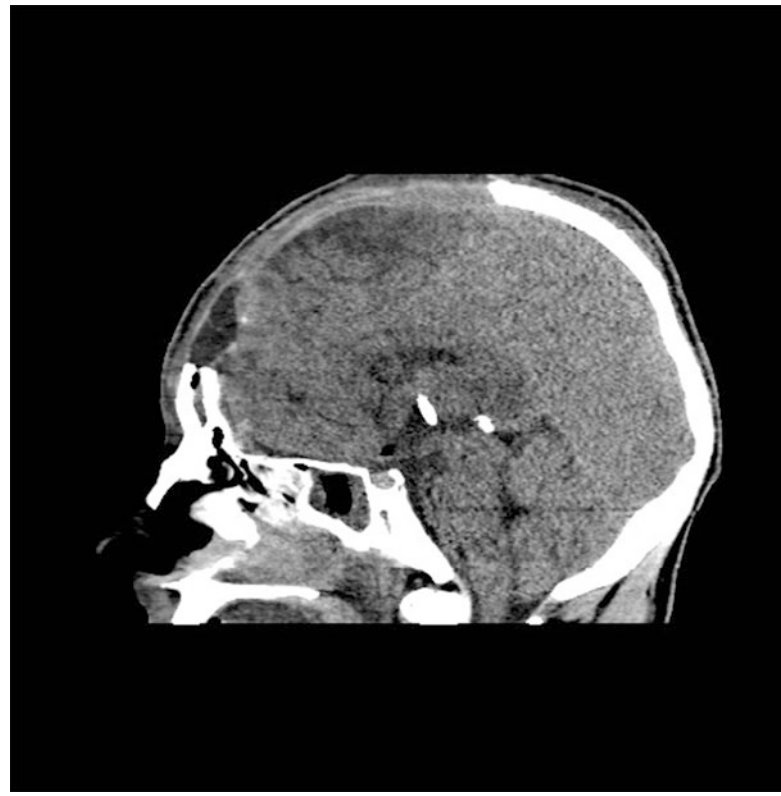

Fig. 19.3 Sagittal CT showing extension of the craniectomy posterior to the coronal suture

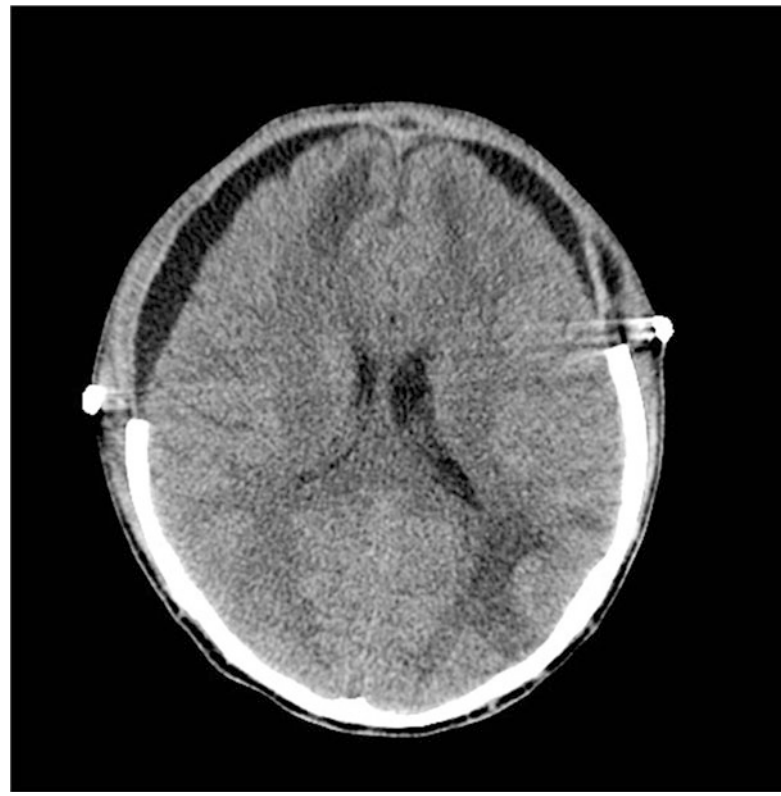

Fig. 19.4 Bilateral subdural hygromas that resolved spontaneously within 3 days

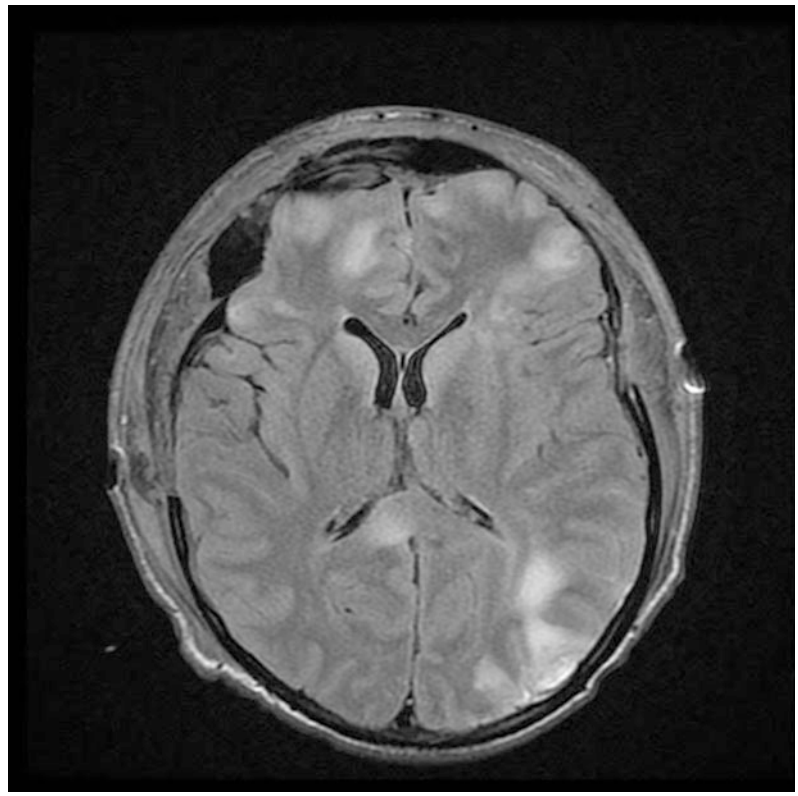

Fig. 19.5 T2 FLAIR sequence 1 month after accident showing signal intensity within the right parieto-occipital, bifrontal, and splenium consistent with diffuse axonal injury

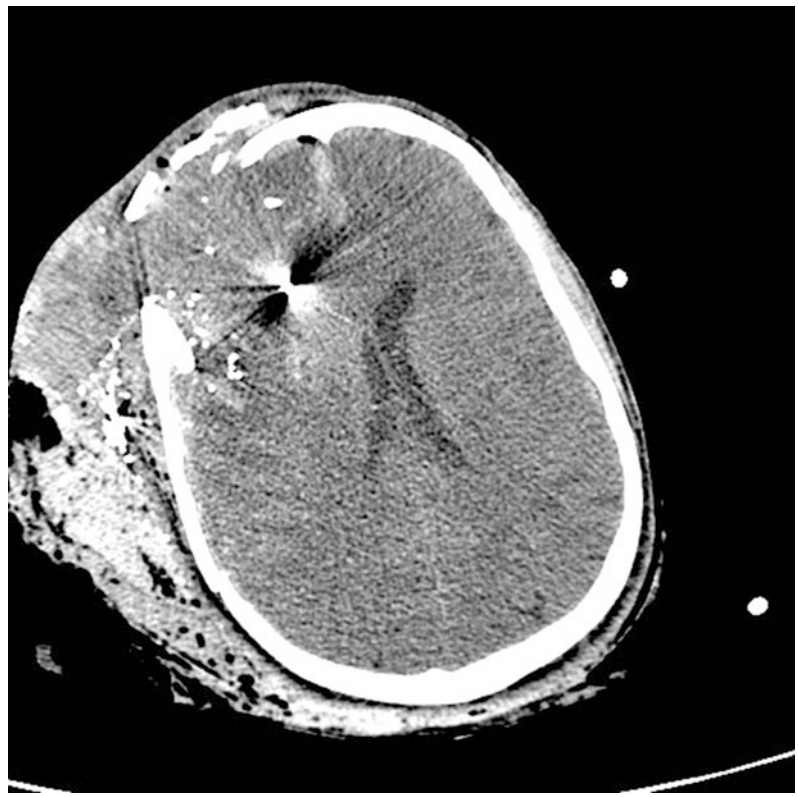

Fig. 19.6 Initial head CT demonstrating comminuted fractures of the frontal, temporal, and parietal bones, metallic fragmentation, traumatic subarachnoid hemorrhage around the anterior falx, and extensive soft tissue hemorrhage

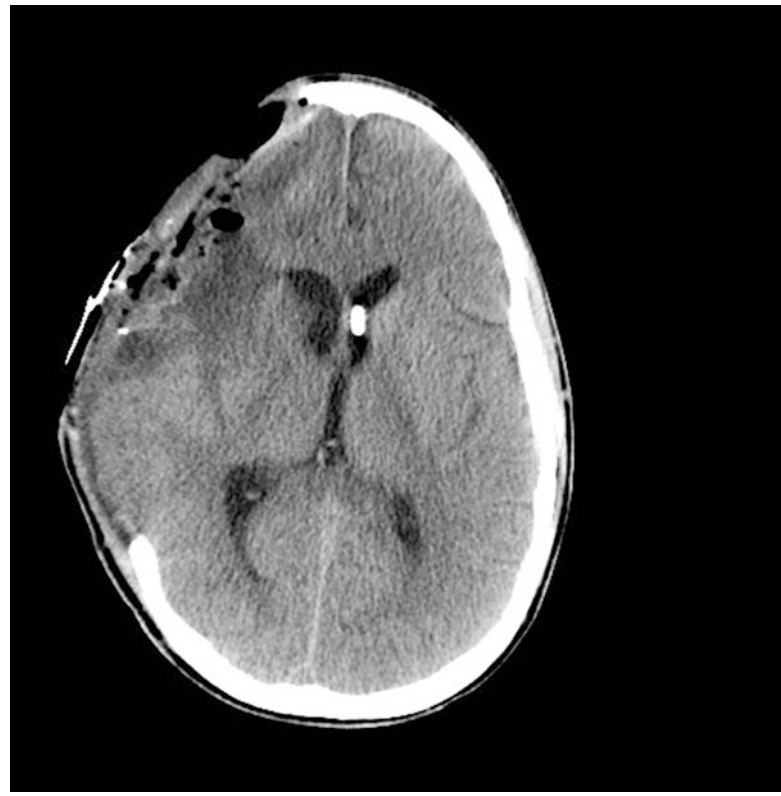

Fig. 19.7 Right frontotemporoparietal craniectomy (11 cm × 14 cm) with a left frontal EVD in place. The posterior extension stopped at a fracture line within the parietal bone and further removal of bone was not thought to be necessary at the time. The craniectomy extended inferiorly to the floor of the middle cranial fossa with less than a centimeter of temporal squamosal bone remaining

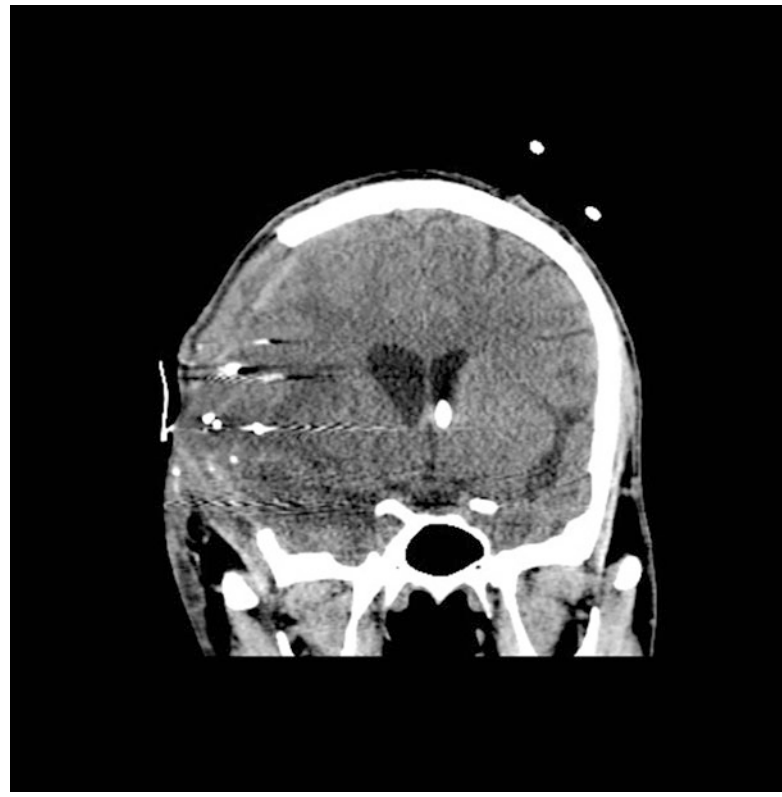

Fig. 19.8 Right frontotemporoparietal craniectomy (11 cm × 14 cm) with a left frontal EVD in place. The posterior extension stopped at a fracture line within the parietal bone and further removal of bone was not thought to be necessary at the time. The craniectomy extended inferiorly to the floor of the middle cranial fossa with less than a centimeter of temporal squamosal bone remaining

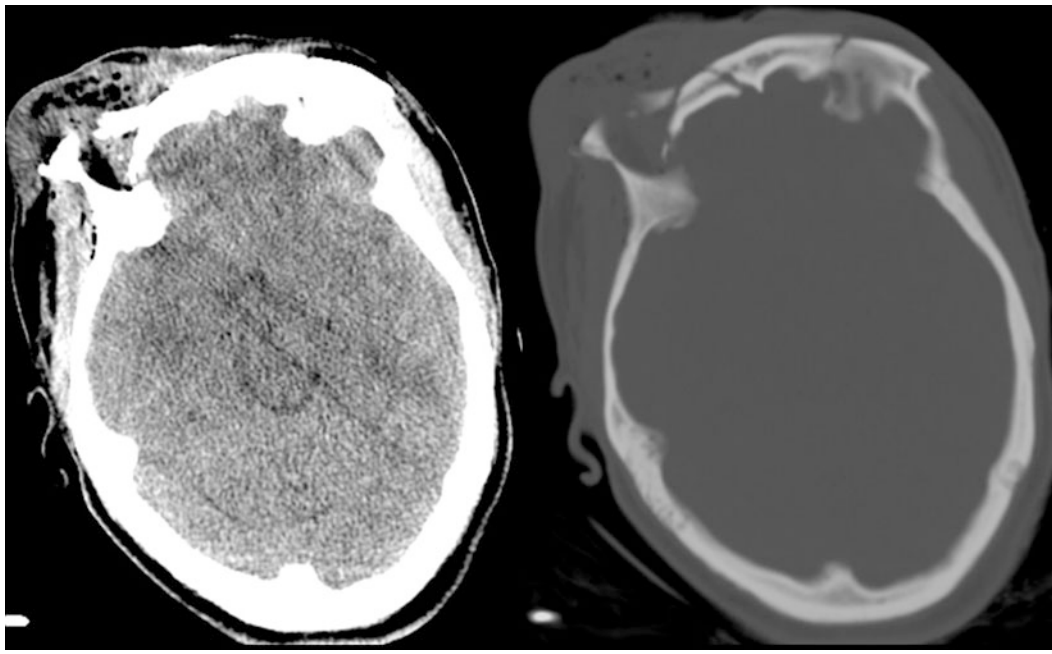

Fig. 19.9 Noncontrasted CT of head demonstrating comminuted fracture of the orbital bandeau and orbital roof and extra-cranial soft tissue swelling

maxillary, orbital, frontal, and zygomatic fractures, retained metal fragmentation within the right frontal lobe and effacement of the frontal horn of the right lateral ventricle. A left frontal EVD was placed but within 24 h his ICPs were refractory to medical management. He underwent a right unilateral craniectomy in theater. He was transferred back to Walter Reed for further care and rehabilitation. One month after the accident he was discharged to neuro-rehab with a GCS 14 and moderate impairment in judgment and insight. He underwent cranioplasty 6 months after the injury.

Case 3: (see Figs. 19.9, 19.10, 19.11, 19.12, 19.13, 19.14 and 19.15)

A 30-year-old female ejected from a motor vehicle after an unrestrained, head-on collision sustained direct craniofacial depression from a highway shoulder rail. On arrival, she was GCS 8T (E2-M5-V1T) and moving extremities symmetrically. She had gross brain matter and mixed serosanguinous fluid draining from an open facial laceration that extended from the middle of her forehead through her upper lip.

There are several intra-operative details that should be considered in conjunction with OMFS, Plastics, ENT and Oculoplastics teams to achieve several goals at the time of surgery: (1) decompression of cranial contents if there is a mass lesion or malignant edema, (2) primary repair of dural injuries using autograft, allograft, or dural substitutes, (3) reconstruction of anterior fossa floor and orbital bandeau, (4) thorough cranialization and exenteration of the frontal sinus, (5) reconstruction of severe, displaced facial and orbital injuries. A bicoronal incision was made and the subgaleal space was dissected anteriorly to the superior orbital rim, keeping the pericranium intact. A vascularized pericranial pedicle was incised beyond the incision posteriorly and up to the superior temporal line bilaterally; the pedicle was carefully dissected anteriorly to the superior orbital rim as well. This maneuver is critical for obtaining a large, vascularized autograft used for dural repair and reconstruction of the anterior fossa floor. A wide bifrontal craniotomy was performed, preserving the orbital bandeau to provide a scaffold for repairing her

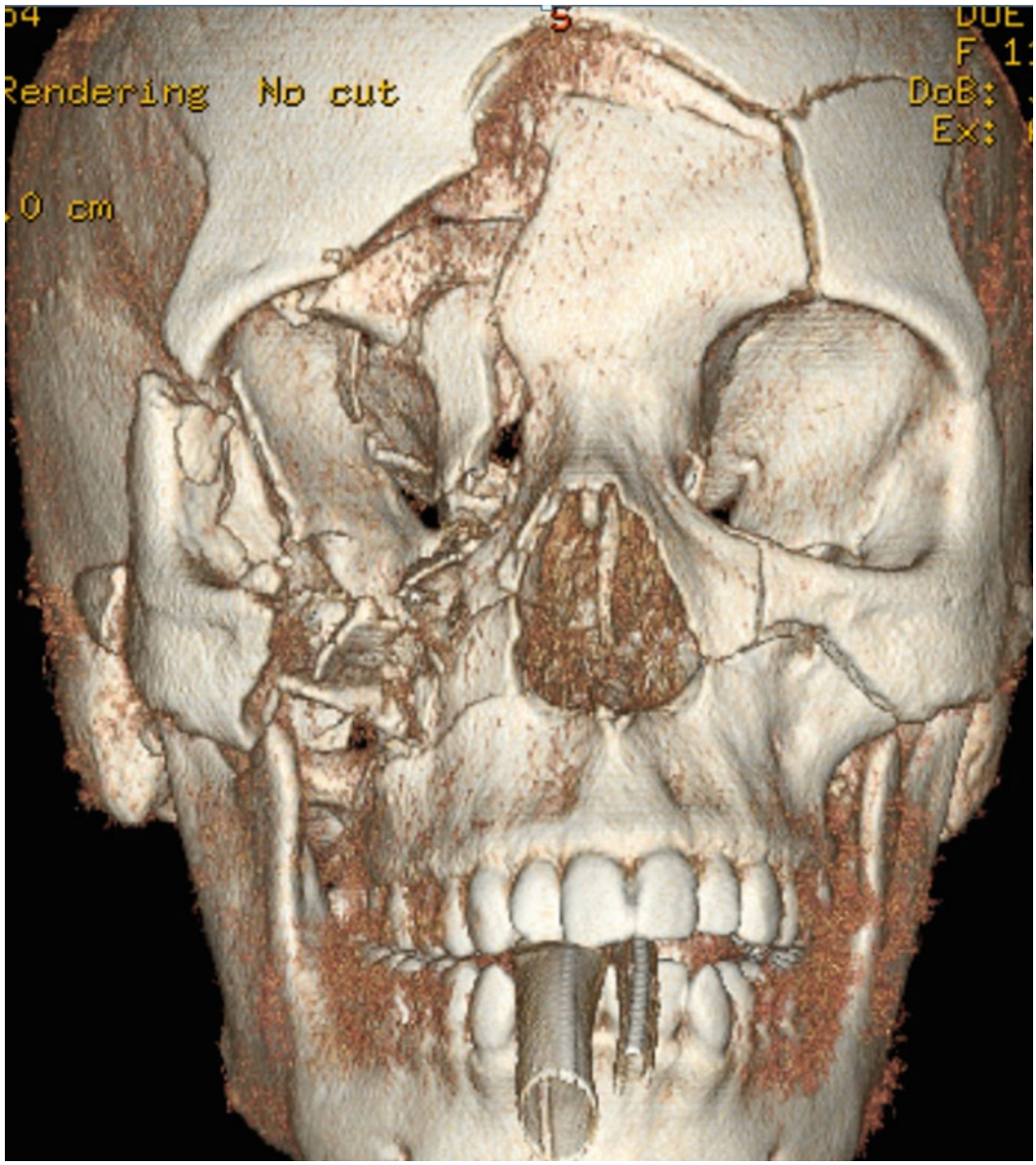

Fig. 19.10 Three-dimensional reconstruction showing complex cranial, facial, and orbital fractures

orbito-facial fractures. Her severe, depressed frontal sinus fracture was elevated and then cranialized and exenterated. The nasofrontal ducts were involuted and packed with muscle, bone chips, fat, and fibrin glue. A 7 cm dural laceration was present that extended from the frontal pole to the anterior clinoid process. The dura was elevated from the anterior fossa floor to visualize the extent of dural injury, and the orbital roof was internally reduced. The uninterrupted dura was opened and reflected medially; the anterior falx was dissected from the crista gali with suture ligation of the anterior superior sagittal sinus. A piece of pericranial graft was harvested far from the laceration site, and the dura was primarily repaired with 4-0 Nurulon suture. The

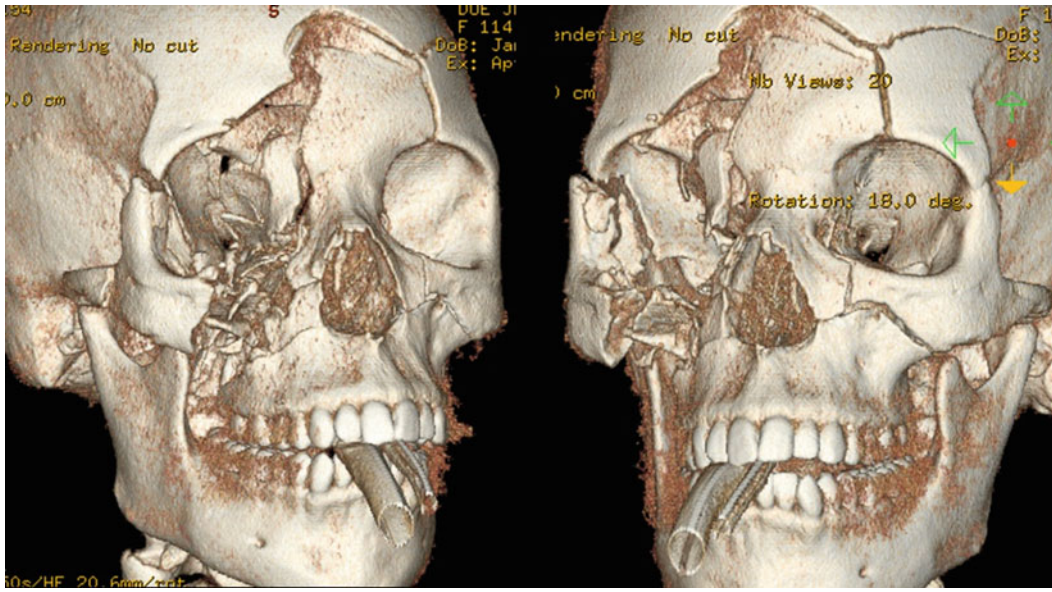

Fig. 19.11 Three-dimensional reconstruction showing complex cranial, facial and orbital fractures

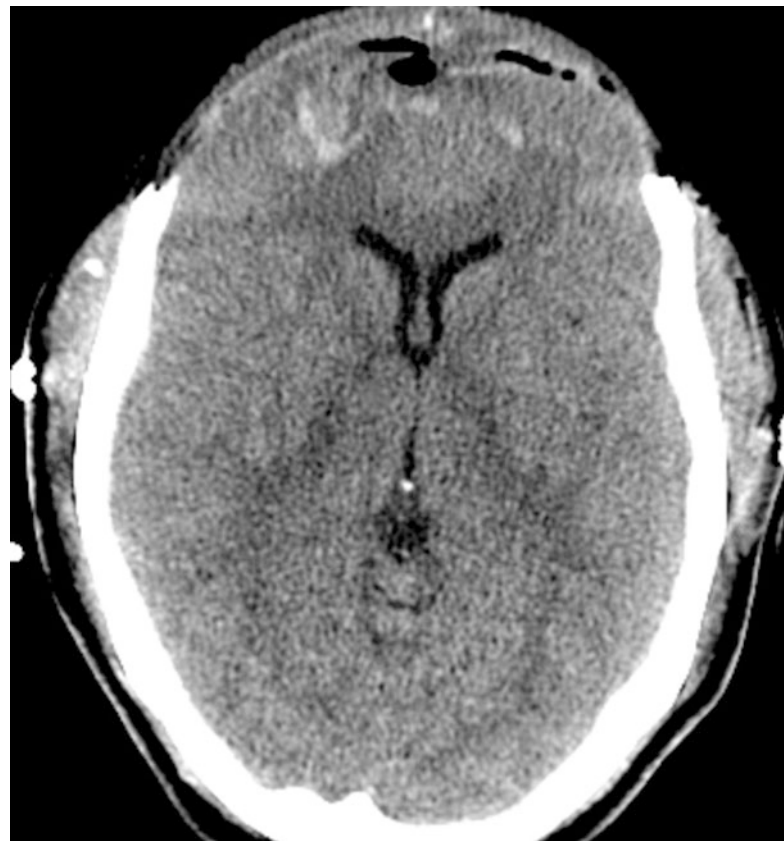

Fig. 19.12 Postoperative noncontrasted CT of head demonstrating blossoming bifrontal contusions

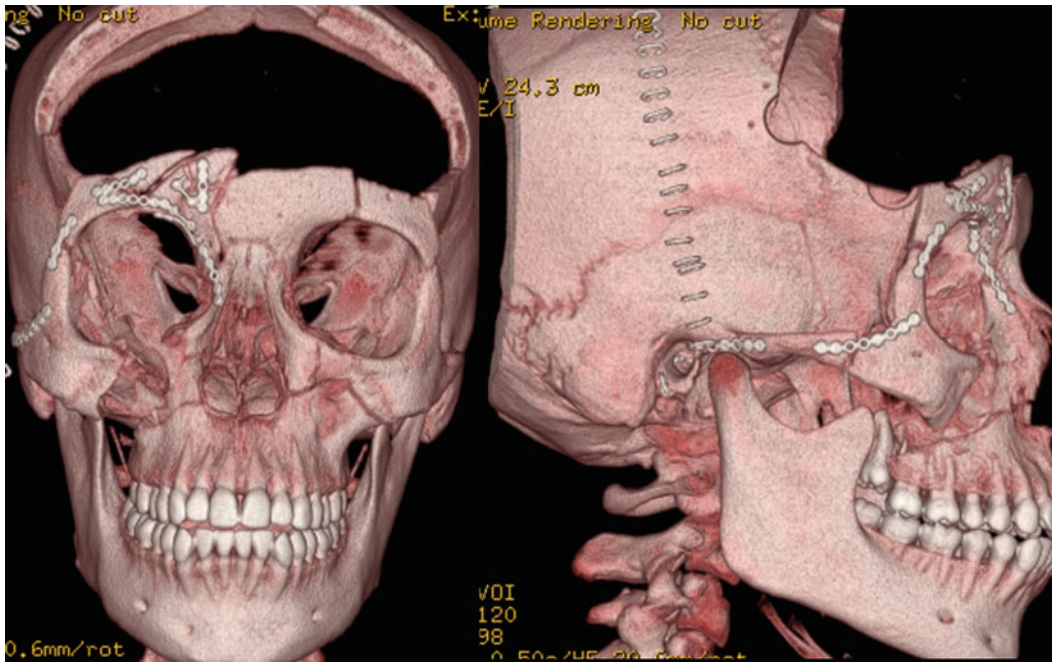

Fig. 19.13 Postoperative three-dimensional reconstruction demonstrating cranial decompression, reconstruction of zygomatic, maxillary, orbital bandeau, and orbital roof fractures

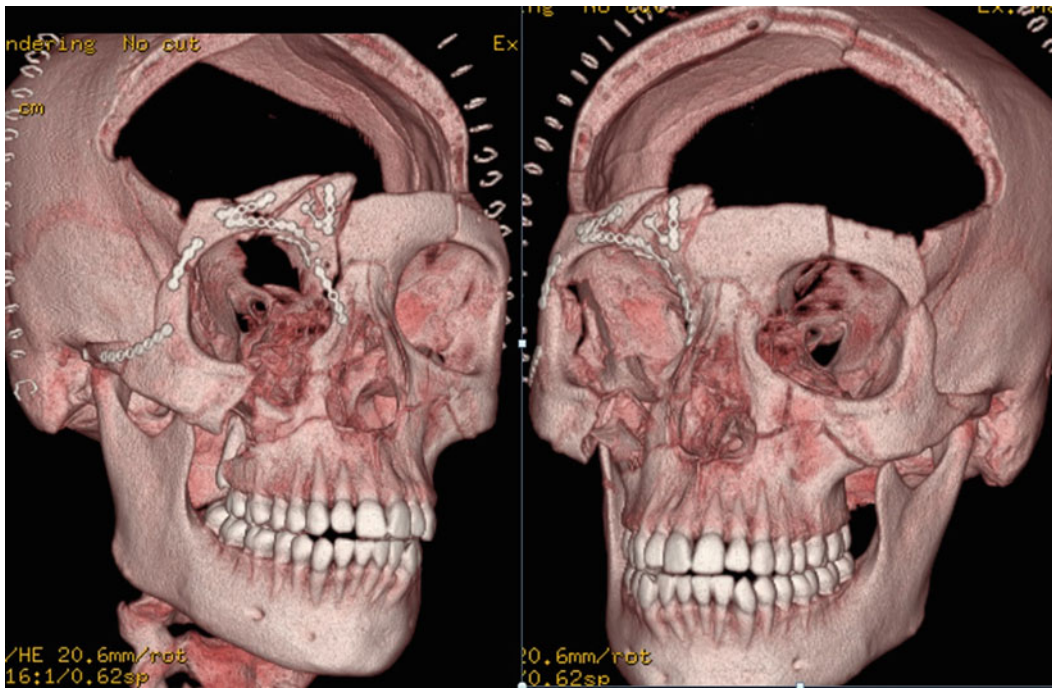

Fig. 19.14 Postoperative three-dimensional reconstruction demonstrating cranial decompression, reconstruction of zygomatic, maxillary, orbital bandeau, and orbital roof fractures

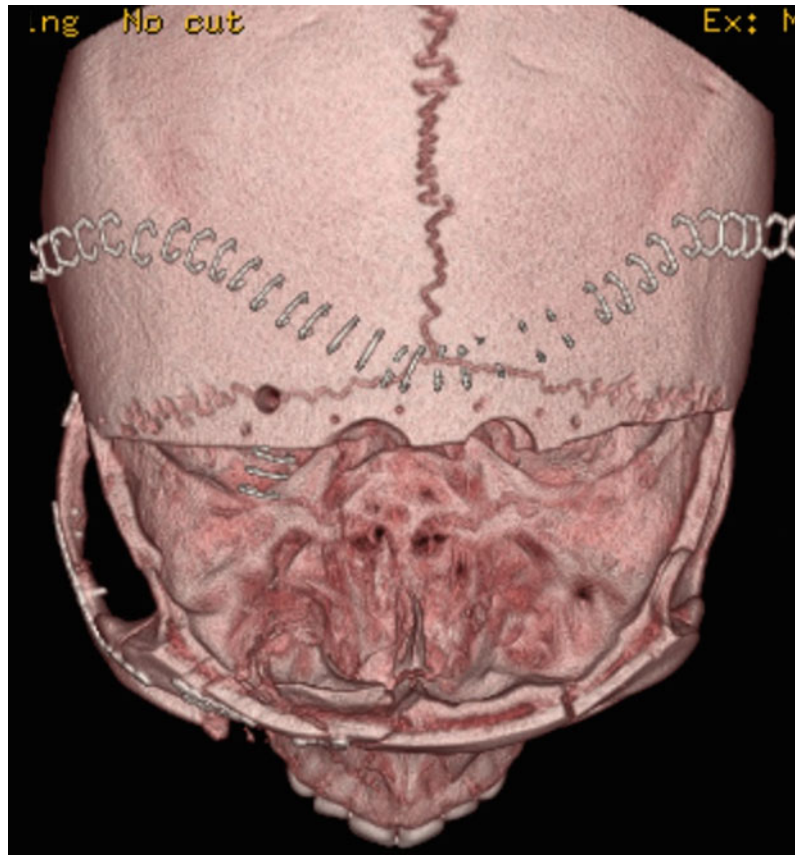

Fig. 19.15 Postoperative three-dimensional reconstruction demonstrating cranial decompression, reconstruction of zygomatic, maxillary, orbital bandeau, and orbital roof fractures

orbital bandeau was carefully reconstructed to provide a scaffold for cranial reconstruction in the future. The remaining vascularized pericranial pedicle was laid on top of the reconstructed bandeau and sutured to the dura at the anterior clinoid process to avoid retraction of the pedicle. The dura was covered with moist gauze and the OMFS team reduced and plated her complex facial fractures. The frontal lobes at the time of closure were soft and demonstrated normal pulsations.

Conclusion

Traumatic brain injury is a serious public health concern. There are more than 50,000 deaths every year with an expected rise in the rate of head injuries as the population expands. There are clinical practice guidelines for the medical and surgical management of severe head injuries but these are based mostly on Class III evidence. There are very few class I studies evaluating the role of decompressive craniectomy in severe TBI. As the survivability of traumatic injuries improves with advancing medical knowledge and technology, more well-developed prospective studies will be needed to help identify who will benefit the most from an aggressive surgical approach, as well as to keep the clinical practice guidelines up to date.

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Part IV
ICU Care

Hemodynamic Considerations in the Polytrauma Patient with Traumatic Brain Injury (TBI)

20

Jing Wang and Laith Altaweel

Epidemiology and Normal Physiology

Traumatic brain injury (TBI) is the leading cause of morbidity and mortality in the United States, especially in the young, affecting more than 1.4 million a year [1]. Serious major extracranial injury, or polytrauma, is commonly associated with TBI, occurring in up to 46 % of TBI patients [2]. Polytrauma is an independent predictor of poor outcome when compared to isolated TBI [3]. This is in part explained by the complications common to polytrauma, such as shock and anemia due to blood loss [4]. These complications contribute to reduced oxygen delivery resulting in delayed, or secondary, ischemic brain injury.

The effects of secondary brain injury are based on derangements in basic physiological principles of oxygen delivery. Normally, the human brain metabolizes oxygen ($CMRO_2$) during oxidative phosphorylation of ATP production necessary for neuronal function. To assure a constant and adequate delivery of oxygen for metabolism, a constant cerebral blood flow (CBF) is necessary. CBF rate varies based on changes in $CMRO_2$ or flow metabolic coupling. The high demand for oxygen, 20 % of the amount available to the whole body, makes the brain sensitive to changes in oxygen delivery (DO_2) [5]. In the setting of polytrauma with TBI, DO_2 can be perturbed due to shock, anemia, hypoxia, pain and agitation, and impaired cerebral autoregulation.

Mathematically, the relationship between DO_2, CBF and cerebral perfusion pressure (CPP) are defined in the following equations:

Equation 1:

$$DO_2 = CBF * [(Hb * 1.39\ mL\ O_2 * SaO_2) + (PaO_2 * 0.003\ mL\ O_2/mm\,Hg/dL)] * 10$$

Equation 2:

CBF if defined by the Hagen-Poiseuille law:

$$CBF = \frac{CPP * r^4 * \pi}{8 * \eta * L}$$

Equation 3:

$$CPP = MAP - ICP - IVP$$

DO_2, oxygen delivery (mL/min); CBF, cerebral blood flow (mL/100 gm brain tissue/min) Hb, hemoglobin (g/dL); SaO_2, oxygen saturation (%); PaO_2, partial pressure of oxygen (mm Hg); CPP, Cerebral perfusion pressure (mm Hg); r, vessel diameter; L, vessel length; η, viscosity; MAP, mean arterial pressure (mm Hg); ICP, intracranial pressure (mm Hg); IVP, intracranial venous pressure (mm Hg).

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The focus of this chapter will be to review the clinical challenges in optimizing DO_2 in the TBI patients with polytrauma. There will be a discussion on maintaining CPP with colloids, crystalloid, and vasopressor; as well as the current data on transfusing packed red blood cells. We will also briefly discuss intracranial pressure management and potential application of brain oxygen monitoring and cerebral microdialysis.

Cerebral Blood Flow

In healthy subjects, CBF is maintained at a constant flow despite fluctuations in blood pressure—mainly by modulating cerebral vessel size—a process known as autoregulation. As illustrated in Fig. 20.1, under normal physiological conditions, CBF remains relatively constant (about 50 mL/100 g/min) for a wide range of CPP (e.g., 60 and 150 mm Hg) [6].

In acute severe TBI, cerebral autoregulation is commonly lost, resulting in pressure dependent flow and increasing the risk for ischemia or hyperemia with relatively minor fluctuations in blood pressure. A reduction in CPP, especially when CPP < 50–60 mm Hg, can result in cerebral ischemia and worse outcomes; [7, 8] while higher perfusion pressure—CPP > 70 mm Hg or SBP > 120 mm Hg—has been associated with better outcomes [9, 10]. Yet, this finding is challenged by animal and human studies suggesting that higher CPP (e.g., CPP > 70 mm Hg), induced with vasopressors, are associated with cerebral edema, acute respiratory distress syndrome (ARDS) and worse outcomes [11–14]. Thus, the optimal CPP is likely within a narrow range, and is reflected in the National Brain Trauma foundation recommendation (Level III) of a CPP range between 50 and 70 mm Hg and SBP > 90 mm Hg, while avoiding a CPP > 70 mm Hg with pressors and fluids (Level II) [15]. For the polytrauma patient, increasing need for higher SBP goals, especially greater than 80–100 mm Hg, as might be necessary in a situation of raised ICP, must be balanced with the increased risk for extracranial bleeding [16, 17]. In order to achieve adequate perfusion goals, a

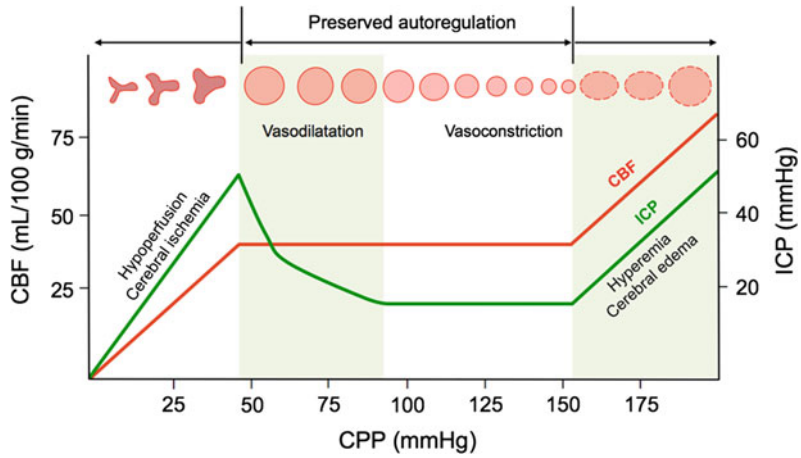

Fig. 20.1 Cerebral autoregulation, modified from [6, 127–129]. Under normal physiological conditions, CBF remains constant (about 50 mL/100 g/min) for a relatively wide CPP (e.g., 60–150 mm Hg), though age and chronic vascular disease may shift this range to the right; acute brain injury autoregulation is lost or narrow, such that the brain is susceptible to injury with CPP fluctuation. At low CPP (in figure above, <50 mm Hg), vascular tone collapses with resultant reduction in CBF and cerebral ischemia. Conversely, extremely high CPP (in figure above, CPP > 150 mm Hg), the myogenic vasoconstriction is overcome to the point of forced dilation and resultant increase in CBF with hyperemia, cerebral edema and intracranial hypertension. At these extreme pressures, cerebral autoregulation is lose, cerebral vascular tone and ICP are passive to CPP. This correlation between ICP and CPP is the basis for PRx [95]

combination of crystalloids or colloids and vasopressors are utilized.

Resuscitation with Crystalloids or Colloids

Patients with severe TBI often presented with concomitant polytrauma and may develop hypovolemic shock that requires early resuscitation. Resuscitation is commonly achieved with the administration of crystalloids or colloids, and vasopressors; with blood products reserved for hemorrhagic shock (discussed in later section). Rapid and adequate volume resuscitation is the first critical step in resuscitating TBI patients, as inadequate resuscitation is an independent predictor of worse outcomes in TBI patients [7], even when adjusted for blood pressure.

In choosing a resuscitation fluid, the general critical care literature lends considerable insight. When comparing crystalloids (e.g., normal saline or lactated ringer) to synthetic colloids (e.g., hydroxyethyl starch or pentastarch) or natural colloids (i.e., albumin) for resuscitation in critically ill populations, especially with sepsis, several large clinical trials have found either no benefit or harm with colloids [18–25]. In the TBI subgroup of the SAFE study, albumin was associated with intracranial hypertension, possibly through albumin extravasation into the brain, and death [20]. Given the clinical evidence against the use of colloids, guidelines recommend crystalloid for resuscitation in the trauma patient [26]. In this regard, the challenges in administering crystalloid will be determining adequacy of resuscitation without causing fluid overload.

Critical to the treatment of shock, regardless of etiology, is the rapid and adequate volume of the fluid. Much of literature on the dose of fluid resuscitation comes from non-trauma critical care studies, and has yielded mixed results. For example, in a mixed etiology ARDS study comparing two strategies, either liberal or restrictive fluid management over the first 7 days post injury, found the restrictive strategy resulted in a negative fluid balance, better oxygenation, reduced duration of mechanical ventilation and need for dialysis, but was equivocal with regards to the primary outcome of survival [27]. A secondary analysis of a septic shock study found higher mortality in the quartile with the greatest fluid balance after 4 days [28]. Conversely, in a recent prospective multicenter observational trial in septic shock patients, greater fluid volume was associated with a survival in patients with persistent shock [29]. Clearly, clinical equipoise persists regarding the effect of high-volume fluid administration in the setting of septic shock. Unfortunately, as a means of gauging the adequacy of volume resuscitation, traditional physiological variables, such as heart rate and blood pressure, are insensitive measures of ongoing hypoperfusion [30]. Initial arterial lactate level and clearance over time are prognostic, and thus could serve as a guide to resuscitation [31], but continuous real-time assessment of volume status is preferable. To this end, newer measures of fluid responsiveness, or need for additional fluid administration, using noninvasive or minimally invasive measures (e.g., straight leg raise or pulse pressure variability) have been studied in septic shock and show promise [32], but have not been studied in trauma and TBI patients.

Even if adequacy of volume resuscitation can be gauged accurately, it is important to note that the effect of fluid restriction may have heterogeneous systemic effect depending on the underlying pathology. For example, while the FACT trial found a negative fluid balance beneficial for lung function, a secondary analysis of the NABISH study (hypothermia in TBI) found that a negative fluid balance in severe TBI was associated with worse outcomes [7] Thus, what may be good for the lung may not be so for the brain, and generalization regarding volume status from non-TBI studies should be done with caution. In the setting of polytrauma with TBI, avoiding inadequate resuscitation may mitigate, to some extent, secondary brain injury.

The osmolality of the crystalloid fluid is also a critical factor in resuscitating the TBI patient. Compared to isotonic solutions, the use of hypotonic solutions (e.g., Ringer's lactate) is associated with an increased risk of cerebral

edema and intracranial hypertension [33, 34]. Surprisingly, the early administration of hypertonic saline has not been shown to be beneficial. In randomized controlled studies, the prehospital administration of hypertonic saline in hemodynamically stable or unstable TBI patients, while lowering ICP, did not improve long-term outcomes [35, 36], with some studies suggesting increased risk for hematoma expansion with hypertonic saline [37]. Clearly, the safety and efficacy of hypertonic saline in the setting of polytrauma needs more study. In conclusion, at a minimum, it seems reasonable to avoid hypotonic solutions while the administration of hypertonic saline should be reserved for treatment of intracranial hypertension.

Vasopressors

In polytrauma, shock is a serious life-threatening event that requires rapid treatment to prevent end-organ injury. In addition to hypovolemic shock, other etiologies include neurogenic, distributive, or hemorrhagic. Defining the etiology allows for definitive therapy (e.g., control of bleeding or chest tube for pneumothorax) if possible, or for initiating adjunct therapy (e.g., antibiotics). As the etiology of shock is being identified and treated, supportive measures may be necessary to normalize CPP, which is typically done with crystalloids, packed red blood cell transfusion, and vasopressors. With regards to vasopressors, optimal use depends on timing. Early initiation of vasopressors in trauma patients has been associated with increased risk of death [38, 39]. However, allowing shock to persist is similarly harmful, as suggested in an 8000 patient observational septic shock study [40]. Choosing an appropriate perfusion goal is also critical. Excessively high MAP to achieve a high CPP (i.e., >70 mm Hg) may contribute to cerebral edema and raised ICP, as well as ARDS [12]. However, in situations of raised ICP, administering vasopressors to achieve higher MAP, and thus adequate CPP, may be necessary to prevent ischemia [41]. Commonly used vasopressors in polytrauma patients include norepinephrine, phenylephrine, dopamine, and vasopressin [42]. It is not clear whether one vasopressors is superior to the rest [43], though animal data suggest a survival benefit with vasopressin in hemorrhagic shock [44], with human trials forthcoming [45]. From a practical standpoint, vasopressors need to be initiated as soon as necessary to maintain adequate CPP, and should be used in combination with crystalloids and packed red blood cells [46, 47].

Packed Red Blood Cell (pRBC) Transfusion

The transfusion of pRBC in trauma patients is critical for maintaining DO_2, with there being two thresholds for transfusion based on hemodynamic status. The more obvious threshold for transfusion is in the treatment hemorrhagic shock, in conjunction with crystalloids, vasopressors and control of bleeding, as reviewed in guidelines [16]. The second threshold for pRBC transfusion is in the hemodynamically stable anemic TBI patient at risk for ongoing secondary brain injury. Regardless of hemodynamic stability, there is a threshold below which cerebral ischemia is likely to be exacerbated by anemia, if not treated with pRBC transfusion. Defining this threshold has been very challenging.

As noted in Eq. 1, it is clear that hemoglobin is a critical component of DO_2. In healthy subjects, acute isovolemic anemia results in a reduction in oxygen content matched; which is compensated by an increase in CBF, mainly due to reduced viscosity and cerebral vasodilation, resulting in a constant oxygen delivery (DO_2) [48]. This reserve is limited, however, and with severe enough isovolemic anemia (e.g., Hb < 6), reversible impairment in cognitive function can be noted on neurocognitive and electrophysiologic testing [49, 50]. Patients with cerebrovascular disease do not have the cerebrovascular reserve of healthy subject, and as a consequence, even mild anemia results in reduced oxygen delivery [51], and potentially secondary brain injury. More easily measurable than cognitive function and secondary brain injury is the overall

functional status, which seems to be adversely affected with anemia in trauma [52], stroke [53] and severe TBI [54, 55].

The seemingly logical treatment of anemia in TBI with pRBC has not been proved in clinical trials of TBI without hemorrhagic shock. To begin with, pRBC transfusion is associated with severe side effects, including transfusion-associated circulatory overload, transfusion-related acute lung injury [56] and infection [57–60]. Perhaps as a consequence of these side effects, observational TBI studies have noted increased morbidity or mortality with pRBC transfusion [52, 61, 62]. However, such studies are limited through confounding by indication [63], whereby anemic TBI patients are likely sicker than those without anemia [64], and also more likely to receive pRBC; thus, making it difficult to differentiate the independent effect of pRBC on outcome from the natural history of the underlying disease. This notion is supported by the results of recent randomized clinical trials in non-TBI critically ill patients. In these studies of more than 4000 patient with sepsis or after cardiac surgery, a liberal transfusion goal resulted in more pRBC transfusions when compared to a restrictive transfusion practice, but did not result in increased harm [59, 60].

Specifically with regards to TBI, a randomized multicenter trial by Robertson et al., comparing a hemoglobin threshold of 7 versus 10 g/dL for transfusion in closed head injury TBI without life-threatening systemic injury, found no improvement in neurological outcome at 6 months as well as higher complication rate with the higher Hb threshold [65]. However, important baseline differences, such a higher rate of fixed pupils on presentation in the Hb 10 g/dL group, could have confounded results in favor of the lower Hgb group. In addition, a post hoc analysis suggested an interaction between the timing of injury (before or after 48 h) and Hb threshold (7 versus 10 g/dL) on outcome, with improved outcomes with higher Hb during the first 48 h, but harm thereafter [66]. This finding is in line with the observation that cerebral autoregulation and cerebral metabolic stress, as measured by cerebral microdialysis, are most abnormal during the initial 4 days after injury [67], suggesting this period to be one when pRBC is most likely to be beneficial.

Furthermore, anemia, independent of cerebral hypoxia, may not be a suitable indicator for pRBC transfusion. This is suggested in an observational study which noted worse outcomes in severe TBI patients with anemia only in the setting of coexistent cerebral hypoxia [68]. In another prospective study of moderate to severe TBI, brain hypoxia improved with pRBC only in the setting of concomitant cerebral metabolic stress, as determined with microdialysis [69]. Future studies will need to consider additional triggers (e.g., $PbtO_2$), timing, and dose of pRBC, while minimizing confounding. In conclusion, in the polytrauma with TBI, it seems reasonable to aim for a higher Hb goal (Hb > 9–10 g/dL) [17], particularly during the first days after brain injury, and if possible, guided by multimodal monitoring (e.g., brain oxygen or microdialysis).

Intracranial Pressure

While the maintaining of adequate CPP is critical to the care of the TBI patient, intracranial pressure (ICP) is similarly a critical component in traditional management, and in effect, is integrally related to CPP (i.e., CPP = MAP − ICP). However, in clinical practice, ICP is considered a clinical endpoint for treatment and prognostication.

ICP is fundamentally a reflection of intracranial compliance governed by the Monro-Kellie hypothesis. Principally, this hypothesis states that the cranial vault is a rigid structure which encloses the brain, cerebrospinal fluid and blood, and all of which are maintained at a constant volume. Thus, additional volume in the form of bleeding or edema or hydrocephalus, must result in displacement of one of the three intracranial components. Initially, venous blood and cerebrospinal fluid are displaced into extracranial compartments (e.g., jugular vein or lumbar cisterns, respectively). If left unabated, increasing mass effect increases ICP to the point of eventually displacing brain tissue (i.e., brain herniation) and resulting in brain injury and ischemia (see Fig. 20.2) [70]. Measuring ICP is thus

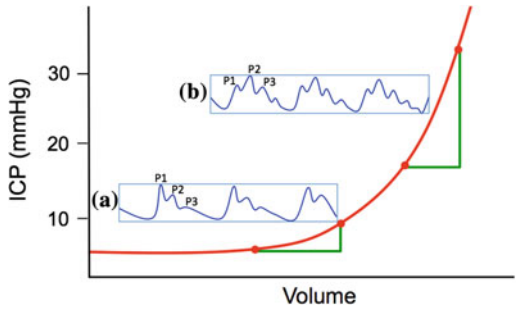

Fig. 20.2 ICP-volume relationship and the concept of the intracranial compliance. Adapted from Avezaat et al. [130]. The ICP waveform is normally comprised of three waves. *P1* is a percussion wave, derived from arterial pulsation; *P2* is a tidal wave, derived from arterial blood volume load and reflective of intracranial compliance; and *P3* is a dichotic wave, derived from aortic valve closure. Intracranial compliance is defined as the ratio of changes in volume over changes in pressure. Note, during normal ICP (waveform shown in *a*) *P1* is greater than *P2*; but as ICP increases with greater volume, (ICP waveform in *b*) *P2* becomes greater than *P1*

fundamental to identifying and treating reduced intracranial compliance prior to herniation. Typically, ICP monitoring is achieved with either intraparenchymal fiberoptic catheter or intraventricular fluid coupled drainage system, with the latter allowing for treatment of raised ICP by facilitating cerebrospinal fluid drainage. The risks of ICP monitor include bleeding during insertion, infection, device malfunction, inaccuracy, and complications related to treatment based on ICP values [71–75].

Indications for ICP monitoring, as per the BTF, are listed in Table 20.1. ICP greater than 20–25 mm Hg is associated with increased mortality [76–80] and morbidity [76, 81, 82], particularly when ICP is refractory to treatment [78]. While raised ICP is clearly associated with worse outcomes, the benefit of having an ICP monitor, and the resultant treatment, is less clear with some studies suggesting improved outcomes [83, 84] and other finding none [85]. A systematic review, consisting only of observational studies, found that ICP monitoring was not associated with lower mortality, though when considering only modern studies, there was in fact a benefit [86]. However, confounding variables, patient selection bias, study heterogeneity limit the generalizability of these data.

Given the clinical equipoise regarding ICP monitoring in isolated severe TBI, Chestnut et al. conduced the BEST-TRIP trial [87]. This study compared acute TBI care based on ICP monitor (ICP group) versus treatment based only on CT scan and clinical exam without an ICP monitor (ICE group). Treatment thresholds for raised ICP were based on TBF guidelines (e.g., CPP 50–70 mm Hg and ICP < 20 mm Hg). The primary outcome, functional outcome at six months, was not different between the groups. However, while 75 % of patients with ICP monitoring had at least one episode of ICP > 20 mm Hg, the median percent of hourly ICP > 20 mm Hg was only 5 %, suggesting an infrequent occurrence of raised ICP, which may explain the comparatively less frequent administration of hyperosmolar therapy in the ICP arm; while a greater administration of barbiturates and less use of hyperventilation in the ICP arm suggests a tailoring of advanced tier treatment only possible with ICP measurement. Given the low incidence of raised ICP, this study may have underpowered to assess the efficacy of ICP monitoring. This hypothesis is supported by a recent multicenter observational study that found ICP monitoring beneficial in patients with the most severe form of TBI (e.g., GCS 3–5) [86]. It is important to note that the treatments of raised ICP(see next paragraph) have not been found efficacious in clinical studies, further complicating the analysis of this study. Nonetheless, given the known association between raised ICP/low CPP and poor outcome, it seems prudent to continue to monitor and treat raised ICP, particularly in the setting of hemodynamic instability common to polytrauma.

The management of raised ICP involves a stepwise, multimodal approach (see Fig. 20.3) [88]. However, most of the treatments outlined in the figure have not been studied rigorously, and are applied with considerable physician variation [89]. Clinical data to help guide timing, duration, optimal combination, and triggers for escalating ICP treatment are lacking. Few clinical trials had studied the complex interaction of available treatments, and most trials attempt to measure the efficacy of a

Table 20.1 Brain Trauma Foundation Indications for intracranial pressure monitoring [131]

• All salvageable patients with severe TBI (GCS 3–8) after resuscitation and abnormal head CT including hematoma, contusions, cerebral edema, herniation or compressed basal cisterns (Level II)
• Severe TBI with normal head CT with >2 of the following (Level III)
– Age > 40 yr
– Unilateral or bilateral motor posturing
– SBP < 90 mm Hg
• Unable to follow hourly neurological exam
– Heavily sedated
– Paralyzed
– Pentobarbital coma
– Induced therapeutic hypothermia

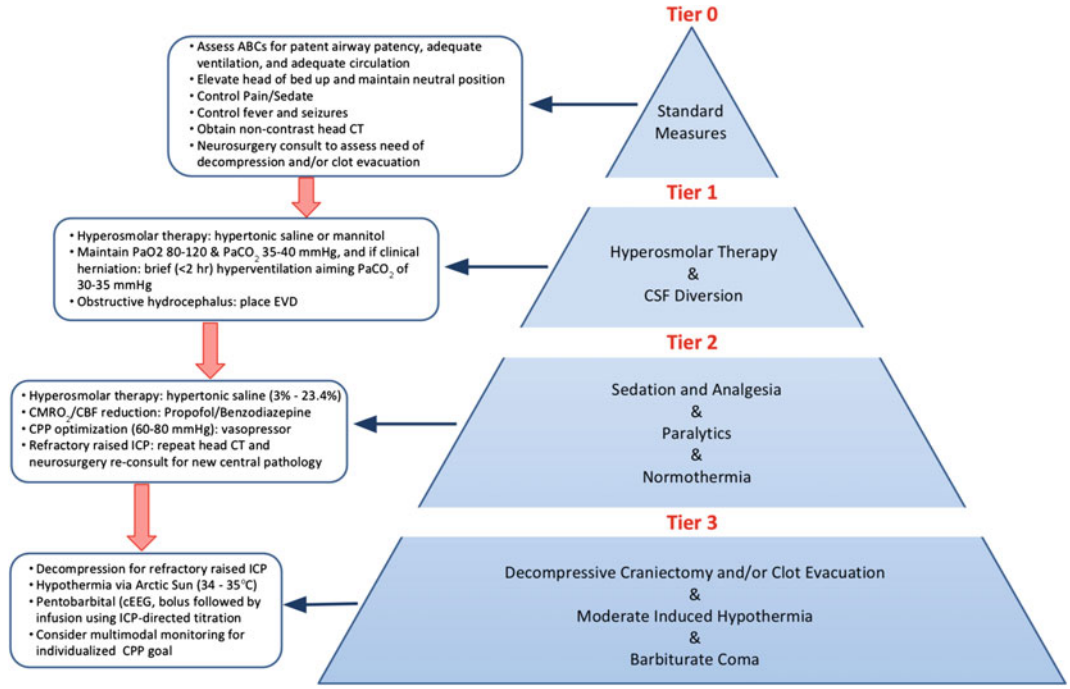

Fig. 20.3 Schematics illustrating the stepwise management of intracranial hypertension [88]

particular treatment, such as therapeutic hypothermia or decompressive hemicraniectomy, alone but not in combination. Even when studied in isolation, the few large randomized trials or systematic reviews conducted in severe TBI have shown harm with third tier treatments. For example, decompressive hemicraniectomy as a salvage treatment for refractory ICP [90], and therapeutic hypothermia (TH) as a prophylactic treatment or upon onset of raised ICP in severe TBI [91–93], have failed to show benefit. A Cochrane review of pentobarbital found no benefit to barbiturates with regards to ICP control or survival [94]. Furthermore, the added complexity of polytrauma necessitates an efficient treatment pathway that addresses brain injury unique to a particular patient's

physiology (i.e., with or without shock), rather than a one-size-fits-all approach. To achieve this goal, investigators have begun to analyze ICP in the context of other physiological variables, such as cerebral autoregulation, brain oxygen, and microdialysis.

As mentioned previously, in normal brain, cerebral autoregulation maintains a constant CBF across a wide range of blood pressure. In acute TBI, however, cerebral autoregulation is blunted resulting in a narrower blood pressure range of constant CBF, beyond which ischemia or hyperemia can result. In clinical practice, direct measurement of cerebral autoregulation is difficult, but some groups have defined surrogate measures by correlating changes in MAP and ICP over time. One such measure is the pressure reactivity index (PRx), which is based on the idea that during impaired autoregulation, cerebral vessels dilate passively with increase in CPP. The dilated vessels increase cerebral blood volume and increase ICP—the correlation between ICP and CPP is thus positive (PRx > 0.2). Conversely, with preserved autoregulation, cerebral vessel constrict with CPP increase, resulting in a negative or zero PRx [95, 96]. The CPP range resulting in a low PRx, suggesting preserved autoregulation, is termed optimal CPP (CPPopt). Observational studies suggest that CPPopt varies between patients and over time, and that the magnitude of deviation between the actual CPP from the CPPopt correlates with poor outcome [97, 98]. Such real-time analysis, if validated, would provide a means of titrating ICP and CPP therapy based on individual patient's physiology rather than the current one-size-fits-all strategy.

Brain Tissue Oxygen and Microdialysis

Normal brain oxygenation depends on adequate CBF and arterial oxygen content to match the needs of cerebral metabolic rate of oxygen consumption ($CMRO_2$). Brain oxygenation is often altered following TBI due to reduced oxygen delivery secondary to (1) hypotension/shock; (2) acute anemia from blood loss; and (3) hypoxia often attributed to co-existing acute lung contusion in the setting of polytrauma, acute pulmonary edema caused by neurogenic stunned myocardium, aspiration pneumonia or ARDS. Alternatively, reduced brain oxygenation could also result from increased $CMRO_2$ related to pain, agitation, pyrexia, or seizure.

Brain oxygenation is measured by one of the two ways, either by local white matter partial pressure of oxygen sampling or via a more global measure by sampling of jugular venous oxygen saturation. Passing a fiberoptic probe through a burr hole into the white matter allows for the measure of local tissue oxygen tension ($PbtO_2$) within a small sampling area. $PbtO_2$ is actually measuring the partial pressure of oxygen within the extracellular space, which equals the difference between oxygen that crosses into brain tissue (arterio-venous oxygen difference [$AVDO_2$]x CBF) and $CMRO_2$ [99]. Thus, reduction in CBF or oxygen content, or increase in $CMRO_2$, can result in low $PbtO_2$. The second and more global means of measuring brain oxygen, entails placing a fiberoptic catheter within the jugular vein at the level of the jugular bulb to measure jugular venous oxygen saturation ($SjVO_2$) to derive oxygen extraction and AVO_2. Brain hypoxia, as measured by either $PbtO_2$ (<15–20 mm Hg) or $SjVO_2$ (<55 %), is associated with worse outcomes in TBI patients [100–103]. Both techniques are relatively safe [104] with $PbtO_2$ possibly being more accurate for a focal area of brain and more commonly used than $SjVO_2$ [105–107].

Interestingly, ischemic $PbtO_2$ values exist independent of ICP [108], making $PbtO_2$ measurement in TBI a potentially useful add-on tool to standard ICP/CPP guided therapy. From a management perspective, low $PbtO_2$ values may be treated by increasing the inspired fraction of oxygen (FIO_2) and blood pressure with vasopressors or fluids; administering sedatives or paralytics; transfusing blood; or administering hypertonic saline [109, 110]. However, with randomized trials lacking, data from observational studies have shown mixed results of $PbtO_2$ monitoring on outcomes [102, 111–118]. Increased fluids and vasopressor administration

guided by $PbtO_2$ monitoring may have contributed to worse outcomes, as suggested in one study [117]. In addition, given the small sampling area of $PbtO_2$, catheter placement is of critical importance, with $PbtO_2$ values near injured brain, but not from unaffected brain, being a better predictor of patient outcome and thus guide to therapy [119], though this has not been a consistent finding [66] and additional studies are needed. Other variables, such as extracellular brain pH [120], may interact with $PbtO_2$ and serve to better discriminate treatment thresholds. Ongoing studies are addressing the utility and efficacy of $PbtO_2$—guided treatment in TBI.

As with $PbtO_2$, local sampling of metabolites of energy (e.g., lactate and pyruvate) or cell injury (e.g., glycerol) is possible by passing a microdialysis (MCD) catheter through a burr hole and into the white matter. MCD can be used to measure extracellular cerebral glycolysis, as represented by the ratio of lactate to pyruvate (LPR). Several studies have found an association between elevated LPR (>25–40), or metabolic crisis, and poor outcomes [121]. In particular, LPR values are elevated during cerebral hypoxia [120], low CPP (<50 mm Hg) [122] as well as high CPP (>70 mm Hg) [123]. Concomitant MCD and PET scan measured $CMRO_2$, LPR > 40 is seen in 25 % of severe TBI patients, but only a small fraction (2.4 %) have concomitant ischemia, suggesting cerebral metabolic stress, and thus injury, occurs by mechanism other than just cerebral hypoxia [124]. Other studies suggest 75 % of moderate to severe TBI patients develop metabolic crisis (LRP > 25 and low glucose) within the first 72 h after brain injury, despite adequate resuscitation and ICP control, with longer duration of metabolic crisis associated with unfavorable outcome [125]. Thus, MCD uniquely offers insight into nonischemic mechanism of brain injury, such as mitochondrial dysfunction [126], offering the potential to identify new therapies for mitigating secondary brain injury.

In conclusion, the management of TBI with polytrauma is challenging given the complexity of secondary brain injury, which is incompletely understood and not easily measurable in clinical practice. Nonetheless, current care is focused on maintaining adequate oxygen delivery by: (1) aiming for a narrow CPP range (e.g., CPP 60–80 mm Hg) with the use of crystalloids and vasopressors; (2) avoiding excessive anemia by pRBC transfuson; and (3) Aggressively treating ICP in a stepwise approach. Studies are ongoing to better define therapeutic thresholds, particularly with the advent of new of technologies.

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Coagulopathy in Traumatic Brain Injury

21

John Dunford

Coagulopathy in Traumatic Brain Injury

The coagulopathy commonly seen with head injury is associated with worse clinical outcomes than trauma without head injury. Head injury is associated with delayed or progressive bleeding, ischemic secondary injury, and microvascular thrombosis [1]. The general prevalence of trauma-associated coagulopathy in trauma can be as high as 97.2 % [2]. Low Glasgow Coma Score, high Injury Severity Score, hypotension on admission, the presence of cerebral edema, subarachnoid hemorrhage and midline shift are independent risk factors for developing coagulopathy in patients with isolated traumatic brain injury [1]. The International Mission for Prognosis and Analysis of Clinical Trials in Traumatic brain injury (IMPACT) study in 2007 showed that an abnormal PT on admission was an independent risk factor for bad outcome after traumatic brain injury [3]. While multiple studies have demonstrated that abnormities of international normalized ratio, (INR) PTT, platelet count, or fibrinogen degradation products are associated with worse outcomes [4]. A coagulopathy after head injury that develops within 24 h is associated with 55 % mortality while the mortality was 23 % for those who developed coagulopathy after 24 h [5]. The pathophysiology of this coagulopathy is a work in progress. Blood loss and hemodilution secondary to fluid resuscitation is not the most likely mechanism for coagulopathy associated with head injury [1]. Direct injury with activation of coagulation by tissue factor, insufficient control of fibrinogenesis and fibrinolysis play a role in the acute coagulopathy of trauma seen in these patients. A basic understanding of the coagulation cascade is essential.

Coagulation begins almost instantly after injury of a blood vessel [6]. Primary hemostasis, the activation of platelets and secondary hemostasis, the activation of the coagulation cascade both occur upon injury. Exposure of blood to the subendothelial space results in the presentation of subendothelial tissue factor to both platelets and plasma factors. The platelets bind to collagen directly with collagen-specific glycoprotein Ia/IIa receptors. With the help of von Willebrand factor, (vWF) produced by endothelium and platelets, collagen binds to the glycoprotein Ib/IX/V on the platelets. Activated platelets release ADP, thromboxane A2, vWF, platelet activating factor, and platelet factor 4. The activated platelets change their shape from spherical to stellate and have an increased affinity of their glycoprotein IIb/IIIa to assist the platelet to bind to fibrin. This change in shape and increased platelet binding to fibrin are important in clot formation.

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Factor VII leaves the circulation through the damaged blood vessel and comes in contact with tissue factor. Factor VII is converted to VIIa. VIIa converts factor X to Xa. Xa combines with factor V to form a prothrombinase complex which activates prothrombin to form thrombin. Thrombin has many effects on both factors and cells. Thrombin activates and releases Factor VIII. Thrombin converts factor XI to XIa. Thrombin converts factor V to Va and fibrinogen to fibrin. Thrombin also activates factor XIII needed for crosslinking fibrin to form covalent bonds in the final clot. High molecular weight kininogen (HMWK), prekallikrein, and Factor XII are all activated by exposure to collagen. Factor XIIa activates factor XI with in turn activates IX. IXa combines with factor VIIIa which forms a Tenase complex that along with Va produces even more thrombin. Activation of HMWK, Prekallikrein, and factor XII are probably more important in inflammation.

Calcium and Vitamin K are important cofactors for coagulation. Calcium is needed for many parts of the coagulation cascade. Vitamin K is needed for factors II, VII, IX, X, Protein S, and Protein C.

The anticoagulant pathways down regulate the coagulation pathway. Thrombin has an important role in modulation of coagulation. Thrombin also combines with thrombomodulin an endothelial cofactor important in inflammation. Thrombin-thrombomodulin acts as a cofactor for protein C activation. Activated protein C along with protein S degrade factor Va and VIIIa. Antithrombin made by the liver, targets factors Xa, IXa, XIa, XIIa, and factor IIa. (Heparin activates antithrombin) Tissue factor inhibitor (TFI) inhibits Xa. TFI-Xa complex binds to the VIIa tissue factor complex further inhibiting Xa production. Plasmin is created by the effect of tissue plasminogen activator released by the endothelium on plasminogen released by the liver. Plasmin proteolytically cleaves fibrin and controls fibrin deposition. The destruction of clot primarily by plasmin with the assistance of other anticoagulant pathways is termed as fibrinolysis.

How drugs effect the coagulation system is enlightening. Procoagulants work on either platelets or the coagulation cascade. Desmopressin promotes the release of von Willebrand factor which can improve platelet function as well as increase factor VIII levels [7]. Cryoprecipitate has fibrinogen, factor VIII, von Willebrand factor, and factor XIII [8]. Fresh frozen plasma contains an unconcentrated source of all clotting factors. Recombinant activated factor VII can increase thrombin production by activating factor X directly [9]. Tranexemic acid and aminocaproic acid inhibit the activation of plasminogen to plasmin [10]. Prothrombin complex concentrate has factors II, VII, IX and X, protein S, and protein C. (Prothrombin complex concentrate contains heparin) [11]. Warfarin affects the production of vitamin k-dependent clotting factors, Heparin, both fractionated and nonfractionated, increases the activity of antithrombin on factors Xa by as much as a 1000 fold. Apixaban is a direct Xa inhibitor. Dabigatran and Bilvalirudin are univalent and bivalent direct thrombin inhibitors [12]. Aspirin inhibits the production of thromboxane from platelets. Clopidogrel blocks the P2Y12 ADP receptor on platelets. Abciximab inhibits GpIIb/IIIa receptors [13].

Laboratory testing for the extrinsic tissue factor pathway is the prothrombin time (PT). The PT is sensitive to dysfunction of factors VII, V, X, and II while the partial thromboplastin time (PTT) is prolonged with abnormal function of factors I, II, V, VIII, IX, X, XI, and XII. Thrombin levels are difficult to measure directly but can be estimated my measuring thrombin antithrombin complex and prothrombin fragments. Thrombin time (TT) is measured by adding bovine thrombin to plasma and seeing how long it takes to clot. Decreased fibrinogen levels or the presence of an anticoagulant can increase TT. Fibrinogen levels can be measured directly. Platelet function can be measured by analyzers such as the rapid platelet function assey. (Verify Now) [14]. The detection of fibrin degradation products suggests ongoing fibrinolytic activity. D-dimers are most commonly measured. Tissue type plasminogen activator inhibitor and plasminogen activator inhibitor are also abnormal during fibrinolysis [15].

Thromboelastography (TEG) has the ability to measure the kinetics of clot formation and stability. It can measure both hypercoagulable and hypocoagulable states. Thromboelastograms typically describe an R value, an alpha angle, a maximum amplitude (MA) and the percentage of clot lysed at 30 min LY30. The R value is a reflection of coagulation factor activity, the alpha angle represents the thrombin burst and fibrin production, the MA measures both platelet function and fibrin level (80/20 %) and the LY30 describes fibrinolysis. Studies have shown goal-directed therapy of coagulation abnormalities diagnosed with TEG might lower the morbidity and mortality associated with trauma [16–18].

The coagulopathy seen after traumatic brain injury is multifactorial. This coagulopathy can occur without significant dilution of clotting factors. Etiologies for coagulopathy after head injury include: Release of tissue factor, production of microparticles, fibrinolysis, platelet function abnormalities, abnormalities of protein C, elevated thrombomodulin, activation of inflammatory mediators, and reduction of factor V levels may all may play a role in the acute coagulopathy seen with traumatic head injury [19, 19].

Tissue factor is released into the systemic circulation which activates factor VII and causes a consumptive coagulopathy. Tissue factor release has been reported in generalized trauma, traumatic head injury, and sepsis in some brain tumor patients [20, 21]. Head injury has also been associated with circulating microparticles released from either apoptotic or activated cells. These micro particles can be of platelet or endothelial origin [22]. Traumatic brain injury is associated with the formation of microthrombi in the small arterioles and venules. A local or systemic coagulopathy triggered by injured brain can contribute to the production of these microthrombi [23]. In animal studies, an immediate postcontusional blood flow reduction is associated with platelet thrombi in the microcirculation [24]. By blocking the microcirculation, the microthrombi can cause both transient and permanent injury to brain tissue. Head injury is associated with elevation of tissue plasminogen activator, increased factor C and depletion of plasmin inhibitor. Increased levels of these factors can result in increased fibrinolysis [25]. Fibrinolysis as evidenced by elevated levels of fibrinogen degradation products is associated with worse outcome in patients with traumatic brain injury [26]. Thrombocytopenia after head injury is associated with increased mortality [27]. Platelets do not function as well after traumatic head injury. An unknown platelet inhibitor or exhaustion of intracellular platelet mediators could be mechanisms of platelet dysfunction [28, 29]. Elevated thrombomodulin is seen in head injury and can be associated with increased activated protein C [4]. Inflammatory mediators such as cytokines or compliment also contribute to coagulopathy. Increases in levels of both coagulation factors and inflammatory mediators can be obtained in the CSF of head injury patients suggesting that there is and arteriovenous difference in these factors in patients with traumatic head injury [30]. Acidosis as a consequence of massive hemorrhage changes the activity of factor VII and to a lesser extent factors V and X [31]. Hypoperfusion in trauma is associated with a marked reduction in factor V activity with a small reduction in II, VII, IX, X, and XI. The marked drop in factor V may represent fibrinolytic reaction because factor V is very susceptible to breakdown by fibrinolysis [32].

Postraumatic abnormalities of the coagulation cascade can result in both hemorrhagic and ischemic complications. Coagulopathy has been associated with the development of new or progression of existing lesions in TBI patients. Hemorrhagic progression or new development of ischemic lesions was found in 85 % of those with coagulopathy on admission while on 31 % of those without coagulopathy had progression of symptoms [33]. Hemorrhagic contusions were the lesions most likely to expand on intracranial CT especially within the first two hours of the trauma. A significant increase in mortality is noted in coagulopathic patients with hemorrhagic progression on follow up CT. The greatest risk factor for progression of hemorrhagic lesion was

coagulopathy within the first 24 h after traumatic brain injury. In one study, patients with an elevated PTT demonstrated a 100 % hemorrhagic progression rate after traumatic brain injury. Thrombocytopenia with a platelet count less than 100,000 was associated with a 90 % progression rate while increased PT was associated with a 70 % progression rate [34]. A review of 113 TBI patients with 229 non-operated intraparenchymal hemorrhages did not show coagulopathy to be a significant risk factor for hemorrhagic progression [35]. Documented mortality rate in trauma patients with fulminant fibrinolysis was 85.7 % compared with 11.1 % those with low-grade fibrinolysis. Patients with fibrinolysis had higher ISS, lower GCS, lower SBP, and higher lactate levels than patients without fibrinolysis [36].

Management of bleeding and coagulopathy following traumatic brain injury is paramount to a successful outcome. Early monitoring of coagulation, early administration of FFP and platelets, maintaining adequate calcium and fibrinogen levels, treatment with desmopressin, prothrombin complex concentrate, activated factor VII, and tranexamic acid may play a role in the treatment of traumatic brain injury.

Early monitoring of coagulation is important to detect trauma-associated coagulopathy. Monitoring can assist in the proper diagnosis of the coagulopathy including possible fibrinolysis. Early therapeutic intervention of coagulopathy based on early goal directed therapeutic treatments has been shown to reduce the need for packed red blood cells, fresh frozen plasma, and platelets [37].

The multidisciplinary Task Force for Advanced Bleeding Care in Trauma guidelines was updated in 2013 [38]. The task force recommend fresh frozen plasma or fibrinogen should be administered very early in the management of trauma patients with massive bleeding. Further plasma should be transfused at a ratio of at least 1:2 with red blood cells. Initial plasma transfusion should be avoided in patients without substantial bleeding [37]. Fresh frozen plasma (FFP) has about 70 % of the normal level of all clotting factors. Decreased mortality has been demonstrated in patients who were able to meet a 1:1 ration of FFP/PRBCs [39]. Use of fresh frozen plasma is associated with increased incidence of post injury multiple organ failure, acute respiratory distress syndrome, infections, and transfusion-related lung injury [40, 41]. Therefore, administration of FFP is most appropriate for patients with massive bleeding or bleeding complicated by coagulopathy. Fibrinogen concentrate or cryoprecipitate should be used to keep the plasma fibrinogen level above 1.5 g/dl [42].

After trauma, it has been found that the platelet dysfunction is noted even before substantial fluid or blood transfusion takes place and continues during the resuscitation period. Severe injury can result in increased platelet activation and abnormal function in traumatic brain injury [38]. This suggests that early platelet transfusion may be helpful [43]. There is evidence to support an appropriate platelet transfusion threshold in the trauma patient both due to thrombocytopenia or pre-trauma ingestion of antiplatelet drugs. In massively transfused patients, a platelet count of 100,000/ml has been found as the threshold for diffuse bleeding [44]. A platelet count 50,000 or fibrinogen level of <0.5 g/l have been found as sensitive laboratory predictors of microvascular bleeding [45]. A platelet count of <100,000/ml was an independent predictor of mortality in patients with traumatic brain injury [46]. A target level of 100,000/ml can be suggested for those with multiple trauma, brain injury and massive bleeding [47, 48]. For the management of traumatic coagulopathy, there is still no high-quality evidence supporting up-front platelet transfusions. A prospective randomized trial evaluating prophylactic platelet transfusion at a ratio to the whole blood of 1:2 versus the same amount of plasma in patients receiving ≥ 12 units of whole blood in 12 h concluded that platelet administration did not affect microvascular nonsurgical bleeding [49]. A metaanalysis of 16 retrospective studies published between 2005 and 2010 that investigated the impact of platelet transfusion in severe trauma and massive transfusion showed an improved survival rate among patients receiving high platelet:RBC ratios [50–52]. High platelet:RBC ratios and high plasma:RBC ratios

are often administered concurrently and it is therefore hard to isolate the benefit of one with the other. A potential shortcoming of ratio-driven blood support is over transfusion with plasma and platelets, resulting in possible increased morbidity from multiple organ failure that can be seen with the transfusion of blood products [40]. Although there is a demonstrated decrease in morbidity due to aggressive use of plasma and platelets, routine early prophylactic platelet transfusion as part of a massive transfusion protocol is probably not justified [37, 53–55].

Platelets should be administered to head injury patients with intracranial hemorrhage who have been treated with antiplatelet agents. Antiplatelet agents, mainly aspirin and clopidogrel, can have an affect on traumatic bleeding. Head trauma (GCS 14 to 15) while on antiplatelet agents is associated with a high incidence of intracranial hemorrhage [56–58]. Patients who used clopidogrel prior to both spontaneous and traumatic intracranial hemorrhage are associated with worsened outcome [59–62]. Compared to controls, patients on clopidogrel demonstrated a 14.7-fold increase in mortality, increased morbidity and a 3-fold increase in disposition to a long-term facility [60, 61]. Pre-injury aspirin did not affect outcomes in mild to moderate head injury or morality. However, greater platelet inhibition was identified among patients taking a combination of antiplatelet agents compared to those on single agents [63–66]. Early platelet dysfunction was found after severe traumatic brain injury in the absence of antiplatelet drugs [67]. These findings coupled with the fact that 20–30 % of patients are nonresponders to aspirin, clopidogrel or both agents suggest that reliable measures of platelet function would be useful in the setting of the bleeding trauma patient to guide therapy [38, 68].

Besides platelet transfusion, other potential antiplatelet reversal therapies can be used [69]. Desmopressin has been shown to improve platelet function in volunteers on aspirin, clopidogrel and perioperatively in patients with mild inherited platelet defects [70–72]. One metaanalysis suggested a benefit of desmopressin in patients taking aspirin [73]. Desmopressin has been recommended in patients taking platelet inhibitors with intracranial hemorrhage [69, 74]. Activated factor VII reverses the inhibitory effects of aspirin and clopidogrel in healthy volunteers [75]. Tranexemic acid and fibrinogen concentrate may also be helpful in improving hemostasis in trauma patients receiving antiplatelet agents [76, 77].

Head injury patients are increasingly on new oral anticoagulants. These agents are indicated for the prevention of venous thromboembolism, prevention of stroke in atrial fibrillation, reduction of cardiovascular events in patients with acute coronary syndrome, treatment of pulmonary embolism, and treatment of deep venous thrombosis. The primary modes of action by these novel drugs are direct factor Xa inhibition (rivaroxaban, apixaban, and endoxaban) or thrombin inhibition (dabigatran) [78–80]. It has been demonstrated that the effect of these drugs on coagulation tests of factor Xa (rivaroxaban) but not of factor IIa (dabigatran) antagonists in human volunteers could be reversed with high-dose prothrombin complex concentrate (PCC) [81, 82]. Anti-factor Xa activity can be measured with a substrate-specific anti-factor Xa test in trauma patients treated with factor Xa antagonists. Factor IIa antagonist treatment does prolong PTT and thrombin time but does not respond to prothrombin complex concentrate [82, 83]. Prothrombin complex concentrate can also be used for the emergency reversal of vitamin K-dependent oral anticoagulants in patients with head injury. The use of PCC carries the increased risks of both venous and arterial thrombosis during the recovery period; therefore, the risk of a thrombotic complication due to treatment with PCCs should be weighed against the need for rapid and effective correction of coagulopathy [84–86]. Thromboprophylaxis, as early as possible after control of bleeding, has been achieved as recommended in patients who have received PCC. Idarucizumab, a monoclonal antibody fragment that binds dabigatran, was approved by the FDA on October 16, 2015. For patients treated with dabigatran when reversal of the anticoagulant effects of dabigatran is needed for emergency surgery or urgent procedures or in life-threatening or uncontrolled bleeding [38, 87, 88].

Recombinant-activated coagulation factor VII can be used for major bleeding and traumatic coagulopathy refractory to usual methods to control bleeding. According to the multidisciplinary task force for advanced bleeding care in trauma, recombinant activated factor VII is not indicated in patients with intracerebral hemorrhage caused by isolated head trauma [38]. Recombinant activated factor VII is not a first-line treatment for bleeding and can be effective only once the sources of major bleeding have been controlled. Once major bleeding from damaged vessels has been stopped, recombinant activated factor VII may be helpful to induce coagulation in areas of diffuse small vessel coagulopathic bleeding that is refractory to standard treatments. These include packed red blood cells, platelets, fresh frozen plasma, and cryoprecipitate/fibrinogen resulting in hematocrit above 24 %, platelets above 100,000 and fibrinogen above 1.5–2.0 g/l, use of antifibrinolytics, correction of severe acidosis, severe hypothermia, and hypocalcaemia [38]. Because recombinant activated factor VII acts on the patient's own coagulation system; adequate numbers of platelets and fibrinogen levels are needed for a thrombin burst to be induced by the pharmacological, supraphysiological doses of activated factor VII with direct binding of activated platelets [89]. Despite numerous case studies and series reporting that treatment with recombinant factor VII can be beneficial in the treatment of bleeding following trauma, there are few high-quality studies [90–93]. The use of recombinant activated factor VII in isolated head injury was found to be harmful in a case-controlled study of patients with traumatic intracranial hemorrhage, with the risk of death appearing to increase with administration regardless of the severity of injury [93, 94]. Reliable evidence to support the effectiveness of recombinant factor VII in reducing mortality or disability in patients with traumatic head injury is small [38].

Transexemic acid is commonly used in the early treatment of bleeding trauma patients within 3 h of injury [95]. It can be administered while the patient is in route to the hospital. The CRASH-2 trial (Clinical Randomization of Antifibrinolytic treatment in Significant Hemorrhage) showed that treatment with tranexamic acid within 1 h was associated with a significant decrease in the rate of death due to bleeding. Treatment of trauma patients with tranexemic acid more than 3 h after injury was associated with an increased chance of death due to bleeding. Therefore, timely administration of tranexemic acid is important. Pooled results from two random controlled trials demonstrated statistically significant reduction in intracranial hemorrhage progression with tranexemic acid and a non-statistically significant improvement of clinical outcomes in patients with traumatic brain injury. A nested prospective placebo controlled trial (CRASH-2 intracranial bleeding study) of 270 adult trauma patients with, or at risk of, significant extracranial bleeding within 8 h of injury, who also had traumatic brain injury, showed that neither moderate benefits nor moderate harmful effects of tranexamic acid in patients with traumatic brain injury can be excluded [96]. As traumatic brain injury is associated with the formation of microthrombi in the small arterioles and venules suggesting a local hypercoaguable state in the brain, treatment with antifibrinolytic therapy on a routine basis for traumatic brain injury needs be made on a case-by-case basis. Regular use of tranexemic acid in patients with traumatic head injury needs further study [97, 98].

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Venous Thromboembolism Prophylaxis

22

Herb A. Phelan

Overview

The Center for Medicare and Medicaid Service's intention to decrease reimbursements for care related to management of venous thromboembolism (VTE) has led to a renewed emphasis on prophylaxis in all spheres of inpatient care. VTE prophylaxis after traumatic brain injury (TBI) and spinal cord injury (SCI) is problematic, however, because of concerns about iatrogenically propagating neurologic injury through the too early administration of anticoagulants. For many providers deliberating the timing of prophylactic anticoagulant initiation, they envision the risks of delaying anticoagulation on the one hand potentially resulting in a conversation in which they tell the patient or their proxy "I'm sorry your leg is swollen but you've developed a blood clot in your thigh." They then mentally balance this against the risks of anticoagulant initiation by envisioning a previously oriented patient's suddenly herniating with consecutive chart notations of "Dr. Smith approving anticoagulant initiation" followed by "Patient going stat to CT scan for abrupt decrease of mental status." When viewed with this risk/benefit profile, the default for many clinicians is therefore perpetual delay. Lest I be accused of exaggerating for effect, I should mention that these stark extremes are mentioned only half in jest as one of my clinical partners verbalized a very similar thought process during the early stages of my group's work in this area. Consequently, since the use of sequential compression devices (SCDs) in this patient population are universally accepted and well tolerated, they will not be discussed here. Instead, this work will concentrate on the controversies in the field of VTE prophylaxis after neurologic injury: pharmacologic prophylaxis and its timing, and prophylactic vena cava filtration.

Traumatic Brain Injury

Geerts' landmark work on deep vein thrombosis (DVT) after TBI in the 1990s showed the magnitude of the problem [1]. In the absence of any prophylaxis at all, 54 % of TBI patients were shown to have VTE prior to discharge when venography was used as the diagnostic method of choice. While this point estimate is certainly lower when mechanical prophylaxis is used, pharmacologic prophylaxis remains the most potent modality to reduce these events.

One contributor to the default to delay pharmacologic prophylaxis on the part of many clinicians who care for TBI patients is a perception that a deep vein thrombosis (DVT) is a relatively benign entity. The sequelae of DVT are not to be dismissed, however, as patients with mild post-thrombotic syndrome have been shown to have quality of life scores lower than age-matched controls with arthritis, chronic lung disease, and

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Fig. 22.1 Whether it is hiking the cliffs along the Rio Grande River in Big Bend for the view of Mexico's Chihuahuan Desert or starting prophylactic anticoagulation after TBI, the principal is the same. The closer you get to the edge, the bigger the payoff; but going too far can be disastrous

diabetes. If the post-thrombotic syndrome progresses to being severe, quality of life drops off below that of patients with cancer, angina, and congestive heart failure [2]. The entity should not be dismissed as clinically inconsequential.

An analogy that I frequently use in discussing this topic is that of approaching the edge of a cliff to appreciate the view: the closer that one gets to the edge, the greater the reward, while going too far can have disastrous consequences (Fig. 22.1). Defining that point at which benefit is exceeded by risk remains the goal of researchers in this field.

Choice of Anticoagulant and Dose

Geerts' work demonstrated the superiority of 30 mg enoxaparin subcutaneously every 12 h over 5000 units unfractionated heparin at the same interval [3] for VTE prophylaxis after trauma, leading to the widespread acceptance of that regimen. Recently, some have begun to question whether unfractionated heparin 5000 units three times a day may confer protection that is equivalent to enoxaparin [4] while being significantly cheaper. The data on this practice after neurologic injury is limited.

Alternative dosing of enoxaparin has been examined in a limited number of studies. Kurtoglu randomized 120 subjects with TBI or SCI to receive sequential compression devices alone or 40 mg of enoxaparin daily as their sole prophylaxis regimens. While the study showed no significant difference in DVT rates between the groups, there was also an alarming fatal PE rate of 3.3 % in the mechanical prophylaxis arm, and 6.7 % in the enoxaparin arm [5]. Recently, Kopelman examined the effects of increasing the

dose of enoxaparin to 40 mg twice a day in a general trauma population. While higher anti-Xa levels were noted, there was no difference in VTE for the 124 subjects in the study [6].

Most studies in of post-TBI prophylaxis utilize enoxaparin as their low molecular weight heparin of choice, but Cothren examined the effect of dalteparin on a subset of 173 TBI patients in 2007 [7]. She found no cases of intracranial hemorrhage progression when dalteparin was started 72 h after injury (albeit with only a 74 % compliance rate). The limited work with other low molecular weight heparins precludes our ability to say much about this option.

An additional complicating factor when discussing the effectiveness of various pharmacologic regimens and doses is the confounding effect of obesity. This was only realized relatively recently, and the data after neurologic injury is limited. Bickford recently showed that an enoxaparin dose of 0.5 mg/kg subcutaneously every 12 h led to target anti-Xa levels in a cohort of obese general trauma patients [8] without an increase in bleeding complications. Given the prevalence of obesity among the American population and the expectation that it will continue to rise, it is likely that this issue will be vetted further in the near future.

Considering the dizzying array of choices and confounders that confront the physician seeking an anticoagulation regimen for their TBI patient, what can be recommended? Our group's practice has been to use enoxaparin 30 mg subcutaneously every 12 h when initiating prophylaxis after neurologic injury (no disclosures). Our choice was made based on the fact that the preponderance of the evidence shows it to be efficacious and safe. Additionally, our desire to investigate the optimal timing of pharmacologic prophylaxis initiation was aided by a choice of a commonly used regimen (as otherwise the studies of timing would devolve into studies of drug choice). To be sure, new possibilities will continue to arise, some of which will be discussed at the end of this chapter, but for now we feel that the greater need for this field is the elucidation of the timing of initiation rather than the method.

Timing of Initiation

When considering the question of the optimal time to start anticoagulation, we saw a recurring theme through most of the literature on this subject: TBI tended to be treated as a homogenous injury. Study after study just considered TBI as a binary phenomenon in which it was present or absent. While it was understandable that it made for greater methodologic ease in studying the phenomenon, this approach was at variance with what we knew to be our clinical experience with the injury. Seen rightly, TBI is a spectrum of disease in which one could place the patient with a small subarachnoid hemorrhage and a normal Glasgow Coma Score at one end, and the patient with a craniotomy, intracranial monitor, and massive cerebral contusions with midline shift at the other. Why, then, should we treat these patients like they were at the same risk for progression of their injury both prior to and after initiation of prophylaxis?

It was in dealing with this discrepancy that we found the work of Berne and Norwood. These investigators had created an a priori set of injuries which they considered to be candidates for receiving enoxaparin 30 mg subcutaneously every 12 h if a CT scan performed 24 h after injury showed no injury progression [9–11]. These injuries (subdural or epidural hematoma no greater than 8 mm thick at their widest, frontal contusion smaller than 2 cm at its greatest dimension, and a single contusion per lobe) showed no greater rates of growth after anticoagulant initiation than historical controls. We added injury patterns consisting of intraventricular hemorrhage greater than 2 cm in maximum dimension and any degree of traumatic subarachnoid hemorrhage with a negative CT angiogram and in recognition of their work called these the "Modified Berne-Norwood Criteria." We subsequently used these injuries as a basis for a comprehensive protocol for the timing of anticoagulant initiation [12], and have recently found that these injury patterns predict two tiers of risk for progression [13] (Fig. 22.2). For the lower risk of progression arm, we recommend

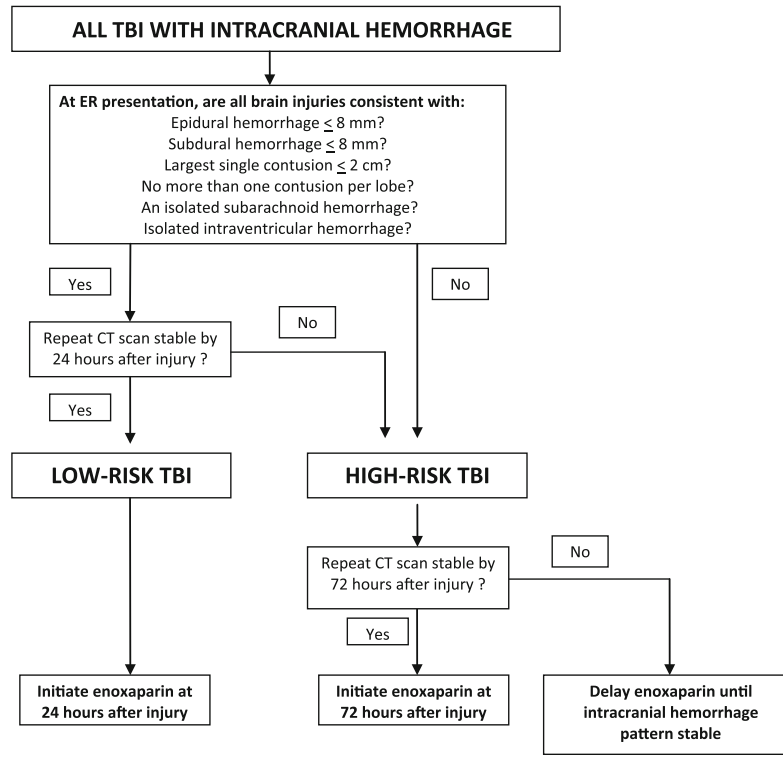

Fig. 22.2 The Parkland Protocol. A suggested algorithm for timing of prophylactic anticoagulation after TBI

initiation of enoxaparin at 24 h after injury if a repeat CT scan shows a stable injury pattern. We have performed a pilot randomized trial called the "Delayed vs Early Enoxaparin Prophylaxis [DEEP] Study" showing that the progression rate after starting enoxaparin is (a) low, (b) similar to placebo-treated patients (indicating that the progression appears to be an evolution of disease rather than iatrogenic), and (c) well tolerated as the few patients who progressed were asymptomatic [14].

Those patients who were originally characterized as low risk but progressed on follow up scanning while enoxaparin-naive are upgraded to higher risk for further progression. They are grouped with those patients who present with injuries larger than the Modified Berne-Norwood criteria, and are considered to be candidates for enoxaparin initiation at 72 h after injury if they have radiographically stabilized by that time. Any patients continuing to experience hemorrhage progression at 72 h after injury are off-protocol and have their decisions about initiation tailored to the individual. In general for these rare patients, we delay enoxaparin until they have had 24 h of radiographic stability, whenever that may be. For patients with an intracranial monitor, we will selectively consider them candidates for enoxaparin if they have stable CT scans and smaller hemorrhage patterns. We simply hold the dose of enoxaparin due before pulling the monitor.

We are currently seeking funding for the powered DEEP II study. Much work remains as we must elucidate the effect of these regimens on the DVT rate (since the endpoints studied so far have been toward progression rates to make sure the practice is safe). Additionally, we have gone to a policy of restrictive repeat scanning on patients who present with high GCS [15]. Since the protocol is based around the performance of repeat scanning, the effect has been that we have seen fewer patients being entered into the protocol's pathway. In reality, this has not mattered as much as would first appear, however, given that most of these high-GCS TBI patients are ambulatory and have short hospital lengths of stay.

Those patients who are getting repeat CT scans of the head tend to be more severely injured and consequently in greater need of prophylaxis.

Finally, when looking ahead to the future, we have noted that what most of our pathway seems to generally lead toward is the initiation of enoxaparin at 24 h after the demonstration of radiographic stability whenever that may be. It may be that at the end of our efforts we find that this will be the simple, take-home message.

National Guidelines

For the busy clinician who may not have time to sift through large amounts of data, or who wants the imprimatur of national organizations as support for decisions, national guidelines exist for recommendations on the question of VTE prophylaxis after traumatic brain injury. The American College of Chest Physicians (ACCP) promulgates a set of prophylaxis guidelines for all manner of surgical and medical patients leading many to consider this to be the gold standard on the subject [16]. Unfortunately, the most recent recommendations from 2012 for prophylaxis on the route, dose, and timing of pharmacologic prophylaxis after TBI are vague. The recommendation for TBI patients is that sequential compression devices be used until the risk of bleeding is felt to have abated and then to institute pharmacologic prophylaxis with no specification of drug or dose. This recommendation is graded level 2C, indicating a medium level of confidence. The Brain Trauma Foundation has (BTF) put forth its own recommendations, most recently in 2007. Only Level 3 in strength, they are similarly vague. The BTF recommends that TBI patients have some form of mechanical prophylaxis until ambulatory, should receive either unfractionated heparin or low dose heparin in conjunction with mechanical prophylaxis, and that anticoagulation appears to be associated with an increased risk of intracranial bleeding [17]. Finally, the Eastern Association for the Surgery of Trauma (EAST) published guidelines in 2002 which are now quite dated [18]. While they address prophylaxis for all manner of trauma patients, their only statements about TBI are to say that neither unfractionated heparin nor low molecular weight heparin have been adequately studied to make any recommendations.

Spinal Cord Injury

VTE rates after spinal cord injury are strikingly high, varying from 49 to 100 % in the first 3 months after injury [19]. Providers are well advised to avoid femoral central venous access in patients with spinal cord injury as this can add venous endothelial injury to a patient who is already at high risk by virtue of stasis and hypercoagulability. Interestingly, the risk abates somewhat after about the first two weeks after injury and this must be factored in when creating a prophylaxis strategy.

Choice of Anticoagulant and Dose

Two recent meta-analyses have addressed the question of the best choice of drug and dose and are to be recommended [20, 21]. Both reviews concluded that unfractionated heparin at 5000 units given subcutaneously every 12 h was no better than placebo in VTE prevention, and that adjusted (i.e., higher) dose unfractionated heparin confers VTE protection over placebo but with higher rates of bleeding complications.

Both meta-analyses considered the comparison of unfractionated heparin versus low molecular weight heparin and concluded that the preponderance of the evidence suggests that low molecular weight heparin (and particularly enoxaparin) was superior to unfractionated heparin in providing protection against VTE. Interestingly, this was despite the fact that both reviews found a lower rate of bleeding complications with enoxaparin.

Having concluded that low molecular weight heparins are superior to unfractionated heparin for prophylaxis after spinal cord injury, both meta-analyses examined the question of whether any particular low molecular weight heparin was better than another. Both reviews found no

differences between enoxaparin and dalteparin based on the limited available evidence. Chen went further to include a study comparing enoxaparin and tinzaparin which also showed no difference.

Conclusions are harder to reach about the optimal dosing regimen for low molecular weight heparins due to the number of permutations that begin to set in when considering multiple drugs with multiple possible doses. A study exists which shows that 4500 units tinzaparin daily are superior to 3500 daily for prophylaxis [22]. Additionally, another retrospective review showed equivalent rates of VTE development were seen with enoxaparin 40 mg once a day and 30 mg twice a day [23]. Additionally, a randomized trial in 2003 demonstrated no differences between enoxaparin 30 mg twice a day and dalteparin 5000 units once daily [24].

National Guidelines

The ACCP's guidelines remain frustratingly vague on prophylaxis recommendations after spinal cord injury with or without spinal surgery, only saying that mechanical prophylaxis should be used routinely and nonspecific anticoagulation should be started when the bleeding risk has abated [16]. The Consortium for Spinal Cord Medicine's 2008 guidelines also state that either low molecular weight heparin or unfractionated heparin with SCDs should be started as soon as bleeding concerns have abated [25]. Gratifyingly, the American Association of Neurological Surgeons/Congress of Neurological Surgeons (AANS/CNS) Joint Guideline Committee has generated guidelines for VTE prophylaxis after SCI which are more specific [26]. As level I evidence, they recommend that low molecular weight heparin be used as prophylaxis, and that unfractionated heparin is an adequate choice only if used in conjunction with mechanical prophylaxis. As level II evidence, the authors state that pharmacologic prophylaxis should be initiated within 72 h of injury, oral anticoagulation alone is inadequate, and that prophylaxis should continue for three months after injury. Finally, the authors make a level III recommendation about prophylactic vena cava filtration which will be discussed below. The EAST guidelines state that low molecular weight heparin may be used after SCI as long as there are no bleeding concerns from other injuries [18].

Prophylactic Vena Cava Filters

The time-honored, universally accepted indications for caval filter placement are VTE and a contraindication to, complication of, or recurrence despite therapeutic anticoagulation. Greenfield and Proctor published a 20-year experience with their device in which they found a 4 % recurrence rate for PE, 2 % rate of strut fracture, and a 4 % rate of caval thrombosis [27], and the PREPIC randomized controlled trial found significant reductions in PE rates for patients undergoing therapeutic permanent filter placement at 8 years after placement [28]. With the development of a percutaneous technique that allowed bedside insertion in a matter of minutes, extension of the technique from therapy to prophylaxis became commonplace after trauma. The development of retrievable filters helped to make the practice of prophylactic filtration become even more accepted as it alleviated the concerns of caregivers hesitant to place a permanent device in a patient with a temporary contraindication to anticoagulation.

Criticisms of prophylactic caval filtration abound. The event that they seek to prevent (clinically significant PE) is rarely seen as these rates are less than 1 % in many series. The devices themselves are expensive and invasive. The reassurance supplied by their retrievability is a false one as the large majority of filters placed ostensibly temporarily do not undergo successful retrieval due to systems issues or poor follow up. Moreover, the long-term follow up for these devices once declared permanent is limited [29] making their placement all the more hazardous in young patients who can be expected to survive their injuries. After all, who can say how these devices will perform in 30, 40, or 50 years? Further, an emerging body of literature suggests

that many of what we are currently calling "early PE" may in fact be primary pulmonary thrombosis [30]. If a segment of these clots are forming primarily in the lung after severe chest trauma, clearly a filter would do nothing to prevent the phenomenon. Finally, the endothelial damage that occurs during filter placement from a femoral approach is actually thrombogenic in and of itself. In other words, we are giving patients DVTs to protect them from PE. As was covered previously, DVT is not a benign event. Finally, due to the relative rarity of clinically significant PE, it has been difficult to statistically establish a benefit to the practice in the literature on the subject. The pioneer for anticoagulation after trauma, Bill Geerts, has performed a power analysis illustrating the difficulties in doing a randomized trial to establish the superiority of prophylactic filtration (Geerts, personal communication, 2012). In order to demonstrate an 80 % reduction in a 1 % symptomatic PE rate with only 20 % dropouts, 4,080 subjects would need to be enrolled. This is obviously prohibitive. Even the best observational study that exists supporting the practice demonstrated a number needed to treat of between 109 and 962 to prevent a single PE [31].

For these reasons, our institution has undergone a significant change in our practice regarding prophylactic caval filtration. Our group historically had a very liberal practice pattern in regard to our use of prophylactic filters. As we noted that we gradually evolved to placing fewer filters while becoming more aggressive with our use of enoxaparin in TBI and SCI patients, we recently completed a QI initiative to examine our symptomatic PE rate in our trauma population over a recent three-year period which saw the most significant drop in prophylactic filter usage. We found that the rate of clinically significant PE was (a) unchanged over all three years despite becoming much more restrictive with prophylactic filter placement, and (b) was <1 % for all three years (unpublished data). Consequently we have all but abandoned the practice.

National Guidelines

The ACCP guidelines are unequivocal on the subject of prophylactic filters after trauma, stating flatly that they should not be used [16]. The Brain Trauma Foundation, meanwhile, does not comment on the practice [17]. EAST is more liberal, stating that prophylactic filtration should be considered for patients with both TBI and SCI [18]. This recommendation should be interpreted with the fact in mind that the state of the science at the time of the guidelines' creation in 2002 has changed markedly. The AANS/CNS Joint Guideline Committee's 2013 recommendation is that prophylactic filters should not be considered a routine method of PE prevention but are "recommended for select patients who are not candidates for anticoagulation [26]." Finally, the Consortium for Spinal Cord Medicine's 2008 recommendation is that providers should consider prophylactic filter placement in those patients who are anticipated to have a contraindication to anticoagulant initiation for >72 h [25].

Future Directions

Clearly, there are many knowledge gaps when it comes to the subject of VTE prophylaxis after TBI and SCI. The difficulties presented by the potential problem of obesity have already been alluded to. Additionally, another potential confounder has come to light in the impact of missed doses of anticoagulation after TBI. Salottolo and colleagues showed that subjects with as little as one missed or interrupted dose of anticoagulation after TBI had a significantly higher chance of DVT development [32]. Given the frequency with which most patients miss doses either due to trips to the OR with other services or through happenstance, this has the potential to be a large contributor to VTE development and deserves more attention. Another potential future direction is that of thromboelastography and its potential

role in decision-making for prophylaxis after neurologic injury. While it is true that a recent pilot randomized trial did not show benefit in regards to VTE development in a general trauma population [33], this area holds considerable potential. Finally, muscle electrostimulation has been examined in the past in preliminary fashion but without a large amount of work. By electrically stimulating the muscles of the lower extremities to contract, a mechanical effect on VTE prevention could theoretically be seen. A small randomized trial did not show a benefit in a general trauma population [34], but it has never been rigorously studied in subjects with neurologic injury.

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Mechanical Ventilation in Traumatic Brain Injury

23

Christopher S. King and Laith Altaweel

Introduction

To date, no pharmacologic therapy has been developed which improves outcomes in traumatic brain injury (TBI). Despite this, mortality following severe TBI has decreased over time, likely due to improvements in critical care management [1, 2]. Current strategies focus on prevention of secondary injury from ischemic insults to the injured brain. Hypoxemia, hypo- or hypercapnia, and hypotension adversely impact outcome following TBI [3–5]. Majority of patients with severe TBI require intubation and mechanical ventilation (MV). While MV is frequently life-saving in this setting, if managed inappropriately it may exacerbate secondary injury and worsen outcomes [6]. The optimal approach to ventilatory support allows neurologic recovery by minimizing secondary injury and also decreases risk for ventilator-induced lung injury.

In this chapter, we will briefly discuss the epidemiology of lung injury and indications for MV in TBI. We will next discuss the effects of mechanical ventilation on intracranial physiology. Finally, a recommended approach to MV in TBI patients will be presented, with special attention to the TBI patient with concurrent severe hypoxemic respiratory failure.

Epidemiology

Lung injury is common following TBI. In 2012, the ARDS Definition Task Force defined acute respiratory distress syndrome (ARDS) as an acute pulmonary process characterized by bilateral infiltrates on chest radiography not fully explained by pulmonary edema. Severity was defined as mild for PaO_2/FiO_2 of 200–300 mm Hg, moderate for PaO_2/FiO_2 100–200 mm Hg, and severe for PaO_2/FiO_2 < 100 mm Hg [7]. If one utilizes this updated definition, the incidence of ARDS following TBI ranges from 5 to 30 % depending on the population examined [6, 8–13]. Risk factors associated with development of ARDS following blunt trauma include: injury severity score >25, presence of pulmonary contusion, large transfusion requirement, hypotension on admission, age >65 years, history of substance abuse, need for vasopressors, and low Glascow Coma Score (GCS) [9, 10, 14]. The incidence of ARDS following TBI follows a bimodal distribution with an initial peak 2–3 days after initiation

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Table 23.1 Indications for mechanical ventilation in brain-injured patients

Neurologic
• Depressed consciousness/inability to protect airway
• Need for sedatives to control intracranial pressure
• Status epilepticus
Pulmonary
• Acute respiratory distress syndrome
- Sepsis
- Aspiration
- Transfusion-related acute lung injury
- Pneumonia
- Fat emboli
• Pulmonary edema
- Neurogenic
- Cardiac contusion
- Fluid overload
• Trauma-related
- Pulmonary contusion
- Pneumothorax
- Hemothorax
- Flail chest/rib fractures
• Venous thromboembolism
Airway
• Head/neck trauma
Other
• Need for procedures/operative intervention
• Need for pain control
• Increased metabolic demands from acidosis/neurohormonal response to injury

of mechanical ventilation and a late peak at 7–8 days. Late onset ARDS is commonly associated with ventilator-associated pneumonia [11, 15, 16]. Development of ARDS in the TBI patient is associated with worsened outcomes including increased intensive care unit and hospital length of stay, decreased number of ventilator-free days, increased incidence of poor neurologic outcome and increased mortality [8, 10, 13].

Indications for Mechanical Ventilation

Majority of patients with severe TBI require MV, although the exact incidence is poorly defined. Indications for initiation of MV in the brain-injured patient can be broadly classified into four categories: neurologic, pulmonary, airway, and other. (Table 23.1) Depressed mental status is a common indication for MV in TBI. General guidance is to intubate patients with a Glascow Coma Scale (GCS) $\leq$ 8 or inability to protect their airway [17]. Patients with intracranial hypertension or status epilepticus also typically require intubation, both for depressed consciousness and to facilitate treatment with sedatives to control their underlying condition. A number of pulmonary conditions commonly complicate traumatic injury, including aspiration, pneumonia, volume overload from resuscitation with fluids and blood products, hemothorax, pneumothorax, and venous thromboembolism. ARDS may be precipitated by trauma, aspiration, sepsis, fat embolism, or transfusion-related acute lung injury.

One condition that deserves specific mention is neurogenic pulmonary edema (NPE), which is reported to complicate approximately 20 % of cases of TBI [10]. The underlying pathogenesis of NPE is poorly understood, but it is believed that increases in intracranial pressure (ICP) lead to the activation of sympathetic nervous system and release of catecholamines with resultant changes in cardiopulmonary hemodynamics and starling forces leading to rapid onset of pulmonary edema [18]. The onset of NPE may be early, minutes to hours after the neurologic insult, or delayed, occurring 12–24 h following injury [18].

In addition to direct insults to the lung, traumatic injury increases cellular metabolism leading to increased oxygen utilization and carbon dioxide production [19]. Furthermore, metabolic acidosis from shock results in increased work of breathing for carbon dioxide clearance [19]. These increases

in metabolic demands, particularly when combined with primary or secondary lung injury, may result in hypercapnic respiratory failure.

Intracranial Physiology and the Effects of Mechanical Ventilation

An understanding of basic intracranial physiology and how it is affected by MV are essential in caring for the severe TBI patient. As mentioned in the introduction to this chapter, avoidance of secondary injury is the cornerstone of TBI management. Secondary injury may result from hypoxemia or inadequate cerebral blood flow (CBF). CBF is determined by the cerebral perfusion pressure (CPP) divided by the cerebrovascular resistance (CVR). As monitoring of CBF is impractical clinically, CPP is typically used as a surrogate marker for adequacy of CBF. CPP is the difference between mean arterial pressure (MAP) and ICP. Given this relationship, inadequate CPP may result from decreased MAP or increased ICP. Hypotension, elevated ICP, and low CPP are associated with worsened clinical outcomes in TBI [20].

Mechanical ventilation (MV) influences cerebral oxygen delivery in a number of ways. The fraction of inspired oxygen (FiO_2) directly affects arterial oxygen tension and in turn, cerebral oxygen delivery. Severe arterial hypoxemia also causes cerebral vasodilation resulting in an increase in ICP [21]. Multiple studies have demonstrated an association between hypoxemia and adverse outcomes in TBI [22–24]. Minute ventilation alters PCO_2, which acts as a potent modulator of CBF. Increases in PCO_2 result in vasodilation, and in turn, increased cerebral blood volume. In an injured brain with decreased intracranial compliance, this can increase ICP and reduce cerebral perfusion. Decreases in PCO_2 result in vasoconstriction and decreased cerebral blood volume. While hyperventilation is sometimes utilized as a short-term management strategy to reduce ICP in a patient with uncontrolled intracranial hypertension and impending brainstem herniation, routine hyperventilation should be avoided as the resultant vasoconstriction may lead to inadequate cerebral blood flow and secondary injury [25]. Studies of prehospital ventilation have found that both hypo- and hypercapnia are associated with increased in-hospital mortality [5, 26].

MV also impacts CPP via positive end expiratory pressure (PEEP). PEEP improves oxygenation and ventilation by recruiting collapsed lung units; however, the increase in intrathoracic pressure may potentially be associated with deleterious effects on the injured brain. PEEP increases intrathoracic pressure, causing decreased thoracic venous return, which: (1) increases cerebral blood venous volume and thus ICP and (2) reduces cardiac preload and cardiac output, and thus reduced CPP [27]. Additionally, when applied incorrectly alveolar overdistension from PEEP can result in hypercapnia, resulting in cerebral vasodilation and raised ICP [28]. While theoretical concerns exist regarding the application of PEEP in the brain-injured patient, the bulk of available studies suggest that the effects of PEEP on ICP are relatively modest [29–34]. Figure 23.1 summarizes the potential adverse effects of MV on the injured brain.

Mechanical Ventilation Strategies

Selection of appropriate MV settings in polytrauma TBI patients requires a comprehensive assessment of the patient's injuries. Selection of the mode of MV should take into consideration the severity of hypoxemic respiratory failure and the presence of intracranial hypertension. The mode of MV selected should correct hypoxemia and hypercapnia, while at the same time limiting plateau pressure and tidal volume to a level that does not potentiate ventilator-induced lung injury. For the majority of TBI patients, we recommend use of volume-assisted control ventilation, as it is the MV mode utilized in the bulk of the ARDS medical literature. It should be recognized that volume-assisted control has not been conclusively demonstrated to be superior to other modes of MV in randomized, controlled trials. Patients who cannot be adequately

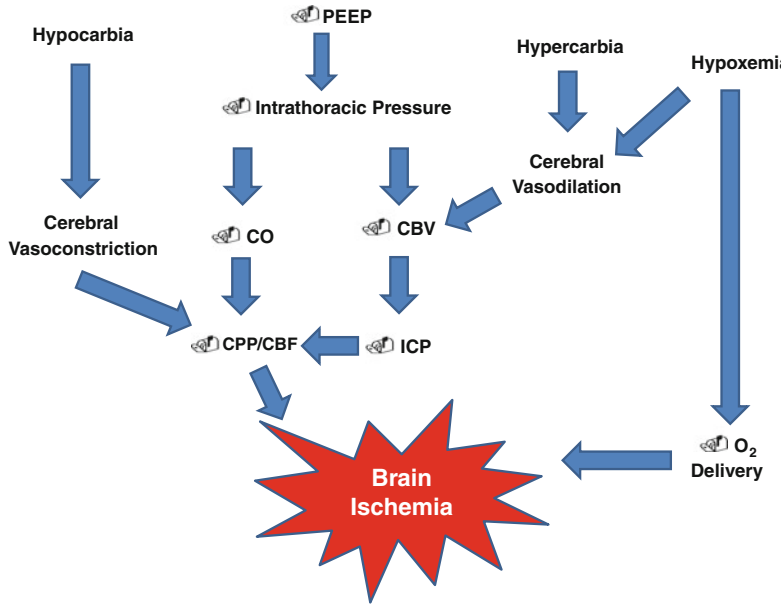

Fig. 23.1 Effects of mechanical ventilation on intracranial physiology

oxygenated or ventilated with volume assist control may require additional rescue therapies. In this section, we will discuss the rationale for selection of tidal volume; PEEP and FiO_2 in patients on volume assist control ventilation. We will then discuss rescue therapies including use of paralytics, prone positioning, nitric oxide, and extracorporeal support.

Selection of Optimal Rate and Tidal Volume

In 2000, the Acute Respiratory Distress System Network (ARDSNet) published a landmark trial comparing outcomes in patients with ARDS ventilated with a low volume strategy of 6 mL/kg of ideal body weight (IBW) versus 12 mL/kg IBW. The trial was terminated early as mortality was significantly lower in the 6 mL/kg IBW group (31 versus 39.8 %, p = 0.007) [35]. The methods of this trial represent the only ventilatory strategy known to reduce mortality in ARDS. Given this, considerable attention has been paid to the limitation of tidal volumes in ventilated patients and some speculate that a "lung protective" strategy may even be beneficial in a non-ARDS population [36]. In fact, high tidal volume ventilation has been associated with subsequent development of ARDS [6, 37].

A low tidal volume "lung protective strategy" is not without risks in the brain-injured population; however, as it has the potential to cause hypercapnia and raise ICP. The low tidal volume also requires heavy sedation in some patients, which limits the utility of the neurological assessment, making an ICP monitor necessary. In light of these concerns and the unclear benefit of tidal volumes of 6 mL/kg IBW when plateau pressure is <30 cm H_2O, a balanced strategy targeting a tidal volume of 6–8 mL/kg IBW and a plateau pressure <30 may be more suitable in the TBI patient [38, 39]. Arterial blood gases should be closely monitored and changes made to target a PCO_2 of 35–40 mm Hg.

The injured brain, particularly with brainstem lesions, may induce periods of rapid or irregular breathing, resulting in ventilator dyssynchrony, contributing to overdistension and effecting gas exchange due to autopeep [40]. In such cases, sedation and possible paralysis will be necessary. As a result of the loss of neurologic

exam, ICP monitoring may be necessary in these patients.

In cases of increased extrapleural pressure, such as from a hemothorax, pleural effusion, or abdominal compartment syndrome, plateau pressures >30 mm Hg may not cause ventilator-induced lung injury since transpulmonary pressure is not increased [41]. However, the effects of such pressures may decrease CPP and increase ICP. Surgical interventions such as decompressive laparotomy may be necessary to lower ICP [42].

Optimization of Oxygenation —Positive End Expiratory Pressure (PEEP) and Fraction of Inspired Oxygen (FiO_2)

Positive End Expiratory Pressure (PEEP)

PEEP therapy is necessary to prevent lung injury due to repetitive opening and collapse of alveoli, or atelectrauma. PEEP may improve outcomes, but only in patients with moderate or severe ARDS by the current definition, suggesting a preferential effect based on lung compliance [7, 43]. As mentioned earlier, increases in PEEP have the potential to reduce CBF and raise ICP, although the effects demonstrated in the limited available studies are variable and mild. In a small clinical series of TBI patients with ICP < 20 mm Hg, an increase in PEEP from 0–15 cm H_2O did not increase ICP [34]. Yet another study suggested that effect on ICP is based on alveolar recruitment. Mascia, et al. studied the effects of increased PEEP in 12 severely brain-injured patients. They found that when PEEP resulted in alveolar recruitment, ICP was unchanged; however, when increased PEEP failed to result in alveolar recruitment, ICP was increased. They hypothesized this was due to alveolar hyperinflation and resultant hypercapnia [28]. A similar study found that increasing PEEP from 0 to 12 mm Hg in mixed neurocritical care patients resulted in decreased CPP and MAP in patients with normal lung compliance, but had no effect on these parameters in patients with poor lung compliance [44].

In a small study of nine TBI patients with polytrauma with hypoxia and elevated ICP, incremental increases in PEEP from 0 to 21 mm Hg improved oxygenation (PaO_2/FiO_2 increased from 128 to 245), while ICP only marginally increased (27–29 mm Hg) and CPP remained stable [45]. A study in mixed neurocritical care patients with raised ICP (18 mm Hg), PEEP up to 15 mm Hg did not significantly alter ICP or CPP [33].

High levels of PEEP for short periods of time, or recruitment maneuvers, as a salvage therapy for refractory hypoxemia have been shown to improve oxygenation [46]. However, in one study, the tradeoff for improved oxygenation in TBI patients was a reduction in jugular venous saturation, concerning for cerebral ischemia, despite an improvement in PaO_2 [47].

Given the paucity and heterogeneity of studies, firm conclusions regarding the use of PEEP in TBI are difficult. Modest amounts of PEEP (5–10 mm Hg) are unlikely to be associated with detrimental intracranial effects. High PEEP (>10 mm Hg) should be avoided with mild ARDS and patients exhibiting minimal improvement of PaO_2/FiO_2 with increasing PEEP, but can be cautiously applied in patients with severe hypoxemic respiratory failure. As PEEP is increased, ICP and CPP should be closely monitored. Decreases in MAP secondary to PEEP should be addressed with fluid loading or vasopressors to prevent resultant decreases in CPP. Few studies have assessed the effect of PEEP >15 mm Hg; so extreme caution should be exercised in applying this strategy.

Fraction of Inspired Oxygen (FiO_2)

As mentioned previously, hypoxemia is associated with worsened outcomes in the brain-injured patient [22–24]. At a minimum, FiO_2 should be set to avoid hypoxia (PaO_2 < 60 mm Hg). Hyperoxia may also be detrimental, though a clear threshold at which negative effects ensue

has yet to be defined [48–50]. Based on the available data, it is reasonable to target a PaO_2 of 80–100 mm Hg in the TBI population to provide some "buffer" against transient insults that may cause hypoxemia while avoiding the possible detrimental effects of hyperoxia as well.

Rescue Modalities for Severe Hypoxemic Respiratory Failure

Salvage treatments can be considered in hypoxemic patients not responding to or not tolerating higher PEEP. Such treatments include airway pressure release ventilation (APRV), prone positioning, paralysis, nitric oxide, and extracorporeal membrane oxygenation.

Airway Pressure Release Ventilation (APRV)

APRV is a pressure-limited, time-cycled mode of ventilation that allows a patient to breathe spontaneously during the application of continuous positive airway pressure [51]. The mode maintains a high pressure for the majority of the respiratory cycle with periodic releases to a low pressure. It allows a very high mean airway pressure to be achieved without high peak pressures which may result in barotrauma. A single case report by Marik and colleagues describes the successful use of this mode in the setting of increased ICP. No significant detrimental effects on ICP or CPP were observed and oxygenation improved significantly [51]. Clarke, et al. reported a similar experience with inverse ratio pressure control ventilation in nine patients with head injury [52]. If inverse ratio ventilation or APRV is utilized in the setting of TBI, it should be done so in the setting of hypoxemic respiratory failure refractory to conventional ventilator settings by a practitioner experienced with the modality. The effects on PCO_2, CPP and ICP should be monitored closely.

Prone Positioning

Prone positioning recruits collapsed lung regions and has lowered mortality in severe ARDS($PaO_2/FiO_2 < 100$) particularly when added to tidal volumes <8 mL/kg IBW [53]. However, proning TBI patients with elevated ICP can raise intrathoracic and intraabdominal pressures, increasing ICP. In an observational study of 29 neurocritical care patients with ICP monitors, prone positioning improved oxygenation at the expense of higher mean ICP and more frequent ICP elevation >20 mm Hg [54]. As with high PEEP, prone positioning has to be undertaken with caution.

Nitric Oxide

In multiple studies, inhaled nitric oxide has been shown to improve oxygenation in ARDS, but without improving outcomes or mortality [55]. Several case reports have described the use of inhaled nitric oxide in the setting of ARDS associated with TBI [56–59]. Some have postulated that nitric oxide may have beneficial effects on both the lung and injured brain in the setting of ARDS in TBI [60]. Further study is required to determine if inhaled nitric oxide truly has a role in the management of TBI complicated by ARDS.

Paralytics

Due to ventilator dyssynchrony from low tidal volume associated dyspnea and hyperventilation from brain injury, as well as raised intracranial pressure, neuromuscular paralysis has the potential to treat ARDS and elevated ICP. Several trials have shown improved outcomes on moderate to severe ARDS patients paralyzed with cisatricurium, without an increase in ICU-acquired weakness [61]. Paralysis is also recommended for management of elevated ICP once adequate

sedation has been provided [62]. Therefore, paralysis seems to be a more suitable initial treatment option for refractory ARDS in severe TBI than prone positioning or use of high PEEP.

Extracorporeal Membrane Oxygenation (ECMO)

ECMO has been shown to improve outcomes in refractory ARDS [63]. ECMO treatment generally requires systemic anticoagulation to prevent ECMO circuit thrombus formation, limiting its use in traumatic injury. However, several small series suggest that ECMO without systemic anticoagulation is possible in TBI patients [64, 65]. If ECMO is pursued as a therapy for ARDS in the setting of TBI, it should be performed at experienced centers.

Conclusion

Majority of patients with severe TBI require MV and many develop concurrent lung injury. Meticulous attention to ventilator management is essential to avoid secondary injury from hypoxemia and hypo- or hypercarbia. A lung protective strategy can be safely employed in most TBI patients. While PEEP has the potential to adversely affect the injured brain, when used judiciously, the effects on ICP are generally modest. For patients with refractory ARDS, potential strategies to address hypoxemia include prone positioning, paralytics, inhaled nitric oxide, and ECMO.

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Nutrition, Antibiotics, and Post-traumatic Seizure Prophylaxis

24

Erik J. Teicher and Christopher P. Michetti

Nutrition in the Intensive Care Unit

Nutritional support is an important component of the care of the traumatically brain injured patient. Patients in a coma after traumatic brain injury (TBI), even without other major injuries, are in a metabolic state similar to patients with major trauma and burns [1]. Caloric expenditure can be almost twice that of the expected resting energy expenditure (REE) and may be influenced by temperature, muscle tone, Glasgow Coma Scale (GCS) score, and time of measurement in relation to injury [2]. The REE in turn is used to calculate caloric needs.

Indirect calorimetry (IDC) is the most accurate form of nutritional assessment. It measures the oxygen consumption and carbon dioxide production from the patient, from which the REE can be calculated [3]. Several studies that include patients with TBI utilize IDC to determine REE in the intensive care unit (ICU) [4]. Most used single measurements of REE to determine total caloric needs but failed to identify optimal timing, duration, or frequency of REE measurement. The use of repeated measurements of REE in the ICU to monitor ongoing nutritional requirements has not been fully assessed.

Predictive equations such as the Harris–Benedict equation, with adjustments based on activity level [5], have been used to determine the REE [6]. Unfortunately, a direct and accurate relationship of these equations to a patient's daily nutritional requirements has not been established. Currently the American Society for Parenteral and Enteral Nutrition guidelines recommend the range of 20–35 kcal/kg/day for adults, depending on the severity of stress or illness. In the critically ill obese patient, 11–14 kcal/kg actual body weight per day or 22–25 kcal/kg ideal body weight (IBW) per day is recommended [7]. In general, ICU patients should receive hypocaloric, high protein feeding. Fat calories from propofol infusions may be factored into the equation.

Protein metabolism after TBI is also similar to that after major systemic injury [5]. Protein energy metabolism is assessed in the ICU by measurement of the nitrogen balance, which is the only marker for this measurement widely reported in the neurological ICU population [8]. The nitrogen balance is the daily difference between nitrogen intake and output. The percentage of calories derived from protein has been shown to increase from the normal range of 10–15 % to upwards of 30 % after TBI [9]. The consumption of lean body mass during this catabolic state may be decreased by providing 100–150 % of expended calories and further decreased by providing a higher protein intake

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[10], however this incurs the risks of overfeeding such as excess carbon dioxide production, and currently a hypocaloric approach is recommended. Attempts to lessen nitrogen wasting after TBI by increasing protein intake beyond 17 g/day results in greater protein catabolism, so that only 50 % of administered nitrogen may be retained. The level of nitrogen intake that results in a nitrogen loss of 10 g/day is 15–17 g/day, or 0.3–0.5 g/kg/day. This represents about 20 % of the caloric composition of most feeding formulas designed for a hypermetabolic patient.

There is a significantly greater mortality rate as a consequence of undernutrition for a 2-week period after injury, as compared to receiving full nutrition by 7 days [11]. Fewer infectious and overall complications have been demonstrated by starting feedings that meet the estimated energy and nitrogen requirements on day one following injury [8]. Patients receiving early feeding are also more likely to have energy and nitrogen requirements met by 1 week. Early feeding is recommended once resuscitation and hemodynamic stability is achieved and therefore should begin within 72 h following injury to achieve full nutritional support by day seven [12].

There is no validated means of measuring the response to nutrition in the ICU setting. However some nutritional assessment parameters, such as the serum albumin level, are excellent prognostic indicators of morbidity, mortality, and ICU and hospital length of stay [13]. Studies have examined the predictive value of a single albumin level measured upon admission to the hospital, within the first few days of admission, or prior to surgery or other planned treatment. Yet the value of using sequential albumin levels for monitoring nutrition progress is low. Spontaneous changes in albumin concentration are expected in critically ill patients. They occur slowly and are affected by acute phase responses and compartmental fluid shifts which occur during an ICU stay [14]. In some patients albumin levels may not change significantly within the acute setting due to the long half-life of 19 days.

Prealbumin has been used frequently as a marker of nutritional response because of its short half-life of 2–3 days, so that significant changes may be detected in days to weeks. Its use has fallen out of favor, as prealbumin levels are also influenced by acute phase responses and do not correlate with outcomes [15].

Body weight is the most commonly used indicator of nutrition adequacy in nonhospitalized patients, but due to the confounding effects of fluid retention and gradual weight loss during acute illness, changes in weight more often indicate alterations in fluid balance [16]. Anthropometric indices such as the mid-arm circumference, triceps skin fold thickness, and calculated mid-arm muscle circumference are typical indicators of somatic protein and fat reserves and may be used to monitor response to nutrition therapy under normal circumstances, but are also confounded by fluid balance in the ICU setting.

The most commonly employed options for nutrition delivery currently are the enteral (gastric or jejunal) and parenteral routes. The enteral method is superior to parenteral nutrition in patients with a functional gastrointestinal tract [17]. Enteral formulations utilize more effective substrates to support cell and organ function, result in lower risks of hyperglycemia or hyperosmolarity, are administered at rates which may avoid overfeeding, and maintain the mass and barrier function of the gut. However, enteral feeding in patients with gastrointestinal intolerance is associated with underfeeding and subsequent malnutrition. Parenteral formulations deliver more dependable nutrient bioavailability, result in greater nutrition effects in a shorter time period, act independently of gastrointestinal function, and avoid gastrointestinal feeding complications such as intolerance, abdominal distention, and diarrhea. However overfeeding, administration of excess dextrose, triglycerides, or calories, and refeeding syndrome (from rapid feeding with preexisting malnutrition) may occur. This may cause certain metabolic complications such as hyperglycemia, hypertriglyceridemia, hypervolemia, and hypercapnia [18]. It has been estimated that at least 20 % of patients with TBI exhibit gastric feeding intolerance within the first week. In this situation, parenteral nutrition may be utilized for initial nutrition support, though improved outcomes from early

parenteral nutrition have not been demonstrated. Jejunal feeding can also be used and provides the benefits of enteral feedings while avoiding the complications of the parenteral route. Although older evidence had suggested that pneumonia rates may be reduced by jejunal feeding due to the reduced aspiration presumed to occur during gastric feeding [19], more recent investigations have found no influence of the delivery route on this complication [20]. Currently, routine nasojejunal feeding is not routinely recommended.

Nutrition support and therapy are important factors in the management of the critically ill patient. Nutritional issues pertaining specifically to the brain injured trauma population have been underestimated and certainly less studied. Additional work is needed to realize outcome benefits that could result from improved nutrition delivery in the TBI population.

Antibiotic Stewardship in the Intensive Care Unit

On any given day in intensive care units (ICU) across the world, about half of the patients carry a diagnosis of infection, and 71 % are receiving antibiotics [21]). This extensive antibiotic use, both appropriate and indiscriminate, has resulted in increased bacterial antibiotic resistance and emergence of multi-drug-resistant (MDR) pathogens that are increasingly difficult to treat [22]. Infections with antibiotic-resistant organisms result in the death of about 23,000 people a year in the United States according to the Centers for Disease Control and Prevention [22].

Indiscriminate use of antibiotics has other serious consequences. In addition to the risk of allergic reactions, ranging from a mild rash to anaphylaxis, organ damage and other adverse events may result from errors in dosing or incorrect choice of drug. Clostridium difficile infection is directly linked to antibiotic use [23]. While this risk increases with the duration of antibiotic administration, and with broad-spectrum as opposed to narrow coverage agents, even one dose of antibiotic may result in fulminant C. difficile infection. The price of MDR infections is high, both financially [22] and in terms of human health. Not only are MDR infections difficult to treat, but they are associated with higher mortality. [21, 24].

Patients with neurotrauma are highly susceptible to harm from both hospital-acquired infections and from the antimicrobial agents used to prevent or treat them. Coma or altered mental status, bedrest, increased risk of aspiration, extended ventilator dependence, and prolonged ICU stays increase the risk of ventilator-associated pneumonia, catheter-associated urinary tract infection, and central line-associated bloodstream infection. In this section, we discuss a common scenario for neurotrauma patients, that is, the use of prophylactic antibiotics for intracranial pressure monitors.

Prophylactic Antibiotics for Intracranial Pressure Monitors

The use of prophylactic antibiotics (PAB) to prevent infection of fiberoptic intracranial pressure monitors (ICPM) and external ventricular drains (EVD) is a common and traditional practice [25], though the efficacy of this practice is still under investigation. The paucity of randomized or prospective data and the significant heterogeneity of the remaining studies account for the lack of definitive recommendations on the use of PAB for these devices. Many design characteristics must be accounted for when examining the literature on this topic, including: the type of device used (ICPM or EVD); method of infection diagnosis (insertion site infection, cultures from drains or lumbar puncture, or clinical signs); the duration of PAB administration (one pre-procedure dose, a few days, or for the duration of the device); the location of insertion (ICU, operating room); the length of time the monitor is in place; degree of sterile protocol and other technical factors pertaining to insertion; the expertise of the proceduralist (attending surgeon, trainee, midlevel practitioner); and not least, the condition for which the monitor is needed (trauma, non-traumatic subarachnoid hemorrhage, hydrocephalus, tumor).

In the setting of traumatic brain injury, the infection rate of fiberoptic intracranial pressure monitors ranges from 0 to 3.7 % [26–28]. Use of PAB has not been shown to affect central nervous system or monitor infection rates in multiple retrospective studies, when administered either as a perioperative dose or continuously for the duration of the monitor [26–29]. Intuitively this makes sense, when one considers the lack of evidence that prophylactic antibiotics affect infection rates for other percutaneous devices such as non-tunneled vascular catheters [30] and drains [31].

The risk of infection for EVDs is higher than for ICPMs, most likely due to multiple factors such as their more invasive nature, wider diameter, and attachment to drainage systems that allow one to break the circuit (e.g., to flush the catheter or change the fluid collection container). Whereas ICPM infection rarely involves more than the local surgical site, ventriculostomy-associated infections (VAI) involving ventriculitis or meningitis pose a greater risk to patients. Most retrospective studies fail to show benefit of PAB on VAI rates [27–29, 32, 33]. Only two randomized studies directly address the question of PAB for EVDs [34, 35].

Blomstedt [34] showed less early (but not late) infections with use of trimethoprim-sulfamethoxazole versus placebo in patients undergoing shunting procedures, and no difference in patients undergoing ventriculostomy procedures. A study from Hong Kong [35] randomized 228 patients receiving EVD to perioperative antibiotics only or antibiotics for the duration of the EVD, and reported a lower rate of CSF infection with prolonged antibiotics (3 %) than with perioperative antibiotics (11 %). However, no statistical methodology was reported in this paper, and with only 15 patients diagnosed with VAI its statistical power is limited. When VAI was diagnosed, more MDR pathogens were isolated in the prolonged antibiotic group, a finding replicated in other studies as well [26, 27]. It is important to keep in mind that sterile techniques in the intensive care unit have changed significantly in only the past decade (chlorhexidine skin preparation instead of betadine, head-to-toe draping of the patient instead of local draping, mandatory full sterile garb for all bedside procedures) such that the results of even fairly recent studies may have limited application to today's healthcare environment.

The 2013 joint guidelines from the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America state that data are insufficient to make a recommendation on use of PAB for EVD or ICPM [24]. Given the current state of evidence, the risk of MDR pathogens, and considering that use of extended prophylactic antibiotics in non-immunosuppressed patients has very few other indications, a restrained approach is preferable. If used for ICP monitors in trauma patients, PAB should be utilized in the manner as for other clean neurosurgical procedures: a single dose of pre-procedure cefazolin; clindamycin for documented beta-lactam allergy; or vancomycin with known MRSA colonization. One should also be mindful of other modifiable risk factors for VAI, including EVD presence for more than 5–7 days, suboptimal sterile placement technique, unnecessary or frequent flushing, and routine catheter exchange. [29, 32, 36, 37].

Pharmacological Seizure Prophylaxis for Patients with Traumatic Brain Injury

Approximately 2 % of patients with TBI who seek medical attention have a post-traumatic seizure (PTS) at some time. The risk of seizures increases with head injury severity, with rates reported as high as 12 % in patients with severe TBI, and approaching 50 % when seizure activity is diagnosed by electroencephalography [38]. A penetrating mechanism is associated with a 50 % rate of PTS [39].

Neurologic damage that occurs after a TBI occurs over hours to days. Mechanisms of injury may be divided into primary and secondary. The primary insult is the initial traumatic injury, can be focal or diffuse, and triggers a cascade of events

that ultimately result in cell death. The secondary insult includes damage that occurs as a result of physiological responses to the initial injury. Since the primary insult currently cannot be therapeutically modified, therapeutic interventions target the secondary insult in an attempt to improve outcomes [40]. Secondary insults include impairment in cerebral blood flow, oxygenation, autoregulation, and metabolic function as well as PTS.

By convention, PTS that occur within seven days of injury are termed early, and those occurring after seven days are referred to as late. Risk factors for developing PTS include age, history of alcoholism, penetrating mechanism, loss of consciousness, focal neurologic deficits, GCS score <10, seizure within 24 h of injury, depressed skull fracture, hemorrhagic mass lesions, presence and location of cerebral contusion, and retained bone or foreign bodies [12, 41]. Risk factors for PTS lean heavily, though not exclusively, on findings from brain computed tomography (CT) scans. Assessment of these risk factors is important for determining the need for a prophylactic regimen against PTS.

The existing science regarding the effect of antiepileptic drugs (AEDs) on early PTS when compared to placebo is limited, with only two Class I studies dating from 1983 [42] and 1990 [43], reporting conflicting results. Both the Brain Trauma Foundation guidelines [12] and the Quality Standards Committee of the American Academy of Neurology [44] have concluded that AEDs prevent early PTS in patients with TBI, the latter reporting this conclusion for severe TBI. Both groups rely heavily on one study [43] in drawing their conclusions. Nevertheless, a Level I recommendation for use of prophylactic AEDs cannot be made due to insufficient evidence [12].

Young et al. [42] reported a randomized double-blind trial of phenytoin versus placebo in 244 TBI patients, showing no difference in early PTS rate between the phenytoin (3.7 %) and placebo (3.7 %) groups. Temkin et al. [43] randomized 404 patients with TBI to receive either phenytoin or placebo, and reported a significantly lower early PTS rate in the phenytoin group (3.6 %) compared to placebo (14.2 %). There was no difference between groups in the incidence of late seizures. The inclusion criteria in the Temkin study were: a GCS of 10 or less *on admission*, cortical contusion, subdural hematoma (SDH), epidural hematoma (EDH), intracerebral hematoma (ICH), depressed skull fracture, penetrating head wound, or seizure within 24 h of injury. Traumatic subarachnoid hemorrhages were not included. While 60 % of patients randomized to phenytoin and 67 % of those receiving placebo had a GCS of 10 or less, the study did not report the percentage of those patients with a normal head CT scan. Though the study describes patients meeting inclusion criteria as having severe head injury, no further description of clinical or radiologic severity was provided. It is unclear how many patients, for example, improved quickly to a GCS of 15 and/or had a normal head CT, or if the groups with a positive head CT were equally matched for the size and severity of their lesions (the study predates the Marshall score and other classification methods).

As demonstrated by Bhullar et al. [45], a review of early seizure rates without pharmacological prophylaxis in eleven publications from 1940 through 2013 showed them to be between 2.2 and 4.7 %, with the Temkin study being the single outlier at 14.2 %. It has been theorized that this critical difference in early PTS rates without AEDs may account for the significant difference achieved by Temkin.

Prophylactic AEDs have not been demonstrated to prevent late PTS, nor does prevention of early PTS improve outcomes of TBI. In light of this, while it seems likely that AEDs given for 7 days after injury prevent early PTS in certain TBI populations, the question of whether this is a valid therapeutic target is left without a definitive answer. The question likely cannot be answered based on older literature, given the highly significant improvements in the early resuscitation of TBI and trauma patients that have occurred in the past two decades alone. The influence that improved resuscitation has on early PTS rates is unknown, but the subsequent study by Temkin and colleagues a decade after the initial landmark trial showed an early PTS rate of 1.5 % with phenytoin [46], less than half that of their previous study. The

greater accuracy of today's CT imaging may impact the question also. Even the smallest hemorrhages, obscured on scans almost three decades ago, are now easily visible. These lesions of uncertain significance would meet the broad inclusion criteria from the sole class I trial supporting AEDs, potentially leading patients with clinically mild TBI to receive unnecessary medical treatment. Future randomized studies are needed with more specific inclusion criteria in order to target the population of TBI patients that will truly benefit from prophylactic AEDs.

Several medications have been studied for AED prophylaxis after TBI, but phenytoin is the drug with the greatest amount of supporting data. Phenytoin has been approved by the Food and Drug Administration for the control of generalized tonic-clonic and complex partial seizures and the prevention and treatment of seizures occurring during or after neurosurgery [47]. Phenytoin exerts its effects within the motor cortex, promoting sodium efflux from the neuron and stabilizing the threshold of hyperexcitability. It requires close monitoring because of its pharmacokinetic properties, and critically ill patients with TBI may have changes in multiple organ systems that can affect drug concentrations.

While the drug has few serious side effects [48], life-threatening dermatologic reactions including toxic epidermal necrolysis and the Stevens–Johnson syndrome have been reported, as have arrhythmias and hypotension during parenteral administration, particularly with rapid infusion [47, 49]. Minor side effects include rash and other hypersensitivity reactions, irritation of the skin, phlebitis, and drowsiness. Phenytoin is also prone to many drug–drug interactions because of its induction of the hepatic cytochrome P450 system and has been shown to exacerbate acute adrenal insufficiency, a phenomenon seen in patients with severe brain injury as a result of decreasing cortisol concentrations [50]. Phenytoin has been associated with significantly impaired performance on neuropsychological testing after 1 month, but not at 1 year after injury [51]. A total serum level of 10–20 μg/mL is accepted as therapeutic, though a specific level for the prevention of PTS after TBI has not been specified. Since the drug is albumin-bound, a free-phenytoin level may be more accurate than serum levels in critically ill patients. It should be kept in mind that phenytoin has a narrow therapeutic index and nonlinear kinetics and so small increases in dose may occasionally result in toxic levels.

Because of these issues, levetiracetam has been investigated as an alternative option. Levetiracetam was approved by the FDA in 2006 and has a number of advantages over phenytoin, including linear pharmacokinetics, easier dosing, no need for monitoring of serum levels, and less potential drug interactions. It has not yet been shown to have hepatic enzyme-inducing properties.

Levetiracetam has been demonstrated to be noninferior to phenytoin for PTS, with no statistically significant difference in terms seizure rate, adverse drug reactions, or mortality [52]. There may be an increase in fatigue and somnolence [53] with levetiracetam use during the acute phase of TBI, resulting in discontinuation in about 3 % of patients [54]. One study found that patients who received levetiracetam demonstrated significantly improved global outcome measures, including the Disability Rating Scale and Glasgow outcome scale, which assess neurobehavioral status after TBI [55]. The cost of levetiracetam is significantly higher than phenytoin, an important consideration in PTS drug choice [56].

In summary, while AEDs are not recommended for every patient hospitalized with a brain injury and a positive head CT, they should be considered for patients with significant risk factors such as moderate to severe traumatic hemorrhage. Phenytoin and levetiracetam are the current options for PTS prophylaxis, and the choice of medication should be made based on individual patient factors and cost.

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Therapeutic Hypothermia for Traumatic Brain Injury and Spinal Cord Injury

25

Shamir Haji and Geoffrey S.F. Ling

Introduction

In clinical practice today, there is no therapy that will cure traumatic brain injury (TBI) or spinal cord injury (SCI). Furthermore, there are no clinically available neuro rescue or neuroprotective therapies. Management of patients suffering from either TBI or SCI is based on optimizing general physiology and avoiding exacerbating conditions, such as seizure, hypotension, or hypoxia. Induced hypothermia or targeted temperature management is a promising potential therapy for TBI and SCI. Preclinical animal models, especially rats and mice, of both TBI and SCI provide provocative evidence that induced hypothermia is highly beneficial for improving both neurological outcome and survival. Unfortunately, similar evidence in humans is lacking. There have been a number of clinical trials conducted but the outcomes have not supported widespread clinical adoption. Nevertheless, the ease of application, relatively low toxicity, dramatic benefit in preclinical models, and lack of any other effective therapeutic options make hypothermia still worthy of consideration.

Background

The central nervous system (CNS) is comprised of the brain and spinal cord. Both have gray matter and white matter. Gray matter is primarily neurons whereas white matter is axons, glia, and astrocytes. The CNS is highly dynamic with a consequently high metabolic demand. To meet this demand, the CNS receives 15 % of cardiac output and accounts for 20–25 % of total body oxygen and 25 % of glucose consumption [1]. Jain and colleagues, employing a noninvasive technique that uses magnetic resonance susceptometry-based oximetry and venous oxygen saturation demonstrate that in humans, global cerebral metabolic rate ($CMRO_2$) is about 130 mol per 100 g per min [2]. Others report cerebral oxygen consumption rate in adults as 3.5 ml per 100 g per min [3]. The gray matter uses about 94 % of CNS oxygen consumption whereas the white matter uses approximately 6 % [3]. Almost 80 % of gray matter oxygen consumption is devoted to glutamate-mediated neurotransmission [1]. Under normal conditions, the blood flow to the CNS is autoregulated to about 50 ml per 100 g tissue per minute. Autoregulation is the process whereby cerebral blood flow is maintained at this constant rate over a wide range of systemic blood pressures.

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When injured, the CNS becomes pressure passive. Autoregulatory function is compromised so the CNS is dependent on the systemic blood pressure for adequate perfusion. So, when the CNS is injured, systemic blood pressure rises. The injured tissue is able to receive the perfusion it requires whereas the uninjured tissue is able to autoregulate so as not to be over perfused [4].

Injury has 2 phases—primary and secondary [4]. Primary injury refers to tissue destruction resulting directly from the inciting event. This occurs virtually instantaneously and is complete very soon after injury. Secondary injury is the cascade of events that include inflammation, free radical production, and release of excitatory mediators such as calcium and glutamate. This develops shortly after injury and develops over time in hours to days. The best approach for mitigating primary injury is prevention. Pretreatment may be an option analogous to aspirin for primary prevention of sudden coronary syndrome. However, a clinically effective TBI or SCI pretreatment therapy has not yet been identified. Secondary injury is an opportunity to treat. The period of development is a window in which an effective treatment can be ameliorative.

Hypothermia is believed to reduce neuroinflammatory processes, cause a reduction in $CMRO_2$, and improve the efficiency of glucose and energy metabolism [5]. Hibernating animals have been shown to tolerate very low perfusion states for prolonged periods. This became a basis for investigating induced hypothermia as a potential treatment for TBI and SCI. Many basic science investigators have and are exploring this field. In 1994, Dietrich and colleagues showed in a TBI rat model that reduction of core body temperature to 30 °C resulted in significantly less neuron necrosis and brain contusion volume [6]. Since then, a number of investigators have confirmed these findings in rats and other animal subject species.

In 2002, two landmark studies were published demonstrating human clinical efficacy for induced hypothermia or targeted temperature management in patients who suffer out-of-hospital cardiac arrest and remain unconscious. One study was performed by Bernard and colleagues in which 77 patients were randomized to either hypothermia to 33 °C or normothermia [7]. Hypothermia was induced within 2 h of return-to-spontaneous circulation and maintained for 12 h. They found that 49 % of the hypothermia patients were able to leave the hospital to either home or a rehabilitation facility versus only 26 % of the normothermia patients. The other study enrolled 275 patients and also randomized them to either induced hypothermia to 32–34 °C [8]. In this group, hypothermia was induced within 4 h of return-to-spontaneous circulation and maintained for 24 h. They were rewarmed over 8 h. The hypothermia group did much better than the normothermia. About 41 % of hypothermia patients died as compared to 55 % of normothermia and, of those who survived, 55 % had favorable neurological recovery versus 39 %, respectively.

A Cochrane database systematic review was conducted in 2012 by Arrich et al. [9]. They confirmed the efficacy of induced mild hypothermia for improving outcome after cardiac arrest. Since its efficacy has been revealed, this therapy has become part of clinical practice guidelines for managing adult cardiac arrest [10].

Unfortunately, a recent 2015 study by Moler and co-workers did not demonstrate the same efficacy when induced hypothermia was used for pediatric patients who suffered cardiac arrest [11].

Thus, for adult patients with impaired consciousness after cardiac arrest, targeted temperature management, or induced hypothermia provides clear benefit.

Traumatic Brain Injury

In 1997, Marion and colleagues demonstrated the first conclusive evidence showing that mild hypothermia had a benefit in improving clinical outcome in patients who suffered TBI [12]. Unfortunately, it was temporary. There were better outcomes with induced hypothermia at 3 and 6 months after injury. However, this benefit

was not sustained so that by 12 months after injury, there was no difference between the hypothermia group versus the normothermia group. Importantly, very severely impaired patients, i.e., those with admission GCS scores of 3–4, did not have any benefit at any time with hypothermia.

An interesting finding of the 1997 Marion et al. study was that both glutamate and IL-1 levels were significantly decreased in the hypothermia group [12]. Glutamate is an excitatory amino acid implicated in secondary neuro-injury. IL-1 is an important proinflammatory cytokine. This suggests that hypothermia did reduce excitatory amino acid release and neuroinflammation as previously hypothesized. However, the study was not designed to determine if lower hypothermia levels would have led to even more glutamate and IL-1 suppression or if even that would have had greater clinical impact.

In 2001, Clifton and colleagues studied whether an earlier induction and longer period of hypothermia would be beneficial [13]. They achieved hypothermia within 8 h of injury and maintained it for 24 h. Unfortunately, outcome and mortality were not significantly different between the 2 groups.

In 2002, post hoc analysis of the 2001 Clifton et al. study revealed that patients who were hypothermic on admission and then subsequently maintained in a hypothermic state had better clinical outcomes [14]. This suggested that the induction of hypothermia very quickly after injury with subsequent maintained cooling could be beneficial. This seemed rational as preclinical animal studies induced hypothermia within minutes after injury and outcomes were significantly better.

In 2010, Clifton and co-workers conducted a trial to test the hypothesis that very early and even longer period of induced hypothermia would provide clinical benefit [15]. Patients were cooled to 33 °C within 2.5 h of injury and maintained for 48 h. Unfortunately, in spite of this achievement, after 232 patients were enrolled, interim analysis did not reveal any clinical benefit. The study was terminated due to futility. Thus, it appears in humans, even very early induction of hypothermia is not beneficial.

In 2015, Andrews and colleagues of the Eurotherm3225 consortium studied the impact of adding induced hypothermia to controlling increased intracranial pressure (ICP) in the setting of TBI [16]. Hypothermia added to standard of care treatments, such as mannitol, was able to control ICP better than without temperature management. Fewer patients needed third tier intervention such as decompressive hemicraniectomy for ICP control. However, an overall benefit could not be demonstrated for adding hypothermia. Instead, there was a worse outcome as more patients had a favorable outcome in the control group as opposed to hypothermia.

For pediatric TBI victims, induced hypothermia also has not been shown to improve outcome. In 2008, Hutchison et al. reported a study of pediatric TBI patients where induced hypothermia was associated with increased toxicity but without benefit [17]. In fact, there was a concerning trend toward more patients with poor outcomes and death in the hypothermia group. This study was followed by a study in 2013 by Adelson and associates [18]. Unfortunately, this study was terminated early for lack of efficacy. Most recently, in 2015, Beca and co-investigators showed no clinical benefit following hypothermia. Thus, hypothermia is not used for improving TBI outcome in the pediatric TBI population.

However, there may be hope for hypothermia as a treatment for TBI. A number of systematic literature reviews have concluded that although there is insufficient evidence presently to endorse the routine use of induced hypothermia for improving TBI clinical outcome, there may be benefit from hypothermia in specific TBI populations [19–21]. The most effective depth of temperature reduction, duration of hypothermia, and other goal directed strategies are needed. They all conclude that additional well controlled randomized studies are warranted.

Spinal Cord Injury

Very few human clinical studies have been conducted evaluating the efficacy of induced hypothermia or targeted temperature management for ameliorating SCI. There is only one prospective study of induced hypothermia as a treatment for acute SCI [22]. The remaining literature is limited to case reports, case series, and retrospective analysis.

In 2008, Kwon et al. conducted a systematic review of the literature of induced hypothermia for SCI. They noted that preclinical animal studies revealed conflicting results. Furthermore, over the prior 2 decades, there were no published peer reviewed human clinical studies using local induced hypothermia for SCI and none ever for systemic induced hypothermia [22].

In 2009, Levi et al. conducted a small retrospective SCI case series that showed that systemic hypothermia with surgery may be beneficial. At 12-months post-injury, 6 patients demonstrated improvement of at least one ASIA grade; 3 patients moved to grade B, 2 to grade C, and 1 to grade D. Any improvement that did occur happened within the first 3-months. The extent that surgical decompression accounted for this improvement could not be determined.

In 2013 Dididze et al. published a case controlled prospective study of induced systemic hypothermia [23]. To date, this is the largest such trial. Most of the hypothermia patients also underwent early surgical decompression. The patients that improved did so within 3 months. As in the Levi study, the relative role of surgical decompression could not be ascertained. Notably, the thromboembolic rate in the prospective cohort group remained significant despite prophylaxis.

In 2014, a small prospective case-series of local epidural cooling was described by Hansebout and Hansebout [24]. All of these SCI ASIA A patients underwent surgical decompression and also received dexamethasone. Most of them (80 %) demonstrated some degree of sensory and motor recovery over the next 5 years. This is important as most patients with complete SCI ASIA A rarely recover any function below the level of injury. Of the enrolled patients, 65 % exhibited some improvement; 30 % improved to ASIA grade B, 25 % to ASIA grade C, and 10 % to ASIA grade D. Two patients even regained the ability to walk. Of note, even though patients uncommonly recover from ASIA grade A to ASIA grade C, when they do, it typically takes 3–5 years. As some patients had a very prolonged recovery, there remains the possibility that some of these may have recovered without hypothermia treatment.

For SCI, there is suggestive evidence that induced hypothermia, either systemic or local, may be clinically beneficial. However, the lack of any randomized well controlled prospective human clinical trials prevents endorsement of either approach as standard of care practice.

Managing Intracranial Hypertension

Induced hypothermia may have utility in reducing elevated ICP. In particular, the use of temperature management may reduce the need for more invasive ICP interventions such as decompressive hemicranitectomy.

An important hallmark of TBI management is keeping ICP below 20 mmHg. A retrospective review by Sadaka and associates shows that there is clinical evidence supporting the use of induced hypothermia to manage elevated ICP [25]. Reducing systemic temperature to between 32°–35 °C can decrease ICP by 5 mmHg [16, 26]. However, this may be accompanied by a reduction in cerebral blood flow. For patients suffering from severe TBI (GCS $\leq$5), Tokutomi et al. advocate cooling to 35 °C instead of lower temperatures to obtain ICP levels $\leq$20 mmHg [27]. Work by Andrews et al. have shown that adding induced hypothermia to clinical management options for elevated ICP recalcitrant to medical therapy can reduce the need for neurosurgical interventions [16]. A cautionary note is that even with ICP control, induced hypothermia has not been shown to improve outcome.

Conclusions

An effective neuroprotection or neurorescue therapy is desperately needed for both TBI and SCI. There simply is no cure for these dreaded conditions. Sadly, at this time, there is insufficient evidence to support the routine use of induced hypothermia or targeted temperature management for improving outcome from TBI or SCI. However, as the investigators all noted, there are still reasons to continue exploring the potential of this therapy.

Disclaimer

The opinions expressed herein belong solely to those of the authors. They do not and should not be interpreted as belonging to or being endorsed by the Uniformed Services University of the Health Sciences, the Dept of Defense or any other element of the US federal government.

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Part V
Follow Up Care and Rehabilitation

Rehabilitation in the Setting of Neurotrauma

26

Daniel Rhoades, Christian Bergman and Paul F. Pasquina

Introduction

The effects of trauma to the central or peripheral nervous system may have profound negative impact on multiple other organ systems, such as system-wide inflammation, excessive metabolic demands, as well as the associated negative consequences of protracted bed-rest and immobility. Furthermore, trauma may lead to a variety of physical, cognitive and emotional impairments, which may cause significant disability, loss of functional independence, and poor quality of life. Acute medical and trauma care protocols are now achieving unprecedented survival rates from injuries that were once considered fatal. The field of rehabilitation is dedicated to ensuring that those who survive trauma achieve the highest level of independent function and return to active participation within their families and communities. This chapter addresses the complexity of organ system changes that occur with neuro-trauma and the rehabilitative approaches to mitigating these adverse effects.

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Negative Effects of Immobility

Musculoskeletal System

Muscle atrophy Immobility may lead to profound effects on the musculoskeletal system, including loss of strength, range of motion, and bone loss. Muscles respond to loading forces, and regular use can result in muscle hypertrophy; likewise, disuse can cause muscle atrophy. Importantly, muscles most used for posture and anti-gravity movements, such as those of the lower extremity and trunk, are typically the earliest to be affected by immobility. Muscle strength loss occurs at a rate of 1–3 % per day from immobility as a result of structural changes within the musculature. In patients with spinal cord injury (SCI), the loss can be even more dramatic, with 18–46 % muscle mass lost from muscle below the level of the lesion just 6 weeks

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after injury. Studies have demonstrated a loss in muscle length and thickness due to the loss of sarcomeres in series and parallel; additionally, loss of mitochondrial density can affect the metabolic efficiency of the muscle. A gradual shift in muscle from type I (slow-twitch, oxidative) to type II (fast-twitch, anaerobic) can significantly affect endurance. The metabolic balance shifts from protein synthesis to proteolysis, which is greatly magnified in the critically ill and injured patient [1]. Additionally, there can be a decreased overall metabolic rate, which can cause increased fat storage and a change in total body fat if intake is not adjusted appropriately relative to the decrease in expenditure [2]. There are numerous changes at the subcellular level as well—from alterations in gene expression to changes in intercellular signaling. Briefly, immobility during injury can enhance the chronic inflammatory system, with an increased production of cytokines like Tumor Necrosis Factor-alpha (TNF-α) and interleukin beta causing inflammation and reactive oxygen species generation which can damage local tissues.

Osteopenia/Osteoporosis Like muscle, bone is dependent on load stress. With the removal of gravity from bed rest and the loss of mechanical stress from muscles due to immobility, there is a decrease in the rate of bone formation compounded by an increase in bone resorption. Weight-bearing structures (femur, tibia) tend to be affected earliest and more significantly than those of the upper limbs. After SCI, individuals with tetraplegia demonstrate more significant bone mineral density (BMD) loss in the upper extremities than those with paraplegia [3] indicating the impact that regular muscle use and weight bearing through the upper arms likely has on bone health. Interestingly, spasticity, despite providing increased muscle tone and some protection from muscle degeneration, was not found to significantly alter rates of decreased bone mineral density [4, 5]. Patients with SCI are particularly susceptible to disuse osteoporosis during immobilization, with a reported 19 % trabecular and 3–4 % cortical bone loss noted up to a year post-injury [3]. Increased bone resorption may also lead to hypercalcemia (often manifesting with abdominal pain) as well as an increase in urinary calcium excretion resulting in nephrolithiasis.

Treatment

The best way to avoid significant muscle and bone atrophy is prevention. Early mobilization, particularly of the critically ill patient, has been well established as the single best intervention, with strength, endurance, and flexibility being key components. In the short-term, it can improve functional exercise capacity and self-perceived functional status [6]. Controlled studies using validated animal models demonstrate that mild to moderate levels of daily exercise can attenuate muscle atrophy [7]. Resistance exercise in humans has also been shown to be beneficial in preventing muscle atrophy from disuse and acute illness [6, 8]. Furthermore, moderate exercise (60–75 % of maximal oxygen intake) may lead to the formation of anti-inflammatory cytokines, providing secondary benefits to wound healing and recovery [1]. Evidence also exists that individuals with SCI may also improve muscle mass with activities such as body weight-supported treadmill training (BWSTT) [2].

Early mobilization, particularly for patients in the ICU setting is facilitated by engaging physical and occupational therapists along with the nursing staff. Evidence suggests that successful programs require “buy-in” from all team members, and that healthcare costs can be contained while reducing the length of hospital stays, time on ventilator assistance, and use of sedating medications [9, 10]. Therapeutic and functional electrical stimulation (TES and FES) can also be used in the prevention and mitigation of muscle

loss. TES uses repetitive electrical stimulation to paralyzed muscle in order to maintain muscle bulk and joint range of motion, whereas FES uses coordinated sequences of electrical stimulation to generate muscle contractions in order to assist patients with completing specific tasks, such as activities of daily living (ADLs), transfers, and ambulation. While direct muscle stimulation has not been demonstrated to have a significant impact on preventing BMD loss, evidence does support that supported standing (e.g., with a long leg brace, standing frame, or standing wheelchair) or treadmill walking can preserve, but not increase, BMD [2]. Exciting new research has demonstrated in animal models that Low Intensity Pulsed Ultrasound (LIPUS) may induce significant recovery of lost BMD after 4 weeks of disuse [11]. While pharmacotherapy options, including bisphosphonates and parathyroid hormone, have been studied in animal models with good results, little traction has been gained for human use at this time. However, good nutrition with supplemental Vitamin D and calcium is encouraged [12].

Contractures

Contractures are defined as a shortening of muscle through flexion, preventing the normal range of motion across a joint. There are two defined types: myogenic and arthrogenic. Myogenic contractures are a result of architectural changes in muscle, tendon, or fascia; when a limb is immobilized in a shortened position for a prolonged period of time intramuscular connective tissue is remodeled to adapt to this new position. Arthrogenic contractures are due to changes in the bone, cartilage, synovium, joint capsule, or ligaments.

Treatment

A preventative approach should be taken in the daily management of the patient. Patient bed mobility is essential so as to avoid prolonged time in a single position. Although there is limited research to support the use of daily stretching, passive range of motion, serial splinting or casting, these treatments are often recommended [13, 14]. If contractures are present and significantly limit the daily function of the patient or cause significant pain, surgical intervention may be indicated.

Spasticity

Spasticity is a velocity-dependent increase in muscle tone as a result of upper motor neuron (UMN) injury. It can be associated with increased deep tendon reflexes (DTRs) and other signs of upper motor neuron disease. Importantly, an acute increase in spasticity can also be a symptom of another underlying problem, such as infection, pressure ulcers, urinary or bowel retention; the spasticity may improve if the underlying condition is properly identified and treated.

Unlike contractures, spasticity is not an alteration in the physical architecture of muscle and joints; rather, it is a functional problem of muscle as a result of lost UMN input. It occurs frequently in patients suffering from traumatic brain injury (TBI) and spinal cord injury (SCI); up to 70 % of SCI patients will develop spasticity [15]. The initial pattern of injury usually trends toward an acute diminishment of reflexes and flaccidity (termed "spinal shock"), followed over days and weeks by a gradual return and increase in reflexive responses and the development of spasticity. While spasticity can result in significant pain, difficulty with transfers and participation in physical therapy, and increased risk of skin breakdown, it can also prove functionally beneficial to the patient. This is specifically seen in lower extremities, where a patient otherwise unable to position himself uses the increased muscle tone for standing during transfers.

Treatment

Treatment should be focused on improving patient function, hygiene, and care. An acute

increase in spasticity may be the result of infection or other pathological condition and should be identified and treated accordingly. For stable spasticity which limits the patient's function, there are conservative pharmacologic therapies available. Manual stretching, range of motion exercises and splinting are potential options; however, there is mixed evidence that one or either improve the incidence of spasticity [16]. Postural management and standing may also be helpful in spasticity. Strength training does not worsen spasticity and may provide improved quality of life, despite having little impact on improvement of spasticity.

There are both oral and injectable pharmacologic agents. It is important to consider the useful benefits of targeted spasticity (e.g., lower extremity spasticity to aid in transfers) before applying these agents. Side effect profiles, patient tolerance, and response to therapy should be considered when prescribing these medications. Oral medications can be used, including GABA agonists (e.g., baclofen), centrally acting alpha-2 agonists (e.g., tizanidine), and skeletal muscle calcium-channel blocking agents (dantrolene); however, a Cochrane review found low-level evidence supporting their use [17]. Cannabinoids is another possible oral medication, but current legal concerns and limited efficacy of the extracts require further study [16]. Local injections of agents such as botulinum toxin or chemical neurolysis with phenol or alcohol can be effective while limiting global effect; low doses of intrathecal baclofen by pump can also provide good muscle relaxation without systemic effect.

Heterotopic Ossification (HO)

Heterotopic ossification (HO) is inappropriate bone mineral deposition in soft tissues not normally ossified. The full mechanism is still not fully understood, but prevailing thought is that dormant osteoprogenitor cells within tissues are inadvertently stimulated (e.g., SCI or trauma, surgery, and stroke), allowing these cells to form into osteoblasts that promote bone formation. Common locations include the hip, knee, shoulder, and elbow. It has been reported that up to 80 % of patients who sustain amputations due to blast injury may develop HO [18]. It can take weeks for HO to fully develop or even be detected by traditional X-ray [19]. Clinical signs, including decreased range of motion, erythema, and swelling of the involved area can mimic other diagnoses, including deep venous thrombosis (DVT), infection or hematoma, and should be fully evaluated.

Treatment

Heterotopic ossification may be prevented through gentle ROM exercises, though more studies are needed. Regardless, range of motion (ROM) exercises are helpful for other complications of the musculoskeletal system and should be performed daily. Passive and active range of motion may keep HO from getting worse; however, surgical management is sometimes required to allow for functional range of motion and improvement in daily functioning [20].

The inflammatory condition of acute trauma appears to play a role in formation; NSAIDs have been shown to help reduce the incidence of HO two- to threefold [21]. Single-dose radiation therapy may also be helpful in the prevention of HO [22]. Therapeutic management of HO includes bisphosphonates like etidronate, which blocks the formation of bone matrix; however, it must be given in high doses during a narrow "window" of detection within the first 3–6 weeks of detection [21]. Recurrence may be halted when surgery is used in combination with single-dose radiation or bisphosphonates [20].

Cardiovascular

Lying supine for extended periods causes a significant shift of up to one liter of fluid from the legs to the thorax. This increases the fluid load on the heart, stimulating an increase in cardiac output. This also activates regulatory mechanisms in the heart (for example, Atrial Natriuretic Peptide, or ANP) to stimulate increased urinary excretion

of fluid and salts, while also decreasing thirst. The resultant decreased total blood volume places a decreased load on the heart, which will adapt by attempting to increase the heart rate. The decreased load also means less work on heart muscle, which reacts similarly to skeletal muscle in disuse and begins to thin and atrophy. Therefore, early mobilization helps mitigate these risks. As in skeletal muscle (discussed in above section "Musculoskeletal"), moderate increases in demand can be beneficial in maintaining heart muscle endurance and strength.

Orthostatic Hypotension

When moving from supine to sitting or standing, gravitational forces promote blood pooling in the thorax or legs. In the setting of reduced total blood volume, cardiac deconditioning, or failure of adequate physiological compensation (vasoconstriction in the periphery), there is a significant loss of cerebral perfusion, leading to lightheadedness, dizziness, loss of consciousness and falls. For patients who experience neurotrauma (especially SCI), orthostasis is often compounded because of decreased muscle tone from the neurological impairment, making venous return more difficult. Medications, such as opioids, which can cause peripheral vasodilation, may also influence the development of orthostatic hypotension.

Treatment

Orthostatic hypotension can be managed through prevention and treatment. Compression stockings and abdominal binders help prevent venous pooling in the lower extremities. Physical therapy that engages bed positioning, standing, lower limb exercises, and the use of a tilt table is also very effective. Pharmacologic interventions are used in conjunction with these therapies, but often reserved because of their potential side effects. Effective medications include: selective alpha-adrenergic blocker (midodrine), or long-acting synthetic mineralocorticoid (fludricortisone) [23].

Deep Venous Thrombosis (DVT) and Pulmonary Embolism (PE)

Classically described risk factors for developing venous clots are referred to as "Virchow's triad", which includes: (1) stasis, (2) endothelial injury, and (3) a hypercoagulable state. The incidence of venous thromboembolic events in the trauma setting is widely variable, reflecting the heterogeneity of injury patterns. Overall incidences have been reported as low as 2 % in severe trauma patients, with approximately two-thirds of those occurring within the first 3 weeks after injury [24]. For patients with complete SCI, however, the incidence has been reported to be as high as 90 %; this is attributed to the loss of both neural and muscular regulation of venous return in lower extremities and increased hypercoagulability due to decreased fibrinolytic activity. In addition, the mortality rate of SCI patients with PE is 35 %, which remains one of the top causes of death in this patient population in the weeks following traumatic injury; [25] this is only partially mitigated through adequate anticoagulation therapy [26].

Treatment

Venous thromboembolism (VTE) prophylaxis may not reduce the incidence or mortality of PE, but significantly reduces the risk of DVT [27]. Current guidelines recommend initiating VTE prophylaxis within 72 h of injury. Current evidence indicates the use of low-molecular weight heparin or adjusted dose unfractionated heparin is preferred to intermittent pneumatic compression devices (IPCs) [28]. However, preferences may change in the setting of significant contraindication to thrombolytic medications (e.g., active bleeding, at risk for intracranial or intraspinal hemorrhage or stroke, thrombolytics within last 24 h). Conversion to warfarin with a target international normalized ratio of 2.5 during the rehabilitation phase should be considered and current recommendations are to continue prophylaxis for 3–4 months depending on the activity level of the patient [29].

Pulmonary

High-level spinal cord injury or severe head injury may have profound negative consequences on respiration, as the breathing centers are controlled within the brainstem and the signal is carried through the phrenic nerve, which is composed of spinal roots C3–5. In addition, significant secondary sequelae result from neurotrauma, including atrophy of the diaphragm and respiratory accessory muscles, especially for patients requiring mechanical ventilation. The diaphragm muscle has been observed to atrophy in just 18 h, and ventilator-induced diaphragmatic dysfunction is responsible for many failures of weaning [30]. This weakness reduces the tidal volume (amount of air inhaled and exhaled during normal resting breathing) and flow rate. Weakened and paralyzed intercostal muscles allow the rib cage to collapse inward, reducing the total lung volume and affecting capacity. Another consequence of weakened musculature is an impaired cough, which can make it difficult to clear secretions. Patients also take fewer deep breaths when lying down, which combined with accumulating secretions can result in the development of atelectasis, further decreasing the functional capacity of the lungs. There is also a decrease in airway diameter, thought to be due to uninhibited vagal tone [31]. As a result, pneumonia remains a leading cause of death for patients with SCI [32].

Treatment

Patients and their caretakers should be educated in the importance of bedside incentive spirometry and its use should be encouraged. While there is no clear evidence that respiratory muscle training like incentive spirometry provide benefit, it may help strengthen involved accessory muscles and the diaphragm, much like regular exercise and mobility do for skeletal muscle [30]. Early mobilization and standing is also helpful. Patients with tetraplegia may actually respire better while supine, because during standing the loss of abdominal tone allows internal organs to passively fall forward, pulling the dome of the diaphragm flat and rendering it less mobile. Respiratory therapists facilitate chest physiotherapy and postural drainage. They also are invaluable in helping to educate the patient and caretaker in long-term care, including techniques for clearing secretions and assisted coughing [33].

Gastrointestinal

After acute neurotrauma, neural communication between the central nervous system and enteric network is disrupted. Additionally, prolonged immobility and supine positioning can disrupt normal GI function. Opioid medications can further decrease gastric motility. There is a slight increase in the incidence of gallstones amongst patients with SCI, possibly due to decreased GI motility [34]. The GI tract is also less efficient at absorbing nutrients. Spinal injury can result in a loss of voluntary sphincter control, causing stool retention or incontinence [35]. Loss of neuromuscular input can make passing stool normally difficult as well; those with high SCIs may rely solely on the diaphragm to generate intraabdominal pressures. Prolonged gastric emptying, increased gastrin production and prolonged supine positioning can all contribute to symptoms of reflux, regurgitation, and heartburn [36, 37]. Traumatic injury also increases rates of metabolism and catabolism; when combined with the dysfunctions of the GI tract, this may result in insufficient nutrition.

Treatment

Encouraging early mobilization and activity, maintaining adequate hydration and addressing nutritional needs are essential intervention strategies. A nutritional specialist should also be consulted early in the course of care. Use of a bedside commode or the bathroom toilet is preferable to a bedpan as it further encourages mobility. Adequate fiber intake, hydration, and retraining of the colon by taking advantage of the gastrocolic reflex can help by ensuring regular emptying of the bowels [35]. Other methods

commonly used to aid in encouraging defecation include bulking agents (docusate or polyethylene glycol), suppositories, and manual stimulation. Educating the patient and the caregiver on how to perform manual disimpaction or self-administer enemas can also be useful in maintaining colonic health. Occasionally, surgical colostomy may be indicated, usually for chronic constipation; this has been shown to improve quality of life, reduce abdominal distention, prevent fecal incontinence, and reduce hospitalizations for bowel dysfunction by up to 70 % [35].

Urinary System

In addition to the decreased urge to urinate while supine, neurotrauma patients may also have reduced sensory input, leading to bladder distension. In addition to the increased infection risk of incomplete urinary voiding, bladder over-distention may lead to reduced bladder wall compliance and increased intravesicular pressure, causing urine backflow, resulting in hydronephrosis and renal atrophy. For patients with injury to the spinal cord, neural disorganization may lead to detrusor sphincter dyssynergia, where the detrusor and external urethral sphincter muscles contract at the same time, thereby counteracting bladder evacuation [38]. Trauma to the pontine micturition center may result in the opposite problem, with urinary incontinence resulting from a low-capacity bladder and loss of awareness of the urge to urinate [39]. Trauma patients are also at higher risk for developing renal or vesical (bladder) calculi (stones) because of the increase in urinary calcium excretion resulting from immobility/trauma-induced bone resorption (see above section "Musculoskeletal/Bone"). Urinary retention and indwelling catheters also promote the colonization of bacteria, which may increase the urine pH, helping to further precipitate stone formation.

Treatment

In the setting of acute neurotrauma, most patients require an indwelling catheter (i.e., Foley catheter) to ensure adequate emptying of the bladder. Indwelling catheters should be removed as soon as medically safe in order to minimize injury to the bladder and/or urethra and prevent stricture formation or infections. After removal, monitoring the post-void residual bladder volume (PVR) is important to ensure adequate bladder emptying. For patients with neurogenic bladder dysfunction, self-catheterization may be necessary. Patient and family/caregivers should be educated on proper clean intermittent catheterization (CIC) techniques [40]. Specialized nurses and therapists may assist with the education and provide additional resources for the patient and healthcare team.

Neurotrauma patients with neurogenic bladder should be placed on a bladder program, which consists of timed voids, self-catheterization (as needed), developing a fluid intake schedule, and employing other techniques, such as the Crede technique (tapping over the suprapubic region) and valsalva maneuvers [39]. There is recent evidence that electroacupuncture in combination with bladder retraining may improve outcomes for patients with neurogenic bladder [41]. Pharmacologic agents with anticholinergic properties are also frequently used to decrease detrusor overactivity. These include: oxybutynin, trospium, and fesoterodine. Alpha-adrenergic agonists may also be helpful, including clonidine and tizanidine, especially to reduce sphincter tone when detrusor sphincter dyssynergia is present. Botulinum toxin injections to the sphincter may also be helpful in refractory cases [39]. Surgical options may include urinary sphincter implantation, augmentation cystoplasty, cutaneous conduits, and urinary diversions [42, 43].

Integumentary System

Neurotrauma and subsequent immobilization can result in the formation of decubitus (pressure) ulcers. Evidence suggests that compression and reperfusion injury, in addition to ischemia, are likely the cause of pressure ulceration [44]. Bowel and bladder incontinence, while not direct

causes of pressure ulcers, may contribute to skin masceration and breakdown. Patients with SCI are particularly vulnerable because of their compromised mobility and impaired protective sensation. Almost one-quarter of patients with SCI will develop ulcers during their treatment and rehabilitation [45]. Bony prominences, including the posterior head, elbow, shoulder blades, sacrum, and heels are at greatest risk in supine patients. The sacrum and ischial tuberosities are at risk in the seated patient. Surgical positioning devices may also introduce pressure and contribute to ulcer formation. Pressure ulcers are known to harbor significant bacterial colonies, a majority of which are antibiotic-resistant [46]. This places the patient at significant risk of developing bacteremia and a poorer prognosis.

Pressure ulcers are staged according to the National Pressure Ulcer Advisory Panel (NPUAP) [47]. It is recommended that the classification of a pressure ulcer remain unchanged, despite healing [48]. Stage I ulcers are defined as non-blancheable erythema. Stage II ulcers are a shallow and open, with partial thickness loss of the dermis and presents as a red-pink wound bed. Stage III ulcers are full-thickness skin loss, with or without visible subcutaneous fat, but without visible bone, muscle, or tendon. Stage IV ulcers are full-thickness tissue loss involving underlying muscle, bone, or tendon. The underlying bone or muscle is palpable. There are two additional classes based on unclassifiable or suspicious findings—Unstageable/Unclassified, which is when an ulcer cannot be probed for depth due to obstructing slough and/or eschar, and Suspected Deep Tissue Injury, Depth Unknown, when there are findings of a deep purple or maroon region with intact skin in an area of pressure and/or shear forces. The area can be painful and feel boggy and soft.

Treatment

Prevention of pressure ulceration can be achieved by implementing a frequent-turning protocol every 2 h for immobile patients. Daily skin inspections, hygiene, improving urinary and fecal continence, proper fitting and padding of supportive devices (e.g., multi-podus boot, cervical collars, casts) are also helpful in prevention and early identification. Pressure-distributing devices, such as those used in surgery (i.e., foam mattresses and sheepskins) have good evidence that they may be effective in preventing pressure ulcers. However, the benefit of other lower pressure devices and techniques, such as seat cushions, limb protectors and alternating pressure is unclear. While these pressure-relieving devices are encouraged, they cannot substitute for attentive nursing and physician care [49]. A specialized wound care team should be consulted at the earliest signs of skin breakdown to assist with treatment and monitoring.

Psychiatric

Psychiatric comorbidities are also common with neurotrauma. Significant physical injury and the events themselves can induce acute stress disorder or post-traumatic stress disorder (PTSD), depression, and anxiety. Both PTSD and acute stress disorder have symptoms of intrusive thoughts, nightmares, and flashbacks of the events, hypervigilance, and sleep disturbances; their diagnosis is different mostly by length of time of these symptoms [50]. Research has found that PTSD can occur in 20–51 % of patients suffering orthopedic trauma [51]; In addition, evidence suggests that psychological stress, depression, and anxiety also adversely impact on sleep, nutrition, exercise, and wound healing [52, 53]. Furthermore, maladaptive behaviors, personality changes, and psychosis may accompany neurotrauma [54].

Sleep disturbances are known to affect immune responses, impair resistance to infection and slow wound healing [55]. It also affects cognitive functioning, mood, and perceived pain, which may impact a patient's willingness to participate in their care [56]. Furthermore, while some evidence suggests that patients in an ICU may get enough hours of sleep, the amount of sleep in the deeper stages (III and IV) was significantly less versus controls and may negatively affect healing [53]. The environment of the hospital can

contribute significantly to the issue of sleep disturbances, in addition to pain and emotional distress [57]. Sleep deprivation, head injury, immobility, sensory deprivation, lack of circadian/daylight cycle, and the use of sedatives (particularly benzodiazepines) and analgesics are some of the risk factors that may influence the development of delirium (fluctuating course of significant mental status changes, confusion, and abnormal behavior) [58]. The unfamiliarity of the hospital environment and the lack of familiar individuals can compound this issue. Other precipitating causes include occult urinary tract infections, pneumonia, skin and abdominal infections, dehydration, hypoglycemia, and drug toxicity. Delirium significantly increases the incidence of complications, including longer ICU hospitalizations, accidental extubations, increased infection rates, and injury to patients and staff [59].

Treatment

Early recognition and intervention of psychological conditions in the acute trauma setting can help improve outcomes. Several validated questionnaires are available to help the clinician efficiently direct resources to support the patient and maximize their participation in their rehabilitation; examples include the PTSD checklist, Patient Health Questionnaire-9 (PHQ-9), Beck Depression Inventory (BDI), and the Generalized Anxiety Disorder-7 (GAD-7) [51]. Engagement with the mental health team should be done as early as is feasible. Interventions should also include patient and caregiver education to help normalize the stress responses and recognize early signs of abnormal behaviors. Specific mind–body and pain counseling may help with coping, and meditation methods may be helpful specifically with PTSD [60]. Other nonpharmacologic interventions include mindfulness, breath-control training, and acupuncture, but evidence supporting their efficacy is limited [61]. There are currently no pharmacologic agents available for prophylaxis of developing PTSD; specifically, research has not found evidence to support the use of prophylactic antidepressant medications for PTSD [62]. Aggressive pain management, however, can be helpful in improving overall outcomes and mitigating risk for poor psychological outcomes in the long-term [63].

Disturbances of sleep can be minimized by actively enforcing "quiet times," allowing the patients time for rest. Research has shown patients report feeling better having some relief from the constant hospital noise [55, 64]. Coordinated interdisciplinary care teams can also improve patient satisfaction with sleep, reduced stress, improved healing, and decreased episodes of delirium [65]. Appropriate sleep hygiene techniques can also be helpful, which include minimizing caffeine intake 4–6 h before sleep, eliminating nicotine products, minimizing exposure to screens on electronic devices, dimming bright lights during sleep, and maintaining a routine bedtime. If pharmacotherapy is required, the use of melatonin as a substitute has been suggested; while studies have been limited at this time, there is evidence that its use can help "reset" a disorganized circadian rhythm, improve total sleep time, improve immune responses, and may be neuroprotective [57]. This medication should be given 3–5 h prior to going to sleep. The use of sedatives such as benzodiazepines are discouraged for first-line treatment due to potential cognitive side effects; however, these are preferable over barbiturates and other agents because they tend to have fewer side effects, and have a lower risk of habituation than barbiturates. Opiates to induce sedation are not recommended, since there is no evidence sleep is improved; however, if pain is the cause of insomnia, opiates may be an appropriate option. (see below section "Pain and Pain Management") [66].

Causes of delirium or other acute mental status changes should be thoroughly investigated. Common sources include urinary tract infection (UTI), occult infection, drug interactions, inadequate pain control, dehydration, and impaired glycemic status. The use of opioids and sedatives may also lead to the development of delirium [67], therefore their use should be used with

caution [58]. Once medical pathology has been ruled out, conservative measures should be initiated, such as establishing a consistent sleep–wake cycle, utilizing daily patient orientation, and encouraging involvement of familiar individuals (family, friends, caregivers). A 24-h sitter may be required during the acute phase in order to prevent harm to the patient and inappropriate removal of intravenous or central lines, extubation, and falls from bed. The use of noise-reducing earplugs at night may also improve sleep quality [66, 68]. Pharmacologic prophylaxis for delirium, specifically with antipsychotics of both typical and atypical classes, demonstrates mixed results [66]. Antipsychotics and physical restraints for the agitated patient with delirium should be used as a last resort.

Pain

Inadequate pain management is common in caring for the critically ill patient [69]. Poor pain management has been linked to delayed wound healing, increased complications, increased hospital costs, longer hospital stays, sleep disturbances, and decreased quality of life [70, 71]. In addition, inadequate acute pain management can alter peripheral and central neuron sensitivity, resulting in the development of chronic pain syndromes [72]. Chronic pain has been linked to an increased risk of depression, altered sleep patterns, and anxiety. It has also been associated with increased burden on caregivers and dependence on medications.

For the neurotrauma patient in particular, the etiology of pain can be of different origins and there are two broad categories: nocioceptive and neuropathic. Nociceptive pain is a sensation derived from actual or potential tissue injury, and is based on stimulation of nociceptors by trauma or inflammation. Nociceptive pain is normally described as sharp, stabbing, dull, or aching and can be increased with direct palpation, position, or movement. This pain can be further categorized as musculoskeletal or visceral depending on the particular etiology. Neuropathic pain is often felt in or near an area of altered sensation, is often accompanied by paresthesias or numbness. The pain can be described as burning, shock-like, or shooting and is often triggered in the absence of stimulation or normally nondistressing stimulation, such as light touch otherwise known as allodynia. It is important for the clinician to clearly differentiate this type of descriptor from that of nociceptive pain. Neuropathic pain may not be associated with a specific neural lesion and does not usually follow specific dermatomes. This pain can vary in intensity and sensation such as burning, throbbing, diffuse aching, hypersensitivity to hot or cold, and can exhibit classic dysautonomia symptoms (localized diaphoresis, skin temperature changes, and discoloration). Unchecked, this can worsen to skin changes, edema, contractures, and bone demineralization [73]. Complex Regional Pain Syndrome (CRPS) is a condition due to a combination of psychological and physiological causes. CRPS includes symptoms such as muscle atrophy/weakness, sweating, headache, limb color changes, skin/nail changes, pain, and sensory changes. This condition may be seen in SCI patients, potentially as an association with wheelchair use and frequent transfers [74].

It is important to briefly acknowledge the impact that psychological factors can play in the individual patient perception of pain. In addition to mental health disorders like depression and anxiety, inherent patient characteristics, such as beliefs, attitude, vigilance, and expectations can also play a significant role [75].

Treatment

The management of pain should be targeted to the source of nocioception (peripheral or central) and involve both conservative and pharmacological interventions. A thorough evaluation and interview should be undertaken to characterize and localize the pain and identify other influencing factors such as preexisting illnesses (e.g., arthritis or diabetic neuropathy) or injuries missed during the initial trauma survey. A multimodal approach to pain management frequently includes consultation by a pain specialist,

especially in the acute care setting in an effort to avoid the development of chronic pain. In cases where mechanical/musculoskeletal pain exists, physical and occupational therapy may be helpful in applying physical modalities (e.g., ice, heat, electrical stimulation) as well as correcting range of motion or muscle imbalance problems. Pharmacological interventions often involve the use of patient controlled anesthesia (PCA) as well as opiates and non-opiates medications.

Morphine, the prototypical opiate medication, has its mechanism of action on the μ, κ, and δ opioid receptors, a class of modulatory G-protein coupled receptors found in the brain, spinal cord, and GI tract. It has analgesic, amnestic, and sedative properties, can be delivered orally or parenterally, has a relatively rapid onset of action, and can be used both as a bolus or low continuous dose therapy. Since this is the prototypical drug, daily opioid dosing and conversion from one opioid to another can be measured in morphine equivalents. Side effects associated with opiate use include: constipation, sedation, decreased respiratory drive, nausea, vomiting, and generalized histamine release causing peripheral vasodilation and hemodynamic compromise. In addition, opioid tolerance, withdrawal, and addiction should be considered. In order to best mitigate these secondary side effects, opioid use should be monitored closely and weaned as soon as possible. High doses of opioids may have a paradoxical effect and increase pain, a condition called "opioid-induced hyperalgesia;" the patient reports increased pain despite increasing doses of the opioid medication(s). Treatment includes a scheduled opioid taper or opiate rotation (conversion to another form of opioid).

Non-opiate medications include nonsteroidal anti-inflammatory drugs (NSAIDs). These medications modulate inflammation in the periphery by blocking the function of cyclooxygenase (COX-1 and COX-2), preventing the production of prostaglandins which propagate inflammation and pain. The prostaglandins produced by COX-1 also promote platelet aggregation and gastric mucus production; this may be more problematic in the neurotrauma patient, as nonselective COX inhibition can promote peptic ulcer formation, dyspepsia (see above section "Gastrointestinal"), and uncontrolled bleeding. While NSAIDs more specific for COX-2 such as celecoxib (Celebrex) have fewer GI side effects, these medications should also be used with caution because of their increased associated risk for thrombotic cardiovascular events. While most NSAIDs must be delivered either by mouth or by enteric feeding tube, Ketorolac is available in an injectable form. It has an analgesic effect similar to other opioids and can be a useful adjunct with opioids [76–78].

Neuropathic pain is often treated with antiepileptic and/or antidepressant medications. Gabapentin and pregabalin are both alpha-2-delta subunit modulators of calcium channels present in the central nervous system, and work by decreasing the release of excitatory neurotransmitters responsible for generating the neuropathic pain signals [79]. Both medications have extensive use in diabetic neuropathy, but have recently been shown to have a significant improvement in SCI patients [80]. Additionally, gabapentin and pregabalin can reduce the overall opioid requirement for adequate pain relief. Antidepressants have demonstrated some evidence of moderate effectiveness in the treatment of neuropathic pain. Their mechanisms of action are varied and mixed depending on their class; some of these actions include shared binding on opioid receptors, inhibiting serotonin, and central norepinephrine reuptake to potentiate inhibitory actions on nociception signaling [81]. Tricyclic antidepressants (TCAs), like amitriptyline, are thought to exert their pain-relieving effects through their increased serotonin release, which can help inhibit afferent pain signals [82]. However, due to their nonselective effects on other receptors, they can cause sedation, urinary retention, constipation, increased spasticity or contribute to delirium due to their anticholinergic effects [83]. Selective serotonin reuptake inhibitors (SSRIs) and serotonin–norepinephrine reuptake inhibitors (SNRIs), may also be helpful due to their more selective receptor activity; however, there is insufficient evidence of their efficacy in neurotrauma patients specifically to support their role as first-line agents [82, 84];

although, their additional benefit of treating depression and anxiety may be helpful in alleviating concurrent factors that may exacerbate or perpetuate pain syndromes.

Anesthetic agents may also be helpful in managing pain in the neurotrauma patient. Peripheral nerve blocks, either by single injection or continuous infusion, can provide excellent localized pain relief while avoiding the systemic side effects, and have been shown to last from hours to weeks [85]. Local injections may also be helpful in the management of CRPS, especially when there is a significant sympathetic nervous system component to the pain. Delivery of local anesthetic to the sympathetic chain near the affected limb, called a sympathetic blockade, can frequently help alleviate the pain and dysautonomia that accompanies CRPS.

An expanding role for alternative medicine has emerged when treating pain. Interventions such as music therapy, self-hypnosis, desensitization techniques, acupuncture, and biofeedback may be utilized in conjunction with other therapies without increased risk of side effects. These are generally well-received and can provide some relief of pain, or the perception of the pain. Heat or ice can also be used as adjunct therapies; these utilize the "gate theory of pain" put forward by Melzack and Wall [86]. This should be used with caution in those with spinal cord injuries or who have altered mental status, as they may not be able to communicate or sense tissue injury caused by excess use of these modalities. Other methods include transcranial magnetic stimulation, transcutaneous electrical stimulation (TENS) unit, and spinal cord stimulators.

Interdisciplinary Rehabilitation Team Members

Rehabilitation interventions can be beneficial, particularly if started early in the neurotrauma setting [87]. Recovery through early mobilization and other modalities, particularly in the Intensive Care Unit (ICU) setting, has also demonstrated significant decreases in a variety of complications, including pulmonary (pneumonia), vascular (DVTs), mental status (delirium), and musculoskeletal [6, 10, 77, 88].

The coordination of an interdisciplinary team is essential to implementing an effective rehabilitation program. The team often includes specialists in: physiatry, physical and occupational therapy, nursing, nutrition, speech/language pathology, orthotics/prosthetics, mental health, rehabilitation engineering, assistive technology, peer support, vocational rehabilitation, case management, and social work. Each team member offers unique skills to the care of even the most complex patients, although their input is most valuable when coordinated with other team members [9]. Early interdisciplinary rehabilitation involvement and education has been shown to provide significant benefit in the ultimate recovery of the patient [89]. While concerns remain about the feasibility and cost of implementing interdisciplinary care, it has been demonstrated to be safe, does not increase cost, and is associated with decreased ICU/hospital length of stays [77, 90].

Interdisciplinary rehabilitation team members include:

- *Physical Medicine and Rehabilitation Physicians (Physiatrists)* specialize in the care of patients with physical, behavioral, and emotional impairments following disease or trauma, particularly trauma to the neurological system. They are uniquely skilled at coordinating care between interdisciplinary team members and integrating the medical and surgical care with rehabilitative interventions. In the critical care setting, physiatrists also provide valuable consultative services to assist with mitigating the risks associated with immobility, developing bowel/bladder care programs, skin and wound management, comprehensive pain assessment and interventions, as well as assistance with formulating continuity of care plans, including discharge planning or transfer to a rehabilitation facility.
- *Rehabilitation Nurses* are integral in the daily care of complex neurotrauma patients. In addition to the traditional nursing functions, rehabilitation nurses are especially skilled at

monitoring and facilitating daily skin care, bowel and bladder management, complex pain assessments, sleep quality, as well as promoting mobility and ADL training. Rehabilitation nurses also serve a critical role in monitoring the patient's cognition, enhancing patient and family education, and facilitating communication between the interdisciplinary team and the patient.

- *Nutritionists* focus on the unique nutritional needs of each patient, which includes determining their daily calorie and protein requirements. Nutritionists also help formulate special diets for patients with concomitant conditions such as diabetes mellitus or renal disease. Adequate nutrition is essential for recovery after neurotrauma, including wound healing, attentiveness, and ability to participate in rehabilitation.
- *Physical Therapists (PTs)* assist in the assessment of mobility and motor function of the neurotrauma patient. Once the initial assessment is performed, therapists can progress the patient through a series of short-term and long-term goals with a multitude of treatments which focus on joint range of motion, bed mobility, sitting, standing, and/or walking with or without assistive devices. Therapeutic interventions within the ICU setting have been shown to reduce the complications of post-intensive care syndrome (PICS) [91].
- *Occupational Therapists (OTs)* evaluate the patient's ability to perform activities of daily living (ADLs) which include hygiene, grooming, dressing, feeding, and toileting. They also assess instrumental activities of daily living (IADLs), which include activities such as managing finances, preparing meals, and doing laundry. Most IADLs often require use of devices such as telephones, kitchen utensils, or appliances. Once deficits are noted, OTs develop an interventional therapeutic plan to help the patient regain functional independence.
- *Speech/Language Pathologists (SLPs)* specialize in disorders affecting speech, swallowing, and/or cognition–communication. SLPs assess the patient's ability to swallow and provide education and training on techniques for modification of eating habits to accommodate the underlying pathology safely. SLPs also facilitate the assessment of a patient's cognition, executive functioning skills, and/or communication ability and develop therapeutic interventions to improve any deficits noted.
- *Orthotists/Prosthetists* specialize in the fabrication and fitting of orthotics (braces) and prosthetics (artificial limbs). Orthotics can be either off-the-shelf or customized and are used to align, support, protect, or improve the function of a body part (e.g., halo cervical device, ankle foot orthotics, wrist splints). Prosthetics involve the custom fabrication of a socket that encloses the residual limb of an amputation and incorporates any missing joints and a functional terminal device (e.g., hand, foot). Numerous advanced prosthetic components are currently available to help accommodate the loss of one or multiple limbs.
- *Mental Health Providers* are uniquely qualified to aid with the psychological recovery of the patient and family. Neurotraumatic injuries have been associated with PTSD rates as high 33–39 % in both military and civilian populations [92]. A preventive psychological approach is beneficial for the patient, family, and caregivers. Therapeutic interventions should also extend to the children of trauma events, as they frequently also suffer from a myriad of consequences stemming from traumatic events [93].
- *Rehabilitation Engineers/Assistive Technologists' (ATs')* special certifications are currently available for providers, engineers, and equipment suppliers to ensure quality in the development, fitting, and use of devices such as wheelchairs, seating/standing systems, communication aides, robotic mobility systems, and adaptive vehicles. Professional societies such as the Rehabilitation Engineering and Assistive Technology Society of North America (RESNA) contribute to the safety and quality of this continually advancing field of health care.

- *Peer Mentors/Visitors* Evidence suggests that individuals recovering from major trauma benefit from the support and encouragement of those who have struggled with similar challenges. Peer mentors are generally not providers, but can be valuable members of the interdisciplinary team to help with education, reduce psychological stressors, and promote participation in health behavior. Peer visitation is especially helpful for individuals with SCI, amputation, vision or hearing loss. Organizations such as the Amputee Coalition (AC) offer specific programs on peer support training.
- *Vocational Rehabilitation (VR) Specialists* assess a patient's physical, cognitive, and emotional impairments and try to identify and support future career goals with vocation reintegration. Working in concert with the rehabilitation team, VR specialists incorporate assistive technology, along with local and regional support programs to help patients to pursue retraining, education, and job placement.
- *Case Managers and Social Work Professionals* are critical members of the interdisciplinary team, often serving as the interface between patients and family members with the treatment team. These specialists have special knowledge of access to local healthcare and support programs to assure the continuity of care of trauma patients from the intensive care setting to community reintegration. They also help coordinate complicated issues such as patient transfers, specialized equipment purchases, transportation, home health services, follow-up care, and home modifications.

Rehabilitation Principles for Special Categories of Patients

Traumatic Brain Injury

Epidemiology According to the Centers of Disease Control and Prevention, emergency department visits for traumatic brain injury (TBI), 715.7 per 100,000 persons, outnumber the amount of hospitalizations for TBI, estimated to be 91.7 per 100,000 persons. Men are slightly more affected than women, with a ratio of approximately 1.3:1. The age group most affected is 15–24 years, at a rate of 981.9 per 100,000 persons. The injury mechanisms associated with TBI-related ED visits vary by age group. Falls are the predominant cause of injury for those less than 4 or greater than 65 years of age. These account for 72.8 and 81.8 % of TBI-related ED visits, respectively. For persons in age groups 15–24 and 25–44 years, the proportions of TBI-related ED visits due to assaults, falls, and motor vehicle events are nearly equal within and across both age groups [94].

Classification Accurate classification of TBI is complicated, primarily because of the significant heterogeneity of injury patterns and patient characteristics. Commonly used scoring systems are described below and summarized in Tables 26.1 and 26.2.

- *Glasgow Coma Scale (GCS)* a score of 13–15 is consistent with a mild TBI, a score of 9–12 constitutes a moderate TBI, and a score of 3–8 is classified as a severe TBI.

Table 26.1 Traumatic brain injury classification and VHA/DoD clinical practice guideline for management

Injury severity	Glasgow coma scale	Post-traumatic amnesia	Structural imaging	Loss of consciousness (LOC)	Alteration of consciousness/mental state
Mild	13–15	<24 h	Normal	0–30 min	A moment up to 24 h
Moderate	9–12	1–7 days	Normal or abnormal	>30 min and <24 h	>24 h
Severe	3–8	>7 days	Normal or abnormal	>24 h	>24 h

Table 26.2 Ranchos los amigos scale

Cognitive level	Outcome	Patient response
I	No response	No response to sounds, sights, touch, or movement
II	Generalized response	Limited response, which is inconsistent and nonpurposeful; responses to sounds, sights, touch, or movement
III	Localized response	Inconsistent but purposeful response in a more specific manner to stimuli; may follow simple commands
IV	Confused and agitated	Confused and often frightened; overreactions to stimuli by hitting or screaming; highly focused on basic needs (e.g., eating, toileting); difficulty following directions
V	Confused and inappropriate	Appears alert and responds to commands; easily distracted by the environment; frustrated and verbally inappropriate; focused on basic needs
VI	Confused and appropriate	Follows simple directions consistently; may have some memory but lacks details, attention span of about 30 min
VII	Automatic and appropriate	Follows a set schedule; does routine self-care without help; attention difficulty in distracting or stressful situations; problems in planning and following through
VIII	Purposeful and appropriate	Realizes difficulties with thinking and memory; less rigid and more flexible thinking; able to learn new things; demonstrates poor judgment; may need guidance for decisions

- *Post-Traumatic Amnesia (PTA)* is defined as the time from the injury to the recollection of daily events assessed by tools such as the Galveston Orientation Amnesia Test (GOAT). The length of PTA can assist in the classification of TBI. If time of PTA is less than 24 h TBI, then severity is mild. If time of PTA is 1–7 days, then TBI severity is classified as moderate. If PTA is greater than 7 days, then TBI severity is severe.
- *Loss of Consciousness (LOC)* This measurement may also be used to determine the severity of TBI. If less than 30 min, TBI is considered mild. If the time of LOC is greater than 30 min, but less than 24 h, the severity is equivalent to moderate TBI. If the time is greater than 24 h, the TBI severity is severe.
- *The Rancho Los Amigos Cognitive Recovery Scale* can be used to describe patients in various stages of awareness, behavior, and cognition throughout the course of recovery post-TBI.
- *Other commonly used outcome tools include* the Glasgow Outcome Score (GOS); Functional Independence Measure (FIM); Community Integration Questionnaire (CIQ); Craig Handicap Assessment and Reporting Technique (CHART); and the Disability Rating Scale (DRS). These tools can be viewed in the National Institute of Neurological Disorders and Stroke (NINDS) Traumatic Brain Injury Common Data Element Standards and have been used in practice.

Common Sequelae and Treatment

Traumatic brain injury is associated with a variety of physiologic, physical, cognitive, behavioral, and emotional manifestations post injury [95]. With the exception of amantadine hydrochloride, which has been shown to accelerate recovery for patients with severe TBI [96], all other pharmacological clinical trials have not demonstrated a beneficial effect in the recovery course of TBI, therefore rehabilitative interventions remain the most appropriate management once the patient is medically and surgically stable. Rehabilitative strategies attempt to target symptomatology associated with TBI, particularly those symptoms which most impair function. A discussion of some of the more common symptoms expressed after TBI is presented in the following section:

- *Headache:* Post-traumatic headaches are the most common physical complaint following mild TBI (mTBI). While most patients report symptom resolution within the first month of injury, some patients develop post-traumatic headaches as late as 3–6 months following injury and their symptoms may persist for years [97]. According to the International Headache Society classification system, headaches can be divided into acute post-traumatic and chronic post-traumatic. Pharmacological management may include nonsteroidal anti-inflammatory medications (NSAIDs), beta adrenergic antagonists, calcium channel blockers, and antiepileptics. Botulinum toxin injections and nerve blocks have also shown efficacy.
- *Agitation/Aggression* Behavioral changes after TBI are common and are often both challenging and troubling to families and caregivers. A multifaceted intervention strategy is required, utilizing family counseling, pharmacological interventions, and psychotherapy. Determining the etiology is important, since concurrent neuropsychiatric conditions, depression, or delirium due to medical illness may be present. In addition to correcting any underlying medical conditions, overstimulation of the patient should be avoided, with dim lighting, reduced noise, and establishing a regimented daily schedule. Pharmacological management often includes atypical antipsychotics, tricyclic antidepressants, trazodone, amantadine, and beta blockers [98]. The uses of benzodiazepines are not recommended for acute aggression since these medications may cause confusion, amnesia, poor balance, and even worsening agitation.
- *Post-traumatic Seizure/Post-traumatic Epilepsy (PTE)* Post-traumatic seizures are classified as either: immediate (within the first 24 h); early (from 1 to 7 days); or late (after the first week). The incidence of early seizures after TBI is reported to be between 2.6 and 16.3 %. The majority of post-traumatic seizures (86 %) occur within the first 2 years of trauma [99]. Risk factors for early seizure development include intracerebral hematoma, subdural hematoma in children, younger age, severity of injury, and alcoholism. Risk factors for late seizures include intracranial bleed, severity of injury, and age greater than 65. Mild head injury without skull fracture with either loss of consciousness or post-traumatic amnesia lasting less than 30 minutes has not been found to be associated with PTE [95]. Current guidelines do not recommend seizure prophylaxis beyond 7 days. Frequently used antiepileptic medications include phenytoin (Dilantin) and levetiracetam (Keppra).
- Conditions such as contractures, pressure ulcers, spasticity, deconditioning, sleep disturbances, heterotopic ossification, and pain syndromes are also commonly associated with TBI and are discussed in other sections of this chapter.

Spinal Cord Injury (SCI)

Epidemiology According to the National Spinal Cord Injury Statistical Center (NSCISC), the annual incidence of SCI in the United States is approximately 12,500 new cases each year. The prevalence is estimated to be in the range from 240,000 to 337,000 persons, with the average age at time of injury has increased from 29 years in the 1970s to 42 years currently. Approximately 79 % of all SCI occur among males. The leading causes of traumatic SCI are from motor vehicle accidents, followed by falls, acts of violence, and sports/recreational activities. The estimated lifetime costs associated with SCI vary depending on age, neurological impairment, and preinjury employment, but have been reported to range between $1.1 and 4.7 million [100].

Classification The American Spinal Injury Association (ASIA) has set forth standards of evaluation for the classification of SCI. According to the NSCISC the most frequent neurologic category is incomplete paraplegia, followed by incomplete tetraplegia, complete paraplegia, and complete

tetraplegia. Classification of acute spinal cord injury is standardized by use of the International Standards for Neurologic Classification of Spinal Cord Injury (ISNCSCI) guidelines. A worksheet may be obtained from the ASIA web site [101]. The worksheet details the exam which incorporates the evaluation of key sensory and motor levels on both sides. With this information, a neurologic level of injury may be obtained and determined to be complete or incomplete. AIS classification can be used to communicate with other physicians or healthcare professionals in other facilities.

Acute Management of Spinal Cord Injury Point of injury care should include spinal stabilization. Early surgical intervention in spinal cord injury is defined as intervention occurring from 8 to 72 h [102]. Although the optimal timing remains unknown, there are purported benefits associated with early surgical intervention in the presence of spinal instability. Current research favors weighing the benefits of early intervention against the greater risks of performing excessive spinal surgeries on patients with multiple injuries [103]. The delay is considered beneficial to provide spinal cord recovery time and optimization of general health. Evidence suggests that a 19 % decrease in odds of mortality was shown with each 24 h increase in time until surgery [104]. While still controversial, high-dose steroid use is not currently recommended [105, 106]. Future research strategies aim to more specifically target post-traumatic inflammation as well as identify biomarkers to better monitor prognosis. Implicated possible biomarkers include: TNFα, IL-1β, IL-6, IL-8, and IL-10 [107].

Functional Outcomes after Spinal Cord Injury Evidence suggests that the level of injury for patients with SCI has the greatest implication for prognosis. Patients with injuries above C4 will most likely require lifetime ventilation, while an injury at the C5 level may allow a patient to drive independently with a specially adapted vehicle. Independence in transfers, feeding, grooming, and bowel/bladder care are frequently achieved by individuals with complete injuries at below the C7 level. The minimal neurologic level for independent, functional ambulation with bracing is L2 (hip flexion) on one side and L3 (knee extension) on the other.

Common Sequelae and Treatment

- *Autonomic Dysreflexia/Autonomic Hyperreflexia* is a unique phenomenon that occurs in approximately 50–70 % of patients with complete spinal cord lesions generally at or above T6 [108]. Symptoms may include facial flushing, diaphoresis, bradycardia, headache, and blurred vision. The most prominent sign is elevated blood pressure 20–40 mmHg over the patient's baseline, but may lead to seizure or even death. Because baseline blood pressures may be decreased following SCI, regular monitoring is recommended. Autonomic dysreflexia occurs as the result of a sympathetic nervous system discharge below the level of injury that persists unopposed by central inhibition from above the level of injury. Immediate recognition and treatment is necessary and typically involves identifying noxious stimuli below the level of injury that initiates the sympathetic reflex. Common noxious stimuli include bladder distension, infection, constipation, pressure ulcers, VTE, ingrown toenails, or renal calculi [102, 109]. Treatment guidelines have been published by the Paralyzed Veterans of America and are publicly accessible [110]. The blood pressure should be monitored and treated with a rapid-acting short-duration antihypertensive, if the systolic pressure is at or above 150 mmHg [111]. Pharmacologic interventions include the calcium channel blocker nifedipine or topical nitrates [102, 104]. Other preventative measures include frequent turning to prevent pressure ulcers and regularly checking for possible sources of noxious stimuli, such as ingrown toenails. In the subacute phase, the use of specific α-adrenergic antagonists such as terazosin may prevent serious consequences [112]. For unresponsive patients or those nonresponsive to therapy, anesthesia (regional or general) may be used to successfully ameliorate

the sympathetic response driving the phenomenon [113].

- *Bladder Dysfunction:* Urinary retention and/or incontinence are frequently encountered after SCI. Detrusor sphincter dysynergy (DSD) remains a frequent problem, leading to elevated bladder pressures and possible hydronephrosis. Further imaging, cystoscopy, and urodynamics may help guide appropriate treatment. (Please refer to above section "Urinary System Treatment")
- *Bowel Dysfunction:* Spinal shock, which is characterized by muscular flaccidity and loss of motor reflexes in all parts of the body below the level of injury, can induce an acute decrease in gastric motility, increasing transit times, prolonging gastric emptying and increasing water absorption resulting in constipation and/or fecal incontinence. If not addressed, this can lead to medical complications and poor functional outcomes. Bowel movements should be closely monitored and pharmacological management may help to prevent constipation. A bowel program can be initiated with a goal for a bowel movement daily to every other day. Digital stimulation or digital disimpaction may be sufficient to produce a bowel movement; pharmacologic treatments used may include bulk-forming agents, stool softeners, oral stimulants, and suppositories. Surgical options may include colostomy.
- *Pain Syndromes:* Multiple sources of nociception are common for patients with SCI, whether centrally or peripherally mediated. Direct injury to the cord or nerve roots may lead to significant neuropathic pain syndromes in a dermatomal or nonspecific distribution. In addition, pain may generate from concomitant fractures, soft tissue, or other organ damage. Two important variants to consider are syringomyelia and cauda equina syndrome. Syringomyelia should be considered whenever there is a delayed onset of segmental pain accompanied by a rising level of sensory loss [74]. Cauda Equina syndrome is associated with lower extremity dermatome pain, bowel and bladder incontinence, and classically saddle anesthesia. Central dysesthesia syndrome may also occur, which typically manifests as diffuse, nondermatomal pain accompanied by hyperalgesia or allodynia.
- Other complications of SCI include spasticity, orthostatic hypotension, skin breakdown, heterotopic ossification, and pain which have been addressed previously in this chapter.

Peripheral Nerve Injuries

Etiology Peripheral nerve injuries may result from direct trauma or as a complication of medical care (e.g., poor fitting orthosis/casts or poor bed positioning) or a complication of surgery (e.g., compression by hardware placement or excessive tourniquet pressure during surgery). Common locations of peripheral nerve injury include: the brachial plexus, ulnar nerve at the elbow (cubital tunnel), and peroneal nerve at the fibular head. In the acute trauma setting, the diagnosis of a peripheral nerve injury may be confounded because of the presence of other more life-threatening injuries. Trauma patients, particularly those with prolonged ICU stays, systemic inflammatory response syndrome (SIRS), and shock [114], may develop a critical illness polyneuropathy (CIP) or critical illness myopathy (CIM), manifesting as generalized weakness, muscle atrophy, and/or impaired sensation. These conditions have been attributed to alterations that occur in the nervous system and/or muscular architecture with loss of protein channels and neural degeneration. There is an apparent increased risk of developing CIM associated with intravenous glucocorticoids used to treat patients with acute respiratory distress syndrome or chronic obstructive pulmonary disease [115]. Other risk factors for the development of long-term critical illness neuropathy include duration of ICU treatment, duration of ventilator support, and a high APACHE score [116]. Recovery from CIM/CIP is generally good although the rehabilitation course typically protracted. Electrodiagnostic testing is often very helpful in the evaluation of peripheral nerve and muscle function. Ultrasound may also

be a useful diagnostic tool for the evaluation of peripheral nerves and is also beneficial when used to guide interventional procedures to avoid potential nerve injury.

Treatment

Prevention of peripheral nerve injuries includes proper bed positioning to avoid common compression neuropathies located at the elbow and fibular head. The use of padding at compression points, splints, and/or activity modification may help to prevent further nerve damage to injured peripheral nerves. Nursing staff and therapists can provide assistance and patient/family education for proper bed mobility techniques and/or use of assistive devices for activities of daily living. Regular exercise and rehabilitation therapy sessions are also beneficial in treating critical illness myopathy (CIM). Just as the causes of CIM are varied, the treatment is also multidisciplinary; nutritional intake, stricter glycemic control and removal or minimizing steroid and muscle relaxant medications all may be helpful [117]. For severe neurologic injury, surgical treatment using grafts may be necessary; a more detailed discussion is beyond the scope of this chapter. Rehabilitation after such surgery is prolonged. Neuro-recovery is dependent on the location of injury and distance to the most distal muscle. In general, reinnervation occurs at the rate of one millimeter per day/one inch per month.

Conclusion

Rehabilitation of the neurotrauma patient is complex, requiring the coordinated care of a specialized interdisciplinary team. Interventions are focused on recognizing the negative effects of immobility, mitigating the risk of secondary complications, identifying functional impairments, and implementing education and treatment strategies to promote recovery, independence, and eventual community reintegration. Frequent barriers to successful rehabilitation include impaired cognition, complex pain syndromes, poor home accessibility (particularly for those with mobility challenges), as well as psychological problems. Therefore, treatment strategies should employ patients, families as well as a multitude of specialists, including assistive technology to overcome barriers and foster appropriate goal-directed care to ultimately restore quality of life and dignity after trauma.

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Craniofacial Reconstruction in the Polytrauma Patient

27

Raymond Harshbarger and Anand Kumar

Introduction

From a medical perspective, the hallmark of the most recent conflicts in Iraq and Afghanistan is improved survivability from severe injury. These current conflicts have produced that greatest numbers of casualties since Vietnam. In Vietnam the casualty to kill ratio was 3:1. Due to advances in body armor, critical care in the battlefield, the current ratio is closer to 8:1. Despite improvements in protection and far forward medical/surgical care, the intensity of combat, with associated weaponry has progressed. Blast trauma predominates in the current conflicts related to use of improvised explosive devices (IEDs), rocket propelled grenades (RPGs), and mortar rounds, and high velocity rifles (AK-47s). Injury patterns have changed with improved protective gear combined with the frequency of blast trauma, leading to a predominance of craniofacial and extremity injuries, with up to one third of all injured patients suffering from head/neck trauma [1]. In order to fully understand the severity of craniofacial injuries received on today's battlefield, one must first grasp the nature of the injury mechanisms encountered on the modern battlefield.

Blast-related injury is more severe than traditional ballistic trauma, and has several characteristic features. When, for example, an IED explodes a shock wave from this blast emits high pressure, and leads to high velocity fragment propulsion, resulting in "traditional" types of ballistic injuries. Craniofacial fractures and soft tissue injury are generated during this phase of the blast. Additionally, the blast wave can propel individuals into the ground or other structures creating a traumatic force resulting in fractures, contusions, and soft tissue injuries.

With respect to craniofacial injury, the current conflicts in Iraq and Afghanistan have generated wounds that are greater in size and increased in number, due to the propensity of blast mechanisms of injury [2]. The fractures have been more complex, with devitalization of bone, and irregular fracture patterns. In many cases there has been composite bone and soft tissue loss from both the face and cranium. The signature characteristic of craniofacial blast injury is brain injury with secondary edema. The acute care far forward in the battlefield addresses this immediate life-threatening complication of blast injury.

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Acute care

Injured personnel who suffer massive blast injury to the craniofacial skeleton often require decompressive craniectomy prior to transport to the continental United States (CONUS) and higher levels of medical care. Decompressive craniectomy has resulted in increased survivability after severe brain injury. In contrast, personnel with massive craniofacial injures injured in previous conflicts may have been treated expectantly. Following decompressive craniectomy and stabilization, these patients were routed through Germany and ultimately to the United States for definitive care. After arrival in the continental United States at a Military Treatment Facility (MTF), (Walter Reed Army Medical Center (WRAMC), National Naval Medical Center (NNMC), and others) more complex and definitive treatments would be rendered. The sequence of care and evacuation scheme for craniofacial trauma patients occurred as follows: Battalion Aid Station, Forward Surgical Team (stabilization, possible decompressive craniectomy), Combat Support Hospital (decompressive craniectomy), Critical Care Transport (CCAT) to, and stabilization in Germany, Level I CONUS MTF- definitive care at WRAMC, or NNMC. Average time from initial injury to definitive care in the US was 7.9 days [3]. Transfers could be made more quickly in unique circumstances.

Care Coordination

Following the initial experience from Operation Enduring Freedom 2003 and Operation Iraqi Freedom 2004, a steep learning curve and development of treatment protocols for severely injured craniofacial trauma patients was developed. Two levels of coordination were achieved.

The first tier of coordination was between neurosurgery and craniofacial surgery. Communications led to optimizing the position of scalp incisions for trauma care. Whenever possible a coronal incision was chosen (replacing the traditional question mark access) not only to provide improved exposure for acute neurosurgical decompression, but also to facilitate acute and secondary reconstructive surgery. The treatment of the cranial bone segments removed during decompressive craniectomy underwent evolution throughout the high volume casualty period. During the earlier period of the Iraq/Afghanistan wars, it was customary to implant the craniotomy bone segment in the abdominal wall until it could be replaced at a later time, as is performed in many civilian centers. Over time this practice was abandoned due to frequent persistent fevers, positive blood cultures, and sepsis, with a potential source being the implanted bone segment. Further coordination between neurosurgery and craniofacial surgery involved the timing of initial debridements and temporary wound closures during the acute phase of treatment. In patients with blast injury and severe brain trauma, stability of cerebral perfusion pressure, and neurologic function were limiting factors on trips to the operating room for debridements/washouts.

Many of the wounded soldiers with severe craniofacial trauma also suffered from extremity and other injuries related to the blast trauma mechanisms described above [4]. It was not uncommon to see anywhere from one to all four extremities affected in various states of injury, amputation, or treatment of wounds. The wounded extremities required frequent washouts prior to definitive treatment. So in addition to coordination of craniofacial care, additional coordination with other services was required, i.e., orthopedics, general surgery, ophthalmology, ENT, etc. Due to the frequency of operative debridements/washouts, several operating rooms per day were designated as multi-trauma rooms.

Infection

One of the more powerful forces affecting the outcomes of casualty management from the Iraq/Afghanistan wars was infection. During the early treatment experience of injured service members, traditional plastic surgery reconstructive methods were utilized. Patients underwent routine skin grafting and rotational or free flap

reconstruction of craniofacial soft tissue loss, and bone graft or implant reconstruction of craniofacial hard tissue. A recurring theme was partial or complete loss of skin grafts and flaps, or infection of implants. It was determined that many of these wounds had unusually high counts of Acinetobacter Baumanii, a gram-negative bacterium. This organism is present in the United States, but rarely as a pathogen. However, the sand in Iraq was found to contain this organism (different strain), which behaved as a true pathogen. Once this was discovered, pre-reconstructive treatment with Dakin's solution to the wounds was effective preventing reconstructive failures, however; proper treatment of A. Baumanii was responsible for delayed definitive reconstruction.

Another challenging aspect of treatment of Acinetobacter Baumanii was the frequency of multidrug resistance. Early in the Iraq/Afghanistan wars once A. Baumanii was discovered as a pathogen, broad spectrum antibiotics were administered in theater (combat environment), leading to the development of multi-drug-resistant strains. Cessation of this practice and wound treatment with Dakin's solution ameliorated this problem.

Challenges of Military Craniofacial Trauma

Treatment of the complex array of injuries to the craniofacial region from the Iraq/Afghanistan wars required assessment of traditional methodologies and incorporation of new developing protocols. This was prompted by the presentation of patients with defects of up to one-half of the cranium with or without concurrent facial injury. Frequently, the overlying soft tissue defects would then create a complex, composite wound requiring both soft tissue and bone reconstruction. In addition, prolonged tissue edema of both of the brain and surrounding soft tissues was routine. Zones of injury were large, and patients frequently had concomitant injuries which influenced prioritization and coordination of care (Figs. 27.1 and 27.2).

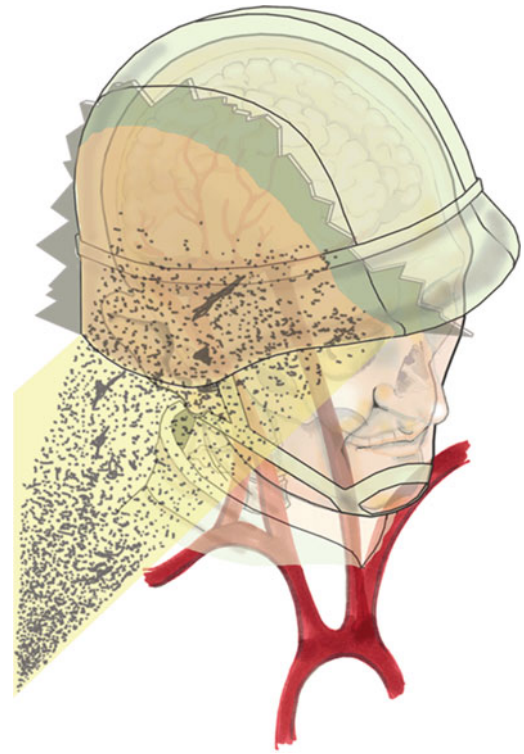


Fig. 27.1 Illustration of blast mechanism from modern battlefield, e.g., IED (improvised explosive device). Vulnerable areas include cranium, face, neck, including vascular supply

Acute Fracture Care

Classic tenets of facial fracture management were challenged by the severe craniofacial blast trauma patient. In traditional management of acute facial fractures, there are two well established windows for open reduction internal fixation (ORIF). Upon initial presentation, without undo swelling or other injuries/issues which are contraindicating, the patient may be taken to the operating room before swelling sets in (within 48 h). A second timeframe, which is the most commonly used is to wait approximately one week after injury (swelling has largely dissipated). It became evident fairly quickly after the start of the Iraq/Afghanistan conflicts that the traditional time frames used for facial fracture ORIF could not be utilized due to tremendous edema within the craniofacial skeleton and the presence of multiple concomitant injuries. In

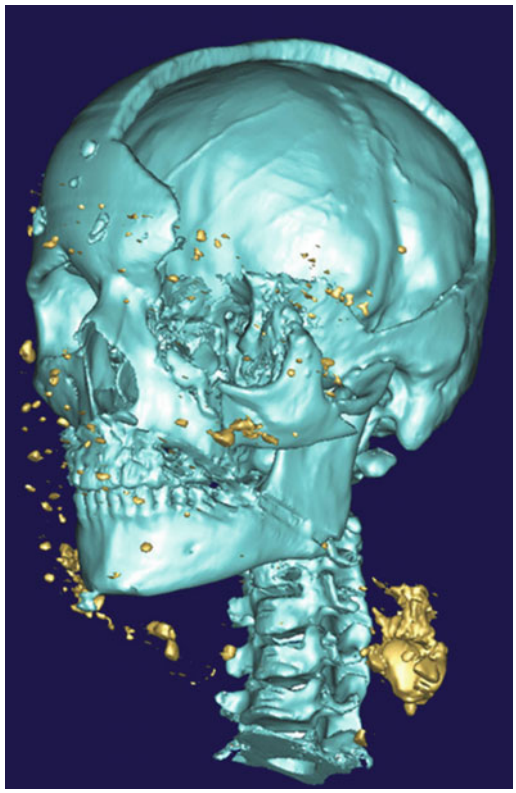


Fig. 27.2 3D CT scan demonstrating blast trauma to L zygoma, orbit, with subsequent decompressive craniectomy. Gold particles represent schrapnel load illustrating entire head and neck as zone of injury

reviewing our acute fracture cohort who had blast trauma, the average time to ORIF was approximately 21 days after injury. This finding was also corroborated in the extremity experience from blast casualties [5]. By this time point some of the swelling had diminished, but there was still persistent inflammation within the tissues that made accurate ORIF more challenging.

In addition to timing, the nature of fracture patterns, and accompanying soft tissue loss complicated the management of acute facial fractures. Given the high prevalence of blast injury and use of high caliber weaponry, many service members suffered complex fractures well beyond the traditional patterns seen in low caliber penetrating or blunt trauma. Bone was frequently devascularized, and rendered unusable in standard reduction/fixation techniques. Often, primary bone grafting was necessary to achieve a stable craniofacial skeleton. Attempts to use alloplastic materials in the maxillofacial skeleton were fraught with failure, most likely due to contact with sinus cavities and nasal flora. Moreover, these areas of complex fracture were compound in nature. With a composite tissue loss, free flap reconstruction brought vascularized tissue to protect and assist in healing of bone grafted regions.

Primary bone grafting and free flap reconstruction provided the foundation for treatment of acute maxillofacial fractures up to and including the orbital bandeau. Above the level of the bandeau, primary cranial reconstruction involved ORIF of fractures, soft tissue coverage with local or free flaps, and cranialization of the frontal sinus. Without stable soft tissue coverage and definitive separation of the nasal and brain cavities, successful secondary reconstruction of the cranium was plagued with failure.

Secondary Reconstruction

Any reconstruction occurring outside of the acute/subacute window (>2 months) was defined as secondary reconstruction. Secondary facial reconstruction consisted of facial osteotomy and repositioning, bone grafting techniques, and free tissue transfer. Cranial reconstruction was typically performed in the secondary time frame; as swelling, limited soft tissue coverage, and frontal sinus injury prohibited definitive primary reconstruction.

Requirements for definitive cranial reconstruction included: cranialization of the frontal sinus (if primarily injured), good soft tissue coverage, and a 3-month infection-free healing period off antibiotics. (Table 27.1) For most patients this would fall around 6 months after initial trauma. Cranialization of the frontal sinus involved removal of the nasofrontal ducts, primary bone grafting (corticocancellous), with a pericranial flap. Many patients were so severely injured that this traditional method of cranialization was not feasible. With large defects free tissue transfer into the anterior cranial fossa was utilized to achieve craniofacial separation, with

Table 27.1 Military protocol for craniofacial reconstruction

Neurological care/ICU
↓
Facial fracture treatment
↓
Infection control-Acinetobacter Baumannii (AB)
↓
3-month infection-free healing (off antibiotics) due to pathogenicity of AB
↓
Craniofacial reconstruction

or without primary bone grafting. With regard to soft tissue coverage, many service members could be healed with wound care, others required local (rare) or free flap coverage to achieve a stable soft tissue envelope. In some cases tissue expansion of the scalp provided sufficient coverage for patients undergoing cranial reconstruction, which would overcome tight scarring and contracture. As mentioned earlier, contamination of penetrating wounds was a significant problem, especially with A. Baumanii. A protocol of 3 months of infection healing off antibiotics was developed to ward off long-term colonization/infection of alloplastic reconstructive materials.

Syndrome of the Trephined

Adaptation of reconstructive paradigms/protocols to account for the unique challenges of military craniofacial trauma was accomplished, which placed cranial reconstruction approximately 12 weeks post injury. However, certain patients were noted to suffer from neurological decline which corresponded to the intense wound contracture phase after decompressive craniectomy [6]. Neuroimaging associated with decreased functioning showed pronounced soft tissue concavity within the cranial defect and midline brain shift, a feature associated with the syndrome of the trephined (Fig. 27.3). These patients underwent cranial reconstruction immediately upon presentation with this syndrome. Notable improvements in neurological

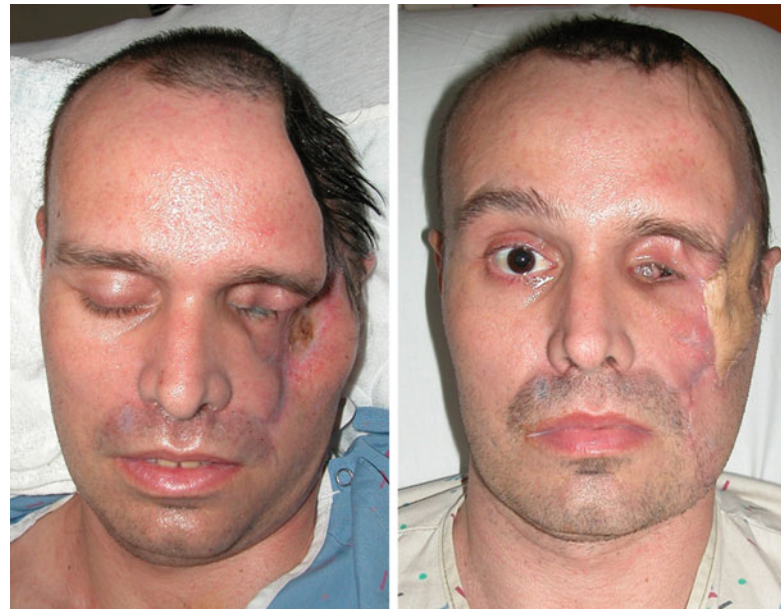


Fig. 27.3 Pt with syndrome of the trephined and large concavity at the cranial defect. Before (*left*) and after (*right*) restoration of cranial vault with custom alloplastic implant and free flap. *Note* improved level of consciousness after restoration of cranial vault

functioning followed the reestablishment of proper cranial space, in this unique subset of traumatic cranial defect patients.

Treatment Methodology

All patients with craniofacial trauma awaiting secondary reconstruction were presented at a multidisciplinary treatment planning conference. Prior to the conference, the patient's CT data were processed to generate a stereolithic skull model. In the early 2000s, software to analyze the patient's CT through use of Digital Imaging and Communications in Medicine (DICOM) data sets was being developed, as were 3D printers to stereolithically print a craniofacial model. Due to the high volume of this type of casualty from the Iraq/Afghanistan conflicts, the military (Walter Reed Army Medical Center) developed a robust 3D Medical Applications Lab to process CT scans and generate Stereolithic models.

Through the aid of advanced processing software and the production of stereolithic models, the process of secondary craniofacial reconstruction was advanced. Using individual patient CT mirror image technology (unilateral defects), or cohort CT data (bilateral defects), a 3D custom patient-specific implant could be generated. Additionally, using the stereolithic printer, a model of the defect could be generated (which could aid in bone graft fabrication). Stereolithic models could also be used to prebend reconstruction plates, and simulate surgery in the preoperative setting, enhancing accuracy and efficiency in the operating room. Finally, stereolithic models could be used to foster "informed consent" of the patients, as they could truly visualize the problem and proposed solution.

Based on multidisciplinary treatment planning, patients requiring large volume cranial reconstruction related to posttraumatic and/or decompressive craniectomy defects underwent either autologous (cranial bone graft), or custom alloplastic reconstruction. Split cranial bone or rib graft reconstruction was performed in patients with smaller defects, failed alloplastic reconstruction, and potential concerns with contamination. Concerns were raised about harvesting essentially a hemicranium to produce enough split bone graft for large-scale reconstruction, especially in the context of significant prior brain trauma and systemic injury. Most reconstructions were performed with in house produced, custom 3D patient prefabricated implants of either polymethylmethacrylate (PMMA) or woven titanium. Patients fell into one of three groups for reconstruction, implant alone, implant with tissue expansion, and implant with free tissue transfer. Most patients with cranial defects and poor soft tissue underwent free tissue transfer in the acute setting; however, some required simultaneous implant/free flap related to dense scarring in the area to be reconstructed.

Reconstructive Materials

While no ideal cranial implant material for large-scale reconstructions currently exists, there are several desirable characteristics. A custom shape is necessary which mirrors the missing segment of cranium. The material needs to be bone-like in its quality. It should have long-term sustainability, i.e., present for long-term brain protection and contour. Even with advanced imaging technology and software which produces a 3D patient-specific prefabricated design, there can be small discrepancies at the time of implantation, such as bone differences or scarring which prevent a native implant from fitting perfectly. In this scenario, implant contouring is required to allow proper fit. Biocompatibility and biointegration is desirable, to reduce long-term risk of infection and/or exposure.

Stable long-term reconstruction of large-scale cranial defects has been a problem vexing surgeons for some time. A variety of reconstructive materials have been used over the years, all with benefits and drawbacks (Table 27.2). While autologous bone grafting is preferred, and has been the gold standard for reconstruction over

Table 27.2 Craniofacial reconstructive materials

Reconstructive materials		
	Benefit	Weakness
Bone graft	Autologous Modify	Resorb Limited donor Hard to shape
Medpor	3D shape "integrateable"	Infection Exposure
PMMA	Custom 3D Modify	Infection Exposure
Hydroxyapatite	Bone growth	Size and shape
Titanium	Durable Custom 3D	Hard to shape Infection Exposure

the years, large segments of non-vascularized bone graft can be subject to resorbtion, donor sites may be limited, and shaping is inherently limited. As mentioned above, hemicranial harvest for split cranial bone graft must be approached with caution in a patient with severe brain trauma and frequently multisystem injury. Autologous vascularized bone reconstruction in composite cranial reconstruction has also been described [7], but only in the civilian population.

Given the frequency of large scale cranial defects, abandonment of abdominal wall banking of cranial segments, and desire to achieve proper 3D reconstructive shaping, a system was developed to design and produce custom 3D prefabricated implants. PMMA was chosen as the primary material being ubiquitous, hard like bone, and displayed good operative contourability with burr or onlay methymethacrylate (Fig. 27.4). With PMMA, true tissue integration is not achieved. No bony ingrowth occurs, and a scar capsule forms over the implant, with acute and long-term issues with infection and/or exposure. To enhance tissue tolerance in alloplastic reconstruction, woven titanium implants were instituted- produced in house with specialized 3D printing using a patient-specific design. The interstices of this implant (Fig. 27.5) were conducive to tissue ingrowth; however, the

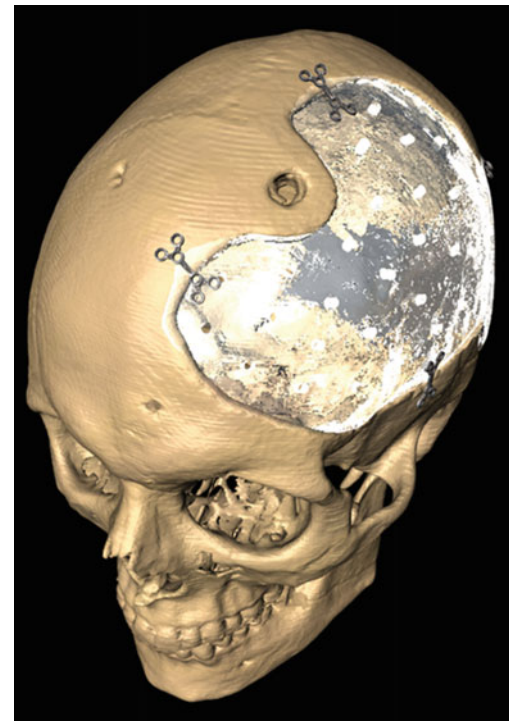


Fig. 27.4 Custom 3D, patient-specific PMMA implant

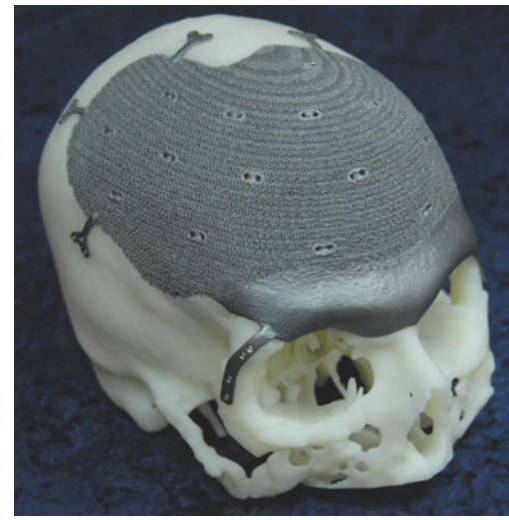


Fig. 27.5 Custom 3D patient-specific woven titanium implant

implant was somewhat brittle, and had virtually no operative contourability. In addition, removal of the implant was arduous, as tissue ingrowth could be somewhat excessive.

Large-Scale Cranial Defect Reconstruction

While there were cases which required temporary removal of implants, custom 3D prefabricated cranial implant-based reconstruction was largely successful (Fig. 27.6). Ninety-nine alloplastic cranioplasties performed on soldiers injured in the Iraq/Afghanistan conflicts were reviewed [8]. The average age was 25. Most (88 % underwent hemispheric craniectomy), will some (12 %) necessitated bifrontal craniectomy related to location of trauma. The average GCS of patients receiving decompressive craniectomy was 9. Approximately 82 % of the patients reviewed suffered penetrating blast trauma, with 50 % improvised explosive device (IED), 24 % gunshot wounds, 7 % mortar blasts, 22 % other. At 6 weeks post implant reconstruction, 92 % of intracranial dead space was resolved, with 7 % developing hematomas or hygromas. At long-term follow up, 95 % of the patients had implant retention. Five percent were removed due to infection. Bacteriologic isolates included Staphylococcus Aureus, A. Baumannii, and Strep Pneumoniae. Analysis of failed implants revealed increase risk for failure when implants were near facial sinuses, and/or extending down into the orbital region. Overall reoperation rate was 18–10 % for hematomas, 3 % hygromas, 5 % removal. Secondary operations were performed for aesthetic reasons, i.e., temporalis resuspension or fat grafting to the temporal hollow. Secondary procedures need to be performed in a judicious manner, as implant exposure can lead to colonization and necessitate removal.

Overall, custom 3D prefabricated alloplastic reconstruction of cranial defects suffered from military trauma can be successful provided specific criteria are met. Soft tissue coverage must be acceptable. The facial sinuses must be separated from the intracranial space with appropriate bone grafting and vascularized soft tissue flaps (pericranial or free flaps) [9]. Perioperative dead space must be obliterated in the postoperative period, i.e., drain usage. Soft tissue contouring may be performed at the initial implant procedure; however, additional procedures may be necessary for final contouring. Last, if these conditions cannot be met, then autogenous reconstruction with split cranial bone graft should be considered.

Successful reconstruction of large-scale cranial defects involves consideration and sometimes treatment of intracranial dead space (Table 27.3). Despite severe trauma mechanisms, most patients who underwent custom 3D prefabricated implant reconstruction after decompressive craniectomy, showed expansion of the brain and intracranial contents up to the level of the endocranial surface of the implant. However, occassionally severely injured soldiers had so much contracture and scarring associated with injury and decompressive craniectomy, initial attempts at reconstruction failed due to incomplete intracranial expansion after implant placement, with persistent intracranial dead space. These rare patients required intracranial free flap reconstruction to diminish dead space prior to successful restoration of cranial skeletal form (Fig. 27.7). Another method of treating scarred dura and a relatively fixed intracranial dead space would be through nonanatomic, cranial reconstruction, ± free tissue transfer [10].

Complex Craniofacial Reconstruction

In addition to the need for large-scale cranial defect reconstruction, many patients suffered composite tissue loss in the head and neck region, requiring reconstruction at various levels. One of the most devastating injury patterns noted involved direct frontal trauma, involving the

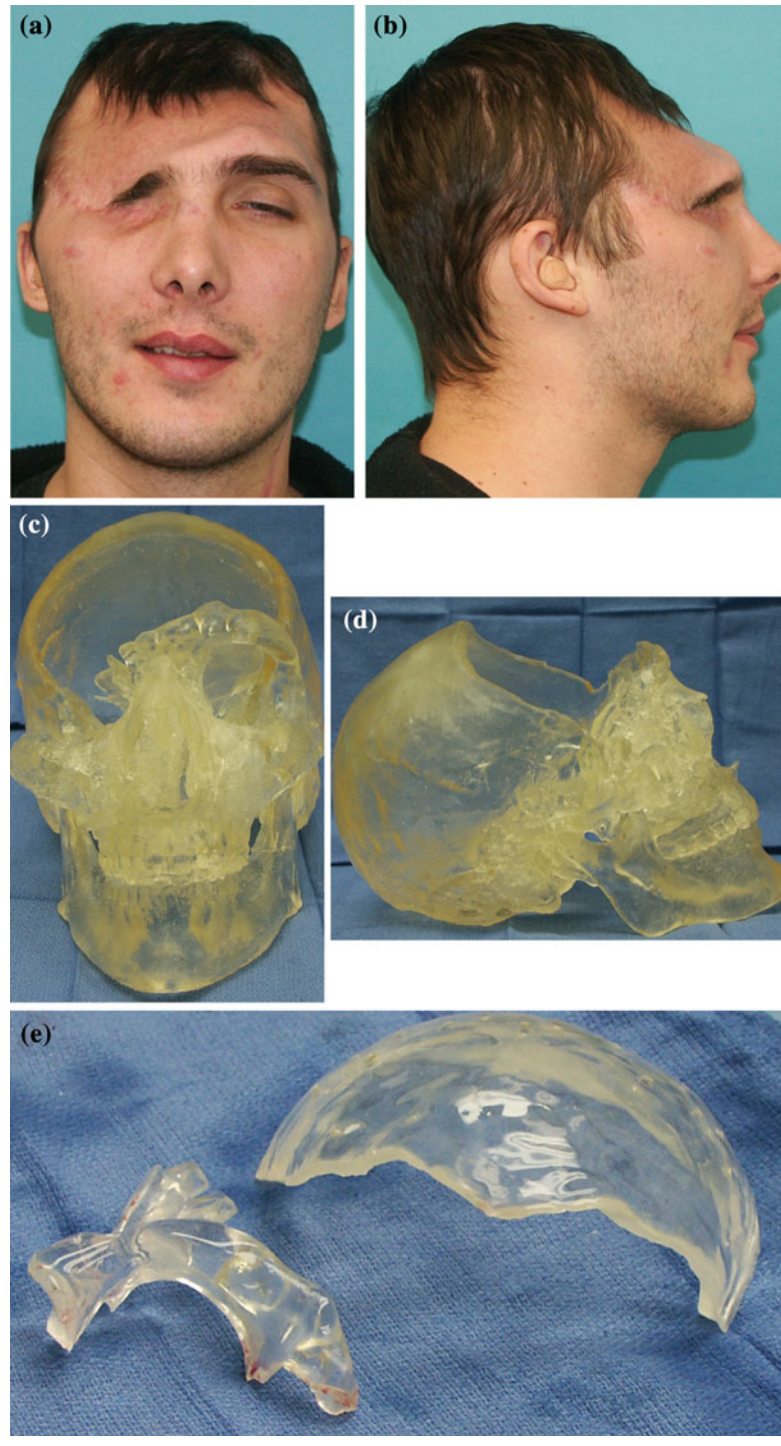


Fig. 27.6 **a–m** Fronto-temporal blast trauma with primary (loss of soft tissue, bone, orbit), secondary blast trauma (deafness), and s/p bifrontal craniectomy. Custom 3D prefabricated orbito-fronto-temporal PMMA implant-two

orbits, frontal cranium, anterior skull base, and nasal sinuses. This type of injury was most frequently associated with an upward blast to the face. To accommodate massive brain swelling, bifrontal craniectomy was performed. Additionally, the orbital bandeau was destroyed, along

Fig. 27.6 (continued)

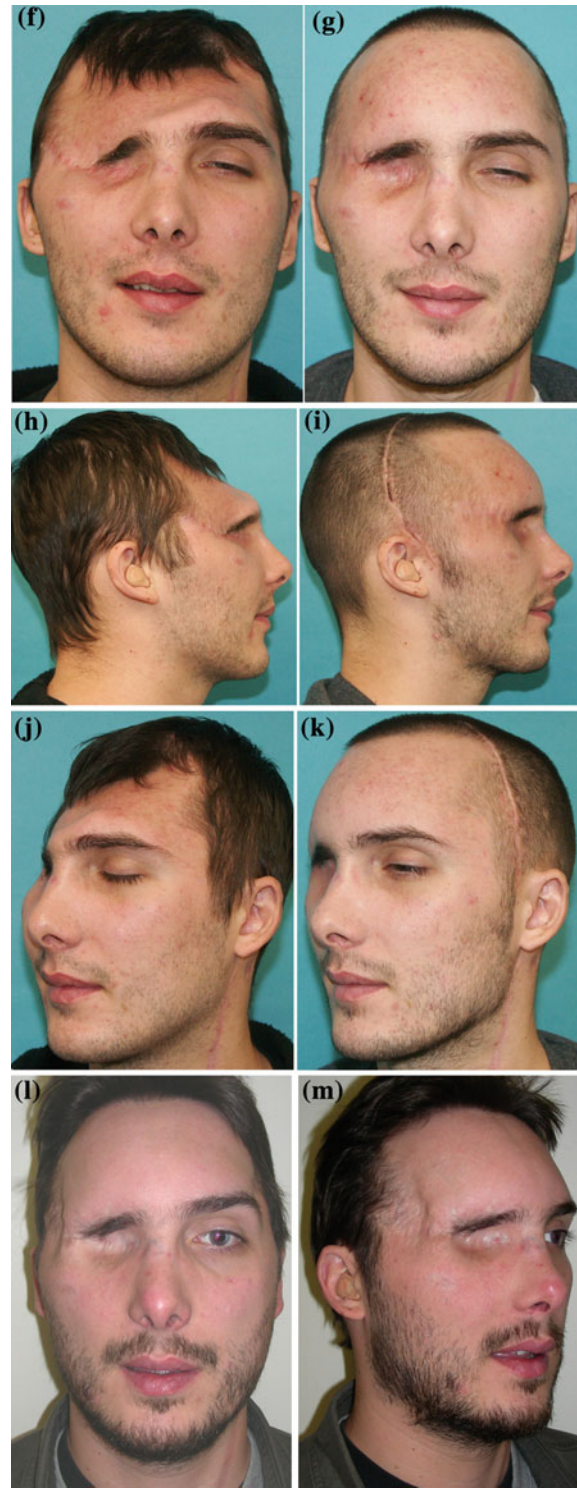
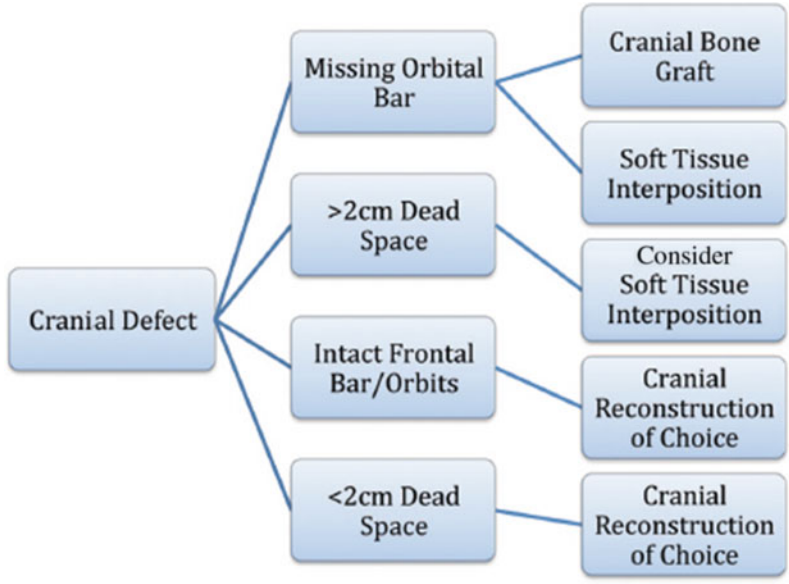


Table 27.3 Algorithim to treat military cranial defects



with creating a direct contamination between nose and brain through anterior skull base/frontal sinus trauma.

Successful treatment of this type of complex craniofacial injury pattern required a) walling off the nose from brain through frontal sinus cranialization and anterior skull base reconstruction, b) orbital bandeau recreation, setting the foundation for cranial restoration, and c) large-scale frontal cranial reconstruction. Through repeated presentation of this type of injury, certain principles were ascertained. In the acute setting, after decompressive craniectomy, anterior skull base reconstruction/frontal sinus cranialization with bone graft and vascularized tissue was required. Due to the frontal mechanism of injury, frequently the pericranial flap, which is the primary local flap utilized for anterior skull base reconstruction, was not available. Intracranial free tissue transfer was required to promote healing between the nasal cavity and anterior skull base, usually latissimus dorsi, or ALT flaps [11]. Orbital bandeau reconstruction is most reliably performed with autogenous bone graft, followed by bifrontal cranial reconstruction with custom 3D prefabricated alloplastic implants (PMMA or woven titanium), or split cranial bone graft. Attempts to reconstruct the orbital bandeau with alloplastic materials was often met with failure, most likely due to contamination from nasal sinuses and/or implant prominence with limited overlying soft tissue. Custom alloplastic implants were quite successful in the bifrontal area as long as the aforementioned criteria of brain/nose separation and autogenous orbital bandeau creation were adhered to.

Composite defect reconstruction in the facial region was successfully performed with strict adherence to use of autologous materials (hard and soft tissue). After primary fracture treatment was completed, many patients required treatment of composite facial defects in the acute/subacute period. Soft tissue reconstruction was almost uniformly completed with free tissue transfer, given the limited local donor sites, although several forehead flaps were used for nasal/paranasal reconstruction. Durable skeletal reconstruction in the face was achieved with use

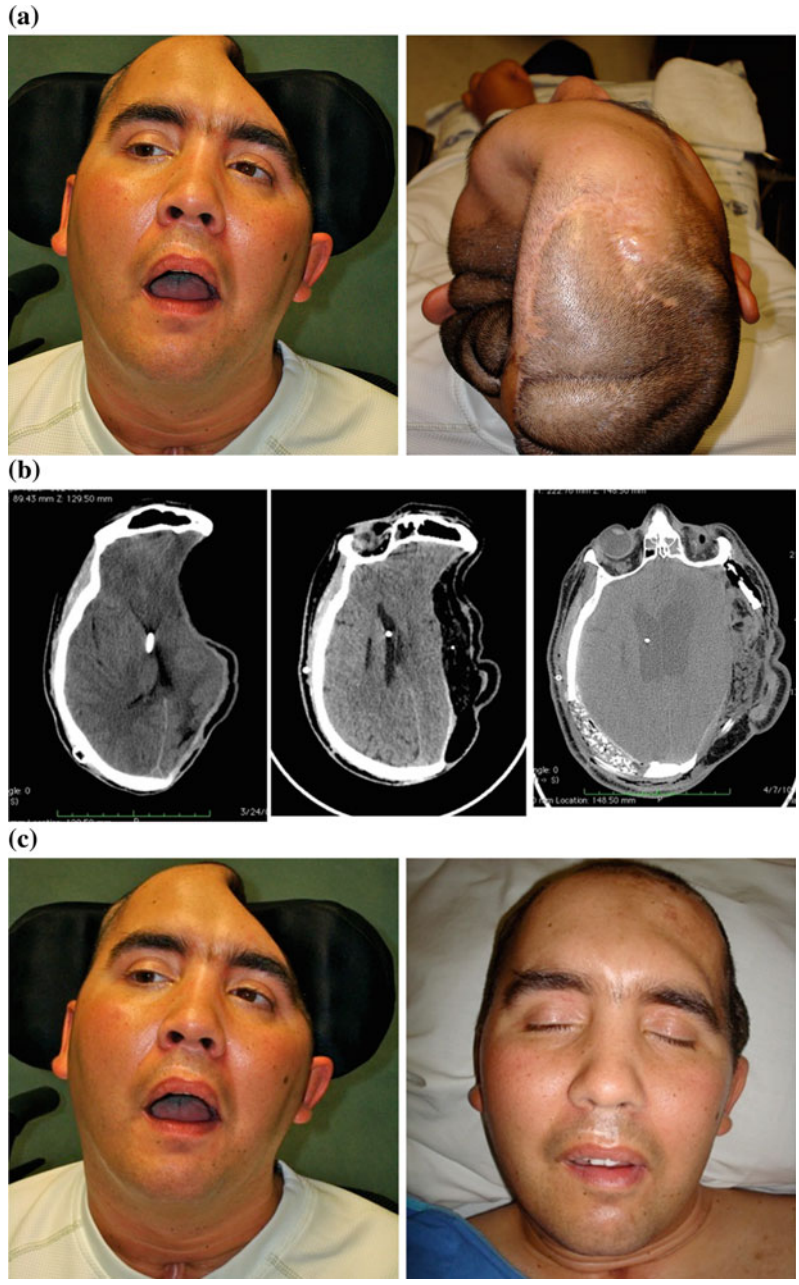


Fig. 27.7 **a** Sunken flap syndrome (aka syndrome of the trephined). Decreased neurological function. **b** Progressive endocranial expansion. *Left*—L fronto-temporo-parietal defect with midline shift. *Middle*—s/p free latissimus dorsi flap, *Right*—after delayed cranial bone graft reconstruction. **c**—L (pre), R (post)- latissimus free flap and cranial bone graft reconstruction

of autologous bone grafts, either nonvascularized or vascularized, depending on size needs. Near complete midface/lower face skeletal reconstruction necessitated free vascularized bone flaps, i.e., fibula, with smaller defects, usually less than 6 cm receiving nonvascularized bone grafts from cranium or iliac crest. Attempts at use of alloplastic materials to reconstruct the facial

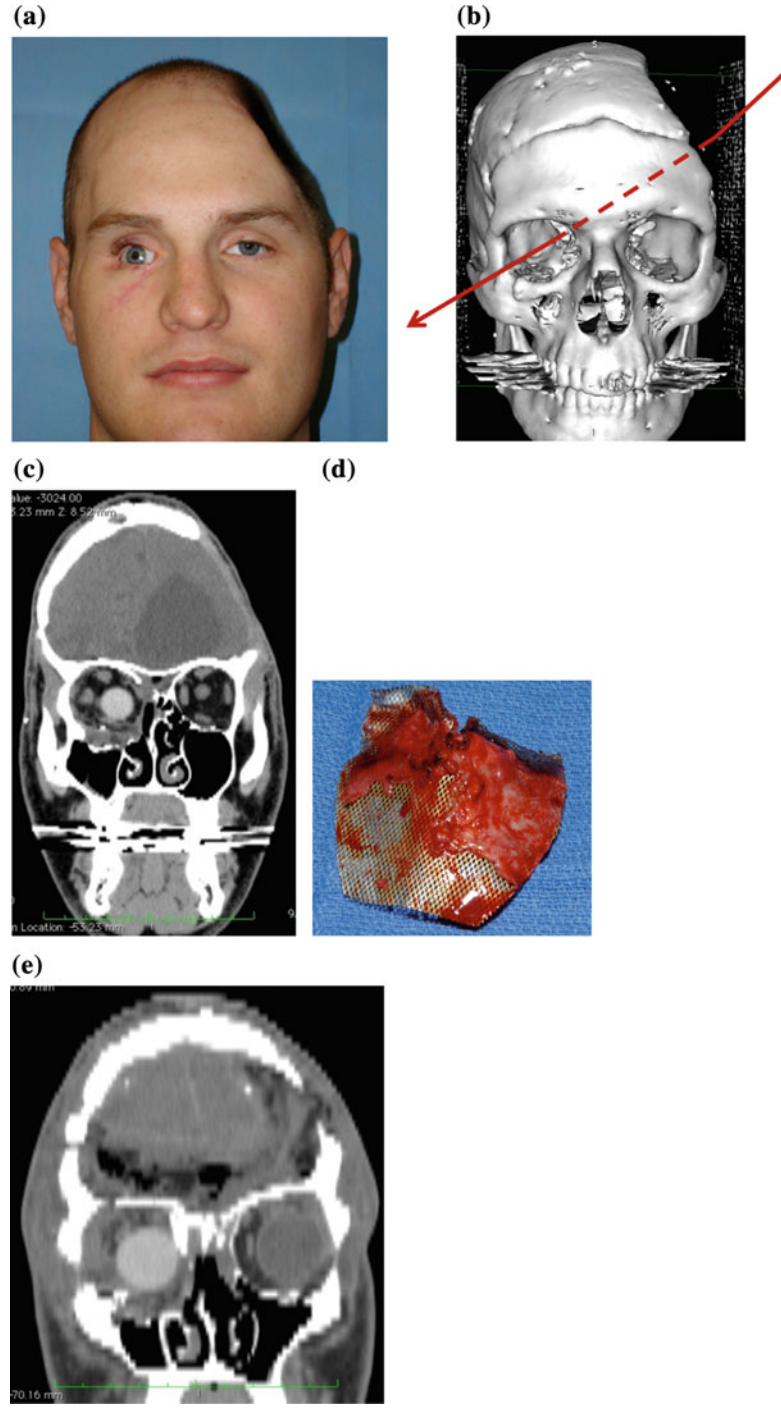
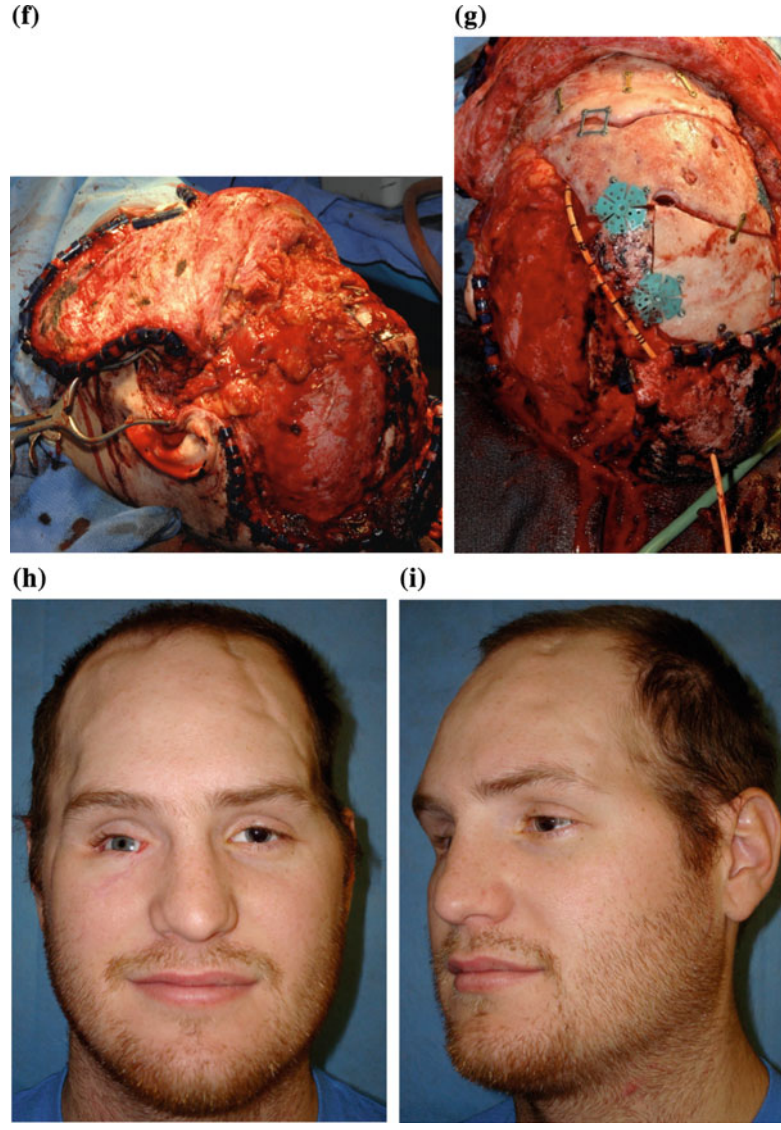


Fig. 27.8 **a**,**b** GSW to head. Injury to anterior cranial fossa, loss of R globe, endocranial dead space created. Trajectory shown in b. L temporo-parietal craniectomy performed for swelling. **c**, **d** Anterior cranial fossa initially reconstructed in field with titanium mesh. Note R globe spacer. Patient suffered purulent infection due to mesh and frontal sinus communication. Mesh is shown with purulence attached. **e** Cranial bone graft reconstruction of anterior cranial fossa/orbital roof. ALT adipofascial free flap used to provide vascular cover to bone graft and fill dead space. **f**, **g** ALT adipofascial free flap shown before and after replacement of cranial bone. Ventricular shunt present. **h**, **i** After L temporo-parietal PMMA implant reconstruction

skeleton were uniformly met with failure. Again, as in cranial reconstruction, the WRAMC 3D Medical applications lab was utilized to create bone graft templates for complex 3D cranial bone graft reconstructions, as well as segmented applications of the free fibula flap.

Microsurgical free flap reconstruction of craniofacial injures was evaluated. A total of 242

Fig. 27.8 (continued)



craniofacial injuries from the Iraq/Afghanistan wars treated at the Military National Capital area MTFs (WRAMC/NNMC), were reviewed. There were 111 cranial, 30 complex face, 15 orbit, 35 maxillary/midface, and 51 mandible. The patients were healthy soldiers ages 22–37, with either close range GSW or blast trauma to the head. There were sixteen flaps in the cohort. No flap losses occurred. Types of flaps utilized were as follows: Radial forearm 8 (two osseocutaneous) ALT 1, Latissimus 1 (vein graft) Osseocutaneous Fibula 6. It was noted on many of these cases, the recipient vessels were covered in a fibrinous peel, much like a radiated patient. The blast wave may have contributed to this phenomenon (Fig. 27.8).

Local flap reconstruction in the head and neck was evaluated in the same cohort. There were seventeen flaps identified. Paramedian forehead 7, Mustarde 4, FAAM 1, and Rotation 5. There were no flap losses. These cases illustrate that traditional local flap reconstruction can be accomplished in patients with high velocity GSWs and severe blast trauma mechanisms.

Conclusions

The Iraq/Afghanistan wars, like any other war in history, have brought about increased understanding of medical and surgical disease. The hallmark of the current conflicts is most certainly the blast injury to the head and extremities, related to improved truncal protection and frequency of IED usage. Soldiers were able to survive formerly life-threatening head trauma through advances in far forward (in the battlefield) care, including decompressive craniectomy. Back at Level I MTFs in the US, high volumes of craniofacial trauma led to the development of novel infrastructure and systems of care to treat these severe injuries. Blast trauma frequently led to multisystem injury. Coordination of complex care amongst multiple treating specialties was required to achieve optimal outcomes.

Through coordination of the efforts of neurosurgery and craniofacial surgery, severe craniofacial trauma patients were able to be treated with improved with refinement of protocols. Incision sites were optimized for trauma and reconstructive care. The role of A. Baumanii in contamination/infection was made clear. Acute fractures could often not be fixated until approximately 3 weeks post-injury, due to massive swelling associated with blast injury. Attention was given to definitive separation of brain and nasal cavities through bone grafting and vascularized soft tissue. Autologous orbital reconstruction provided a successful foundation for alloplastic cranial reconstruction. The planning for and production of patient-specific 3D prefabricated cranial implants was developed as an intrinsic mechanism to treat a high volume of cranial defects. Adequate soft tissue coverage and intracranial dead space management was key to cranial implant retention. Liberal use of free tissue transfer was incorporated to aid in reconstruction of composite defects.

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28 Functional Restoration for Neurological Trauma: Current Therapies and Future Directions

James Leiphart

Functional Restoration for Neurological Trauma: Current Therapies and Future Directions

Neurological trauma is frequently associated with disruptive or disabling neurological symptoms and deficits. The annual incidence of traumatic brain injury in the United States has been estimated at 1.5 million with approximately 300,000 hospitalizations and over 50,000 deaths [1–4]. It has been estimated that these traumatic brain injuries lead to over 120,000 people with long-term disability annually [2], resulting in 1.1 % of the US population with disability from traumatic brain injury [5]. Traumatic brain injury is associated with posttraumatic epilepsy [6–10], impaired attention, memory and concentration [11–13], disabling neurological symptoms such as headache, dizziness, sleep disturbance, tinnitus and imbalance [11], emotional problems including depression, anxiety and posttraumatic stress disorder [11, 12, 14], social impacts including difficulties with school, employment, and marriage [11, 14], and in the most extreme conditions spasticity, minimally conscious states and persistent vegetative states.

Spinal cord injury affects an estimated 273,000 people per year in the United States [15]. Spinal cord injury frequently results in loss or limits in the use of the extremities as well as spasticity and pain [16–18]. The prevalence of peripheral nerve injury in one series was 2.8 % within the trauma population [19], with a 1.64 % incidence among patients with extremity trauma [20]. Peripheral nerve injuries can result in loss of motor and/or sensory function and can also lead to development of complex regional pain syndrome [21, 22]. These effects of neurotrauma can be mitigated by modern neuromodulation surgical techniques and devices. This chapter will review the neuromodulation techniques currently part of standard practice as well as those in development and potential future technologies that may provide alleviation of the negative sequelae of neurotrauma.

Posttraumatic Epilepsy

Head trauma is associated with an incidence of posttraumatic epilepsy to a degree commensurate with the severity of the head trauma. Seizures following head injury are classified as early posttraumatic seizures (EPTS) which occur within the first week following the head injury and late posttraumatic seizures (LPTS) which occur at any time later than 1 week following head trauma [6]. Studies have shown the

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incidence of EPTS in adults (>16 years of age) with severe traumatic brain injury to be 8.4 %, and in children to be proportional to the severity of injury with moderate to severe traumatic brain injury resulting in 12 % EPTS [23] and severe traumatic brain injury resulting in 19–25 % EPTS [6, 24]. EPTS are associated with a higher incidence of LPTS and posttraumatic epilepsy [6]. LPTS and posttraumatic epilepsy also appear to occur more frequently in more severe traumatic brain injury. The incidence of LPTS was 2.1 % in all types of traumatic brain injuries [8]. 10 % in patients with traumatic brain injuries having positive head CT findings [7], and 25.3 % in patients with traumatic brain injuries severe enough to require rehabilitation services [6]. In one study, 77 % of patients having LPTS went on to develop posttraumatic epilepsy [8]. The incidence of posttraumatic epilepsy is the highest in penetrating head trauma with 53 % of patients having posttraumatic seizures of which 92 % went on to have posttraumatic epilepsy [9].

Posttraumatic epilepsy has significant impacts on many aspects of life. Patients with LPTS have a higher disability rating, lower life satisfaction scores, and have a higher utilization of public transportation due to inability to drive compared to traumatic brain injury patients without LPTS [25]. In a study comparing mortality rates of traumatic brain injury patients over a 8–15 year post-injury period 27 % of LPTS patients died compared to 10 % of those without LPTS [26]. Clearly, interventions to prevent the development of posttraumatic epilepsy and prevent seizures in patients who do develop posttraumatic epilepsy would positively impact clinical outcomes. Anti-seizure medications have demonstrated efficacy in reducing the incidence of EPTS [23, 27] but no medication has proven effective in preventing posttraumatic epilepsy [27–29]. A proposed trial of levetiracetam for prevention of posttraumatic epilepsy may hold promise but has not yet yielded results [30–32].

Once posttraumatic epilepsy has developed, surgical approaches to seizure control have proven effective. A review of all extratemporal lobe resections for posttraumatic epilepsy at a single institution showed a 28 % seizure free rate [33], but another study demonstrated higher seizure free rates for posttraumatic frontal lobe epilepsy surgery at 33 % and posttraumatic temporal lobe epilepsy surgery at 69 % [34]. These outcomes are similar to outcomes for epilepsy surgery of non-traumatic origin as well [35, 36]. The surgically implanted vagal nerve stimulator has also been effective in control of posttraumatic epilepsy. Although few patients are seizure free with the vagal nerve stimulator, 4.6 % in a review of studies [37], the majority of patients benefit from the therapy with 50–56 % of patients having greater than 50 % reduction in their seizures [37, 38] and an average reduction in seizures of 62–73 % at 2 years [38, 39]. Other promising surgical techniques for seizure control include the Neuropace RNS device which was recently approved by the US Food and Drug Administration (FDA). This device provided 54 % of patients greater than 50 % seizure reduction [40]. The medtronic deep brain stimulator has been effective in reducing seizures by stimulation of the anterior nucleus of the thalamus. This therapy is not yet FDA approved but is being used internationally and has demonstrated a 50 % or greater reduction in seizures in 54 % of patients [41].

In animal studies vagal nerve stimulation has demonstrated a positive impact on other aspects of trauma. In animal models of brain injury, vagal nerve stimulation was able to decrease edema and the inflammatory response [42, 43], decrease disruption of the blood–brain barrier [44], and protect GABAergic neurons [45]. Vagal nerve stimulation in animal models of brain injury has also produced improvements in behavioral outcomes with improved performance on motor tasks [43, 46–48] and a cognitive task [48]. Although these results are promising, vagal nerve stimulation is not currently being utilized in humans for traumatic brain injury therapy other than for the treatment of posttraumatic epilepsy.

Memory, Cognition and Consciousness

The detrimental effects of traumatic brain injury on memory and cognition, including the effects on concentration necessary for memory and

cognition, are frequently transient but can lead to significant disability when they are persistent. In one study, 22 % of traumatic brain injury patients reported persistent memory or thinking problems [11]. The effects of traumatic brain injury on neuropsychological tests of memory and cognition seem to be dependent on severity of the brain injury. Patients with mild traumatic brain injury had impairments in pooled neuropsychological testing compared to controls. Their average results on the various tests were 13–24 % below the average results of the control subjects [49]. Mild traumatic brain injury patients appear to have greater impairments in attention where moderate to severe traumatic brain injury patients have greater deficits in memory and learning [13]. Severely brain injured patients have shown more cognitive difficulties than mild to moderate brain injured patients [12] and decreases in neuropsychological testing performance correlate with higher levels of injury severity on the Glasgow Outcome Scale in moderate to severe brain injury patients [14]. One to 55 % of patients with mild to severe brain injuries had moderate to severe cognitive impairment on a battery of neuropsychological tests [50]. A review of the neuropsychology of brain injury literature suggested a dose dependent effect of brain injury on cognitive impairment with a clear decline of cognitive functions following penetrating brain injury [51].

Brain stimulation may hold promise as a therapy for the treatment of cognitive deficits and may play a positive role in the treatment of cognitive deficits due to traumatic brain injury. Deep brain stimulation is most widely utilized for the treatment of movement disorders and has proven effective in the treatment of tremor related to traumatic brain injury [52, 53]. Several animal models of traumatic brain injury have had improvements in the resulting memory deficits with deep brain stimulation of the hippocampus [54, 55], fornix [56], and the medial septal nucleus [57]. A few cases of deep brain stimulation for the treatment of memory deficits or improvement of baseline memory have been conducted in humans, but mostly in dementia patients, not trauma patients with cognitive deficits. The oldest of these is a case report of stimulation of the basal nucleus of Meynert in a patient with Alzheimer's dementia. The stimulation produced no significant clinical improvement [58]. Memory improvement from stimulation of the fornix and hypothalamic area in a person with normal cognition initially prompted enthusiasm for this target as a treatment of dementia [59]. Deep brain stimulation of the fornix and hypothalamus region in a small group of patients with dementia produced some improvement in memory or slowing of cognitive decline [60, 61], but the effects have been mild. More recently, visual-spatial memory improvements but not improvements in verbal or naming memory were demonstrated with stimulation of the fornix in patients without dementia being monitored for medically refractory epilepsy [62]. A study of nucleus accumbens deep brain stimulation in patients with treatment-resistant depression suggested a trend toward cognitive improvement [63]. However, a review of the literature concerning deep brain stimulation as a treatment of Alzheimer's disease warned that the data is preliminary and limited [64], making it far from use in other pathologies with memory deficits. Non-invasive brain stimulation techniques have also had some limited success. Repetitive transcranial magnetic stimulation of the left dorsolateral prefrontal cortex improved outcomes in several neuropsychiatric measures and significantly decreased post-concussive symptoms in patients with mild traumatic brain injury [65]. The United States Defense Advanced Research Projects Agency has invested in an ambitious project to develop a memory prosthesis device [66, 67] so a neuromodulation device for the treatment of posttraumatic brain injury memory deficits may be available to patients in the near future.

The more significant effects of severe brain injury on consciousness are always disabling when they persist. They lead to significant health care costs as well as emotional distress for the patients and their families. In one hospital's experience, 0.6 % of all patients admitted with head injury had prolonged unconsciousness for over two weeks [68]. In a population study of traumatic brain injury it was estimated that 0.3 %

remained in a persistent vegetative state and 0.8 % remained in a minimally conscious state 1 year after the head trauma [69]. Another study of severe traumatic brain injury reported 7.2 % remained in a persistent vegetative state and 2.4 % were in a minimally conscious state [70]. The persistent vegetative state has been defined as a complete lack of awareness of self and environment with no purposeful or voluntary response to stimuli but with preserved sleep-wake cycles, hypothalamic function, and brainstem autonomic functions [71, 72]. In the minimally conscious state the patient is able to follow simple commands, respond yes or no verbally or with gestures, have intelligible verbalization and/or have purposeful behavior without achieving functional interactive communication or the use of two or more different objects [73]. The prevalence of persistent vegetative state has been estimated at 0.2–6.1 patients per 100,000 population [74], which would be approximately 640–19,500 in the United States alone. The average lifetime cost of care per patient with severe traumatic brain injury has been estimated at $600,000–$1,875,000 [4], with those in a persistent vegetative or minimally conscious state being at the higher end of these costs. The humanitarian and economic impact of any intervention that could improve the level of consciousness in these patients would be significant.

There have been reports of improved levels of consciousness in patients in a permanent vegetative state and minimally conscious state with brain stimulation. The foundation for brain stimulation is found in the results from animal model studies. Deep brain stimulation of the thalamus [55, 75, 76] and hippocampus [75] in animal models of traumatic brain injury have demonstrated increases in measures of arousal. A group of clinical investigators in Japan has produced several reports of positive outcomes with over a 10 year follow up in a group of 21 patients in a persistent vegetative state who received deep brain stimulation of the mesencephalic reticular formation or the centromedian parafasicular complex of the thalamus [77–82]. They report that 8 of the 21 patients had improved consciousness to the level of being able to follow commands. These results have not been replicated by others in the literature. The same group reports positive results from the use of deep brain stimulation and spinal cord stimulation in patients in a minimally conscious state [80, 83]. All five of the patients receiving deep brain stimulation had stimulation of the centromedian parafasicular complex of the thalamus and the ten spinal cord stimulator patients had electrodes placed in the epidural space from C2 to C4. They report that all 5 of the deep brain stimulator patients and 7 of the 10 spinal cord stimulator patients emerged from the minimally conscious state to be able to functionally use two different items and have functionally interactive communication. Deep brain stimulation of the central thalamus has been attempted by others for the treatment of patients in a minimally conscious state. In one case report [84] and a report of single-subject studies which appears to present the same data as the case report [85] a group of investigators describe increases in measures of arousal, communication, and motor function with deep brain stimulation of the central thalamus of patients in a minimally conscious state. However, with limited data it is difficult at this point to determine how successful this therapy may be.

The less invasive techniques of transcranial stimulation have also been attempted in these two patient populations. In a randomized double-blind placebo-controlled crossover study of transcranial direct current stimulation of the left dorsolateral prefrontal cortex, the group of 30 patients in a minimally conscious state showed benefit in a measure of coma, but a group of 25 patients in a persistent vegetative state did not [86]. In another study of transcranial direct current stimulation of the left dorsolateral prefrontal cortex or the left primary sensorimotor cortex none of the seven patients in a persistent vegetative state improved in a measure of coma but all three of the patients in a minimally conscious state had improvements [87]. A case report of transcranial magnetic stimulation for a patient in a minimally conscious state reported an increase in meaningful behaviors interpreted as a clinical benefit [88]. These results hold promise for a minimally invasive therapy for the minimally conscious patient population. Another less

invasive surgical option has been considered for the treatment of traumatic brain injury patients with disorders of consciousness as well. Given the encouraging basic science results of vagal nerve stimulation in animal models of traumatic brain injury [42–48], a study of vagal nerve stimulation in patients with traumatic brain injury and persistently vegetative or minimally conscious states has been proposed [89].

Depression

Major depressive disorder remains a significant problem in patients with traumatic brain injury. Among all traumatic brain injury patients 22 % self-report feelings of depression [11], whereas 33–53 % of traumatic brain injury patients fulfill objective criteria for major depressive disorder within the first year after injury [90, 91]. Post-concussive disorder is highly associated with the development of depression [92]. The development of depression also seems to be relative to the severity of the traumatic brain injury with 3.6–11.6 % of mild traumatic brain injury patients developing depression at 1 year [93, 94], and 21.2 % of severe traumatic brain injury patients developing major depressive disorder after their injury [95]. Traumatic brain injury patients who developed depression had lower health-related quality of life measures [95] and poorer functional outcomes as measured by the Glasgow Outcome Scale [93, 96]. Medical therapy and psychosocial interventions are currently employed for the treatment of traumatic brain injury-related depression, but as a recent systematic review of the literature has demonstrated [97] the success of these interventions is modest. There are only two studies with class I evidence. One is a study of sertraline in which 59 % of the treatment group and 32 % of the placebo group were responders with a 50 % or greater decrease in their baseline Hamilton Depression Rating Scale (HAM-D) scores. The other is a study of multidisciplinary psychosocial intervention that resulted in no statistically significant difference in the Hospital Anxiety and Depression Scale between the intervention and the placebo groups. The other studies showed varying degrees of improvement, but without class I evidence it is difficult to determine how successful these interventions would be in the traumatic brain injury population.

Neuromodulation techniques have been applied to general major depressive disorder without specifically targeting traumatic brain injury-related depression, but the outcomes may prove to generalize to traumatic brain injury patients as well. Deep brain stimulation has been preliminarily investigated as an intervention for the treatment of major depressive disorder. The most commonly studied deep brain stimulation target for depression is the subcallosal cingulate gyrus. The original group of 20 treatment-resistant major depressive disorder patients implanted in Toronto, Canada have reported follow-up outcomes up to 3–6 years after surgery [98–100]. Utilizing the Hamilton Rating Scale for Depression and considering patients with greater than 50 % reduction from baseline responders, at 12 months this group of 20 patients went from a mean score of 24.4 to a mean score of 12.6 [98] with a responder rate of 55 % [99]. They reported a 60 % responder rate at 3 years with a 40 % remission rate [100]. Deep brain stimulation of the subcallosal cingulate gyrus has been reported in multiple studies from seven medical centers that included a total of 56 treatment-resistant depression patients [101–105]. From combined data of these studies, at 6 months after surgery there were 28/56 (50 %) responders and 8/35 (22.9 %) remitters, at 1 year after surgery there were 16/43 (37.2 %) responders and 9/22 (40.9 %) remitters, and at 2 years after surgery there were 11/12 (91.7 %) responders and 7/12 (58.3 %) remitters (one study did not report remission rates, only response rates). Another promising deep brain stimulation site for depression is the ventral capsule/ventral striatum region which was used in 15 treatment-resistant patients with response rates of 46.7 % at 3 months, 40 % at 6 months and 53.3 % at last follow-up [106]. Deep brain stimulation of the nucleus accumbens and caudate nucleus was attempted in four treatment-resistant depression patients with no responders at 6 months but three responders at 1 year with

nucleus accumbens stimulation, one of whom was in remission [107].

Spasticity

Spasticity is one of the potential sequelae of severe traumatic brain injury that can lead to discomfort, disability, and difficulty with care. In a review of patients with severe traumatic brain injury requiring rehabilitation, 25.8 % had increased muscle tone consistent with some degree of spasticity [108]. Forty percent of these patients required some intervention for their spasticity. Traditional medical treatment modalities for traumatic brain injury patients with spasticity include medications, muscle stretching, orthoses, nerve blocks, phenol neurolysis, BoTox injections [109, 110], ambulation, serial casting, electrical stimulation, and robotics [111]. Medications used orally for traumatic brain injury spasticity are baclofen, tizanidine, cannabinoids, benzodiazepines, clonidine, and dantrolene [111]. Traditional surgical therapies included surgical muscle lengthening, transfers, or releases [109], as well as rhizotomies [111].

Neuromodulation for spasticity by intrathecal infusion of baclofen provides a nondestructive surgical therapy. The standard measure used to grade spasticity is the Ashworth Scale [112] which is graded as follows; 1 no increase in tone, 2 slight increase in tone with a catch that releases, 3 more marked increase in tone but able to move extremity through range of motion, 4 significant increase in muscle tone making movement difficult, 5 rigid in flexion or extension. The traditional protocol for implantation of in intrathecal catheter and pump for long-term therapy is to begin with a trial of 50 micrograms of intrathecal baclofen to evaluate the response. One paper evaluating the intrathecal baclofen trial in a spasticity population primarily containing traumatic brain injury patients (10 out of 11) reported a decrease in the average lower extremity Ashworth scale from 4.2 to 2.2 at 4 h after administration of the baclofen [113]. Two other studies of 58 total patients, 29 of which had traumatic brain injuries, found that the average lower extremity spasticity decreased from a baseline of 2.0–2.4 to 1.6 at 2 h, 1.4–1.5 at 4 h, and 1.3–1.4 at 6 h [114, 115]. Pooled data from the traumatic brain injury patients reported in five different studies of long-term intrathecal baclofen infusion by programmable pump demonstrated clear benefit of this therapy in upper and lower extremity spasticity [116–120]. Included in these five studies were 42 patients with spasticity from traumatic brain injury who were followed anywhere from 3 months to 5 years. The average lower extremity Ashworth score decreased from 3.7 to 1.6 and the average upper extremity score decreased from 3.1 to 1.8 demonstrating a benefit for the upper extremities as well as the lower extremities. Intrathecal baclofen therapy is effective if implemented early, as early as 3 months after traumatic brain injury [119], and the benefit is prolonged, reportedly lasting 14 years and longer [121].

Spinal cord injury has a high association with traumatic brain injury, especially cervical spinal cord injury [122]. It has been estimated that over 200,000 people in the United States have a spinal cord injury with persistent neurological deficits [16]. Among patients with chronic spinal cord injury, a 65–78 % incidence of spasticity has been reported [17, 18]. A survey of patients with spinal cord injury showed that arm and hand function was the most important to the quality of life of those living with quadriplegia, and both walking movement and chronic pain were ranked with middle importance to the quality of life for those with paraplegia [16], all of which could potentially be improved with better control of spasticity when spasticity is present. In three clinical series including a combined total of 174 patients having continuous intrathecal baclofen therapy for spasticity of spinal origin, 29–41 % of which were traumatic spinal cord injury patients, the average Ashworth scale results decreased from a baseline of 2.5–4.2 down to 1.3–1.9 at 3 months or last follow-up [123–125]. Intrathecal baclofen therapy has relatively low risks, with the majority of risks coming at the time of pump and catheter implantation including reported 3.3 % pseudomeningocele, 2.9 % constipation, 2.4 % headache, and 2.2 % cerebrospinal leak [126], and long-term complication rate of 0.13

complications per pump-year [127] with the most common long-term complications being catheter kink or catheter migration at 4 % and infection at 1.2 % [126]. Studies have shown that intrathecal baclofen therapy for severe spasticity is successful in improving quality of life [128] and cost savings over time [129]. These results support the clinical application of this therapy which should be considered for appropriate patients following traumatic brain or spinal cord injury.

Pain

The pain syndrome most commonly associated with traumatic brain injury is headache with an estimated 57.8 % prevalence [130]. Traumatic brain injury can also be associated with complex regional pain syndrome, mostly due to the sequelae of the brain injury neurological deficits [131]. Recommendations for medical treatment of posttraumatic headaches are limited and include opioids for a short period of time then nonprescription pain relievers [132]. For patients with posttraumatic headaches that continue for a prolonged period of time and are refractory to any medical therapy, neuromodulation techniques may provide an opportunity for relief. Two case reports of high cervical spinal cord stimulation showed effective posttraumatic headache relief, with 90 % pain relief in one patient [133, 134]. Stimulation of the great auricular nerve produced 90 % posttraumatic headache relief in a case report of a single patient [135]. Motor cortex stimulation has also been reported in one patient to be effective in relieving posttraumatic facial pain due to injury [136]. Pain from spinal cord injury can be complex including one or several pain syndromes depending on the individual patient [137]. The prevalence of spinal cord injury associated pain varies based on clinical study, being anywhere from 26–96 % [137]. A review of the literature concerning spinal cord stimulation for spinal cord injury associated chronic intractable pain showed moderate benefit, with significant long-term pain relief in only 18–40 % [138].

Treatment of complex regional pain syndrome from extremity injury may also be controlled by neuromodulation. Complex regional pain syndrome can result from injury of an extremity, especially with the presence of a peripheral nerve injury. The prevalence of peripheral nerve injury in a population of patients with multiple injuries was 2.8 % [19]. There was a high association between peripheral nerve injury and head injury, with 60 % of the peripheral nerve injury patients having a head injury as well [19]. Complex regional pain syndrome, which frequently results from extremity and peripheral nerve injury, has an incidence in the population of 5.46–26.2 per 100,000 person years [21, 22] and a prevalence of 20.57 per 100,000 [22]. Complex regional pain syndrome can be challenging to treat with only 30 % having resolved symptoms, 16 % reporting progression of their symptoms and 31 % unemployed at 2 year or more follow-up [139]. Sixty percent of patients with spinal cord stimulators implanted for complex regional pain syndrome type 1 continued to use their stimulator for effective pain relief in a follow-up to 12 years [140]. In a randomized, prospective controlled trial of spinal cord stimulation for complex regional pain syndrome, stimulator patients had an average decrease in their 10 point visual-analog scale of 2.4 points compared to controls who had an average increase of 0.2 [141]. There was no significant improvement in their functional status, but the patients who had stimulators implanted had improvement in their health-related quality of life. The benefits that the patients with implanted stimulators enjoyed persisted through a 5 year follow-up period [142]. An economic analysis of these patients showed an initial $4000 higher cost for each patient implanted with a spinal cord stimulator, but a projected $60,000 savings for each spinal cord stimulator patient over his or her lifetime [143]. Although spinal cord stimulator therapy does not completely eliminate the pain

from complex regional pain syndrome, it provides clear benefit to patients.

Robotics and Brain–Machine Interface

Recent advances in robotics and technologies of brain–machine interface hold promise for devices that could provide increased function in post-trauma patients. Robotic exoskeleton systems are commercially available and have been FDA approved for work with spinal cord injury patients in the clinical environment [144–147]. Seven clinically available robotic exoskeleton systems were identified in a 2015 review article [147]. The significant limitation of these devices is that they are not approved to be utilized at home and in the community. The promise of this technology will only be fully realized when combined with brain–machine interface technologies which are in the process of development and implementation. People with tetraplegia have successfully utilized current brain– machine interface technologies to independently move and meaningfully utilize advanced robotic upper extremity prosthetics directly or in virtual reality environments [148, 149]. Brain–machine interface technology has been utilized by spinal cord injury patients in a virtual reality environment to operate a walking simulator [150] providing proof of concept that robotic exoskeleton technologies may someday be effectively operated directly by the individual's brain activity. Once realized, this technology combination would be extremely powerful in expanding functionality for the patient with trauma related disability.

Conclusions

The long lasting detrimental effects of neurological trauma can lead to significant pain and disability, but these effects can sometimes be mitigated by neuromodulation techniques. Established therapies include resection and stimulator implantation surgeries for epilepsy, intrathecal baclofen pumps for spasticity, and spinal cord stimulators for pain. Other therapies like deep brain stimulation for depression, memory deficits and disorders of consciousness show promise but are currently in limited clinical trials. Case reports suggest that other stimulation modalities for chronic intractable headache may be helpful. Future restorative therapy involving robotics and brain–machine interface technology are in development and could have an important impact on restoring function to severely injured patients.

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Part VI
Special Considerations

Pediatric Neurotrauma

29

Ann-Christine Duhaime

Epidemiology

While the vast majority of both pediatric head injuries and extracranial injuries result from falls, the majority of these are associated with injuries at the milder end of the injury spectrum. Severe and fatal injuries, including those with significant polytrauma, typically result from higher energy events, such as those involving motor vehicles, falls from heights, firearms, or inflicted injuries [1, 2]. While ground-level sports and recreational injuries most often are relatively mild or involve only one or two systems, those involving motor vehicles, such as all-terrain vehicles or motorbikes, can be associated with major polytrauma [3]. In the United States, transportation-related motor vehicle passenger fatalities have decreased steadily, largely due to injury prevention efforts including seatbelts, child restraints, airbags, and other engineering improvements. During that same time, motorized recreational injuries have increased [4–6]. From a global perspective, neurotrauma continues to increase as a cause of fatality worldwide. As access to motorized transportation expands, more children are subject to risk as passengers, pedestrians, and cyclists in contexts in which traffic and vehicle safety developments may not have kept pace with the increase in volume. In addition, serious injuries related to military conflict continue to occur in many regions around the world, in which children are usually bystanders, and sometimes combatants [7–9].

Injury Classifications: Injury Type, Mechanism, and Severity Interactions

Head injuries in patients of all ages can be classified by pathoanatomic injury type (such as skull fracture or epidural hematoma), by mechanism (such as motor vehicle-related trauma or sports injury, or by specific types of forces, such as impact vs. inertial events), and by severity (most often designated by the effect on level of consciousness, typically measured by the Glasgow Coma Score or one of its many pediatric analogues, discussed in more detail below) [10]. As a general rule, many patients have more than a single injury type and more than one type of force responsible for their injuries, as forces tend to happen together; for instance, the patient who is moving at a velocity and whose head impacts an object sustains both contact forces at the site of impact as well as inertial forces as the brain decelerates rapidly. Typically, the heterogeneity

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and magnitude of the forces involved in the injury correlate with the pathoanatomic heterogeneity and severity of the resulting injuries. There are caveats to these rules, however, and some of these are particularly relevant to children. For instance, particularly in a child with a malleable or relatively thin skull, a very focal injury such as a depressed skull fracture with underlying cortical damage may *not* be associated with an overall alteration in mental status, leading to a spuriously "mild" injury severity designation by GCS, but may result in a potential long-term disability in motor or cognitive function, which may become more apparent with maturation. In young children, the long-term effects on neurocognitive and/or social function of various types of traumatic brain injury may not be apparent until demands on these networks increase with age [11–13]. Thus, the severity of an injury with respect to long-term outcomes may be incompletely predicted by the usual acute severity metrics when these are applied to young children.

Pediatric Considerations in Acute Assessment and Management

History

When a seriously injured child arrives at the care facility, a flurry of activity typically ensues, and obtaining the history can be overlooked. However, obtaining a focused, accurate history can (a) direct which aspects of immediate care are prioritized; (b) help predict which problems are at highest risk for evolving and require preventative strategies; and (c) avoid inefficient and costly errors. Because first responders typically arrive and leave promptly, often before specialty providers or their more experienced supervisors have the opportunity to ask questions, important details relevant to that specialty—with our focus here on neurotrauma—can be missed. Thus, attention to specific details can be helpful in optimizing information transfer by those members of the team who have that opportunity at the time of the child's arrival. This information is incorporated into a general assessment and management algorithm which helps to determine what problems are likely to evolve from that particular injury scenario based on the history, initial neurologic assessment, and imaging findings (Table 29.1).

There are several features of the history with particular relevance in children. The exact mechanism of injury relevant to the child is of great importance in predicting the type and severity of injury; it is insufficient, for instance, to just know the child was a passenger in a car crash. Was the child restrained? In what way? Was there intrusion into the vehicle? Was the child ejected? For all injury mechanisms, if the event was witnessed or caregivers arrived at the scene promptly, it is helpful to try to create a "mental video" of events as they unfolded. If the mechanism was a fall, what was the head to ground height? What position was the child in when discovered, and what happened next? What was the initial and the best exam at the scene—was the child unconscious initially, was the child ever see to be crying, speaking, eyes open, moving all extremities with full strength and good excursion? Were there asymmetries in the exam? Was there any evidence of apnea, or seizure activity? Was there a need for resuscitation, and for what indications? What kind of immobilization was performed, what kind of airway protection was required, and what drugs and doses were given, and when? The latter is critical in interpreting the examination on arrival—is this child still pharmacologically sedated and/or paralyzed? (Having a twitch monitor and reversal agents readily available in the Emergency Department can be extremely helpful in early assessment when pharmacologic interference is uncertain.)

In addition, it is important to document, as much as possible, who are the parents/guardians, and if there are additional victims of the injury scenario, what is their relation to the child. First responders may not know past medical history, and it needs to be determined as efficiently as possible who knows the child and is able to provide this information. Often it is best to dispatch a member of the team to interact with or

Table 29.1 Initial assessment includes a structured basic data set of specific elements from the history, physical examination, and imaging findings

Head injury: initial assessment and management for neurosurgical consultants	
Basic minimum acute data	
History	
• Time of injury	
• Mechanism	
–Kinematics; energy, speed, height	
–Struck head?	
• Best exam at scene	
–Loss of/level of consciousness	
–GCS	
–Asymmetry (pupils, motor)	
– Moved legs?	
• Exacerbators	
–Apnea	
–Shock	
–Prolonged extraction	
–Other injuries	
–Resuscitation	
Exam	
• Via standardized tool (GCS, motor, pupils, other)	
Imaging	
• Time of imaging	
• Is there a mass lesion causing symptoms or significant tissue shift now or with predictable worsening?	
Swelling-prone (deterioration- prone) injuries	*Nonswelling-prone injuries*
Acute subdural hematoma (not in atrophic brain)	"Pure" diffuse axonal injury
Multifocal/large contusions	Isolated focal lesion not near brainstem, falx
Temporal or posterior fossa lesions	Chronic subdural hematoma
High energy contact injury	Atrophic/encephalomalacic brain
Gunshot wound	
+ Exacerbators	

The scheme helps divide injuries into "swelling/deterioration-prone" and "nonswelling/deterioration-prone" categories, based on their overall propensity to be associated with dangerous tissue shifts associated with deterioration. These principles are consistent with international efforts to classify and manage patients along multimodality schemes rather than just utilizing severity of injury to guide therapy. Adapted from [1], with permission

contact relatives who can determine whether the child has allergies, was premature or has other preexisting neurologic or general medical problems, and what other aspects of the child's baseline are relevant. This is particularly true for very young children—does this child normally talk? Ambulate? With whom does the child reside? Additionally, since there can be many variations in family structure and custody arrangements, and since injury to a child can be a volatile issue among family members, early involvement of the social work team can be

invaluable in obtaining this information, providing initial support to the distraught family, and providing a communication and "social management" plan early in the course of treatment. This is helpful to the entire team, but also to the clinicians who must interact promptly with the family to provide information about the injuries and treatment plan, to set the stage for an ongoing positive care team/family relationship, and to involve the correct members of the family appropriately in decision-making. Making assumptions that an adult who gives consent for an intervention is the legal guardian of the child can be the source of later difficulties.

Initial Resuscitation

Airway considerations follow general pediatric trauma resuscitation guidelines. In a significantly injured pediatric polytrauma patient, the airway should be secured by an experienced clinician. Often Pediatric Emergency Medicine physicians, Trauma team members from General Surgery/Pediatric Surgery, and Pediatric Anesthesia participants are present very early in the acute care course, and whose job it is to secure the airway should be determined by established protocol to avoid confusion or inefficiency. Use of a checklist has been shown to increase resuscitation efficiency [14]. In young children, significant air accumulation in the stomach can lead to physiologic compromise and so needs to be avoided or relieved promptly if it occurs.

Because of the small blood volume of young children but robust compensatory mechanisms, the risk of shock is increased in specific situations (outlined below) and can become manifest suddenly when decompensation occurs. Use of isotonic or, sometimes, hypertonic solutions typically enables prompt and assertive fluid resuscitation with minimal risk of fluid overload in most children with good baseline cardiopulmonary function, and is more likely to protect against rather than exacerbate neural injury [15]. When in doubt, slight over-resuscitation is generally better tolerated than under-resuscitation in most polytrauma settings in children from the neurotrauma point of view.

Neurologic Assessment

Older children and adolescents with a clearly decreased level of consciousness are examined similar to adults, using a systematic approach to determine level of responsiveness and presence of focal neurologic deficits. Once the pharmacologic status has been determined (especially, if a child might be under the influence of a paralytic agent but not a sedative), children should be approached calmly by first speaking clearly and close to the ear (shouting is not necessary), asking questions using the child's name, and then using progressive levels of stimulation as needed. Some children have a paradoxical response to the application of painful stimulation, which will make them more withdrawn and less responsive, so a gentler approach to the exam can be helpful. Manually opening the eyelids, sometimes accompanied by slight manual movement of the head (depending on the level of concern for cervical injuries,) can be an effective and painless way to encourage alerting and interaction. It should be remembered that Horner's syndrome, which can reflect cervical or cerebrovascular injury, is manifested as failure of the affected pupil to dilate in dim light, so in an appropriate clinical context, this should be specifically assessed. Trapezius pinch and nail bed pressure can be used as needed to check for general level of alertness and to examine the strength in each extremity; the latter also can be assessed by observation of spontaneous activity during maneuvers such as blood draw.

Despite decades of use, aspects of the basic neurotrauma exam are sometimes implemented variably and inconsistently. Although the Glasgow Coma Scale does include a "motor" component, it is designed to assess level of consciousness, and does not include a specific strength exam, which must be performed separately. Rather, the GCS motor score assesses the ability of the brain to recognize input and respond

with appropriate motor patterns, which must be tested systematically. As one common example, "localization" on the GCS is an important finding with considerable prognostic and acute management significance, and assessment for this feature should be performed by a standard and reproducible protocol, upon arrival and in serial exams. For children older than about 18 months, the author prefers bending the elbow and placing the forearm at the patient's waist. Localization is confirmed if a pinch of the anterior trunk elicits flexion of the arm so that the hand moves toward the noxious stimulus, and a second pinch at the lower trunk or thigh results in extension of the arm toward that stimulation. Nonspecific reaching for an endotracheal tube can be an unreliable indicator of the ability of the injured/recovering brain to accurately identify the specific source of noxious stimulation, and should not be used as part of a GCS determination.

Children and adolescents with less severe brain injuries who can be moved safely are most effectively examined by turning on the lights, removing bedcovers, speaking gently to the child, and when possible, sitting the child up on his or her own power, which aids in alerting. When allowable, a cold drink or ice chips can help a child awaken so that the neurologic status can be separated from the lingering effects of deeper stages of sleep. Considerable clinical information can be gleaned from this type of approach rather than applying noxious stimulation as the first maneuver.

Several clinical presentations can appear to represent behavioral issues in children presenting with head injury when in fact they arise from neurologic dysfunction. First is behavioral disinhibition and irritability. Head-injured patients, particularly adolescents, may alternate between obtunded and explosive, combative, and rude, even in youngsters who are calm and polite at baseline. This can cause both involuntary emotional judgments and failure of recognition of neurologic dysfunction on the part of clinicians as well as consternation of parents, and should be both recognized and explained as something that reflects consequences of the injury. Similarly, extreme irritability, especially when coupled with arching or opisthotonic posturing, can indicate incipient herniation in younger children.

A second scenario is unrecognized aphasia. This occurs most often in children with dominant temporal lobe contusions, and can appear superficially to reflect uncooperative or disinhibited behavior, or decreased mental status. If a patient appears alert but does not follow command, aphasia should be considered.

An additional acute assessment pitfall in children is cortical blindness. This can occur in otherwise relatively alert-appearing children, typically after an impact to the back of the head (such as falling from a swing). Young children may be very frightened by their transient blindness and yet unable to express what is wrong, so may appear inconsolable or combative. Cortical blindness almost always resolves in the first day or two, and should be kept in mind in the setting of a confusing presenting exam.

Infants and young children present their own assessment difficulties. A number of analogues of the GCS for preverbal children have been developed over past decades, and most of these have never been fully validated as predictors of outcome, although they can be useful in older babies. Younger infants can be particularly challenging, as the GCS contains behaviors that are not part of the normal infant repertoire (such as localizing painful stimulation). For this reason, the Infant Face Scale (IFS) was designed as a 3–15 point scale analogous to the GCS but with specific assessment of age-dependent normal and abnormal response patterns after traumatic brain injury [16]. The scale pays particular attention to the fact that very young infants can appear superficially "awake" even with major cortical damage, due to the persistence of brainstem modulation of behavioral patterns. The severity of injury can be identified, however, by diminution in grimacing or crying to noxious stimulation; this can be assessed even while a child is intubated. The scale also takes into account the fact that infants can demonstrate

movements that superficially may appear voluntary but in fact reflect seizure activity, which is common after trauma in this age group.

One should not wait for a change in the GCS or IFS score to recognize deterioration. These scales reflect the best that a patient can do, but do not reflect subtle changes that an experienced provider, such as the bedside nurse, will recognize. These subtle findings include longer latency between stimulus and response, increasing requirement to repeat the request or stimulation to garner a response, impersistence of the response, and a lower excursion of movement. In general, a patient who "sleeps unless stimulated" is a patient with the potential to worsen, and should be observed especially closely.

Imaging

Radiation doses to which children are exposed in an acute polytrauma evaluation are considerable, and the smaller and younger the child, the greater is the potential for damage. Both increased risk of malignancy and potential cognitive injury have been reported from CT scans in children [17–19]. For this reason, much effort has gone into reducing unnecessary examinations and reducing the dose of those undertaken (for instance, the Image Gently campaign) [20]. Both head and extracranial CT protocols exist with reduced radiation, and these typically are sufficient for initial assessment. However, for further assessment of both significant brain and spine injuries, MRI has more sensitivity and specificity for parenchymal assessment, especially in comparison to reduced-dose CT scans in which resolution is lost. In addition, for assessment of vascular injuries, while both CTA and MRA can be performed, MRA is often sufficient with no additional radiation exposure, although this should be decided on a case-by-case basis.

Rapid MRI techniques as well as tailored examinations can be performed with little or no sedation in many clinical scenarios, and often give additional information about acute injury as well as unfolding pathophysiology of injury. Thus, MRI is used increasingly both in the Emergency Department and as the follow-up imaging modality of choice in many pediatric settings [21]. The National Institutes of Health, along with other government agencies, sponsored the creation of Common Data Elements for Traumatic Brain Injury, including parameters for both CT and MR imaging in children, which can be used to guide imaging decisions, protocols, and interpretation in children [22, 23].

Spine Evaluation

The level of suspicion for spine injury in children is dependent on patient age, mechanism, history, and initial exam [24]. Specific scenarios are described in more detail below. As a general rule, the spine should be appropriately immobilized until it can be adequately assessed either on clinical or radiologic grounds. Even young children usually can be assessed via appropriate clinical examination, and not every child requires imaging. When imaging is necessary, it should be kept in mind that preadolescent children have a higher risk of ligamentous, rather than bony, injury, and often are optimally assessed with MRI depending on the specific scenario, though this evolving area continues to evoke considerable controversy [25–27]. From a systems point of view, having a coordinated spine trauma service, typically involving pediatric neurosurgery and orthopedic surgery, is helpful in management decisions. While in infants, ligamentous injuries may heal spontaneously with appropriate immobilization, the trend has been toward early instrumentation in older children with unstable spine injuries. Distraction injuries are a special category in young children, and are discussed in more detail below.

Risks Associated with Sedation

Since an association between neurotoxicity and exposure to common anesthetic agents in immature animals and possibly in children was

discovered, parents and clinicians have expressed increasing concern about possible deleterious effects from sedation for procedures, imaging studies, or as part of medical care [28–30]. For this reason, specific choices of agents may be preferred by pediatric anesthesia providers and critical care specialists. As a general rule, procedures and imaging studies requiring sedation should be as efficient, tailored, and as brief as possible, and sedation in the emergency department or intensive care unit likewise should be as brief and as safe as possible. Using sedation and sedating analgesics only as needed and at the lowest doses possible also enables serial neurologic exams, which can be of great help in following the neurologic status during injury progression.

General Algorithm for Tailored Acute Triage and Initial Management

While many "guidelines" for acute management of head injury have been utilized, most of these are based on the GCS at presentation and have been applied primarily to those at the severe end of the injury spectrum. In "severe" pediatric head injury, there are few topics on which management can be recommended at a high level of evidentiary certainty, with the majority of attempts to compile literature-based recommendations for management existing at the "option" level of evidence [31]. Because of limitations in the GCS in capturing all the elements that go into decision-making about acute management, there has been an effort in the head injury community to better tailor management to other features of the specific injury, including the pathoanatomic type of injury and other exacerbating injury or host factors [10]. In addition, algorithms need to include patients with less severe injury presentations, but who may be at risk for deterioration, including children who may be difficult to assess. To this end, a characterization of injury based not only on severity, but also on history, mechanism, examination findings, physiologic stressors, host factors, and imaging findings has been developed, which uses these various features to characterize injuries as "swelling/deterioration-prone" versus "nonswelling/deterioration-prone" injury patterns (Table 29.1). This characterization is then the starting point for a simple algorithm to help guide initial triage and management, in order to promptly attend to immediate problems and treat evolving patterns before deterioration (Fig. 29.1). While some of these principles may be obvious to the experienced neurosurgeon, the algorithm can serve as an initial guide for communication among team members as to why different patients with similar clinical appearances with respect to GCS score may be handled in different ways. The general principle is to intervene proactively to prevent or promptly manage those problems which are known to evolve in the acute and subacute management epochs under specific types of scenarios, and can be associated with increased morbidity or mortality. The tools include surgical intervention, medical management, and continuous close observation and monitoring. This algorithm can be applied to pediatric or adult patients [32].

Communication Among Team Members/Specialties and Families

The family of an injured child is a family in crisis, and often relatives are unable to fully process the initial information provided. Also, many parents are preoccupied with a sense of failed responsibility to protect their child, concern for additional injured family members, or with anger at others who they see as responsible for the injury.

In the author's experience, it is helpful to sit down with the family after the initial assessment, along with the other care providers (e.g., trauma surgeon, orthopedic surgeon, emergency and/or critical care physician, social worker, etc.), to provide a simple overview of what the overall status is, who is who on the team and who is "in

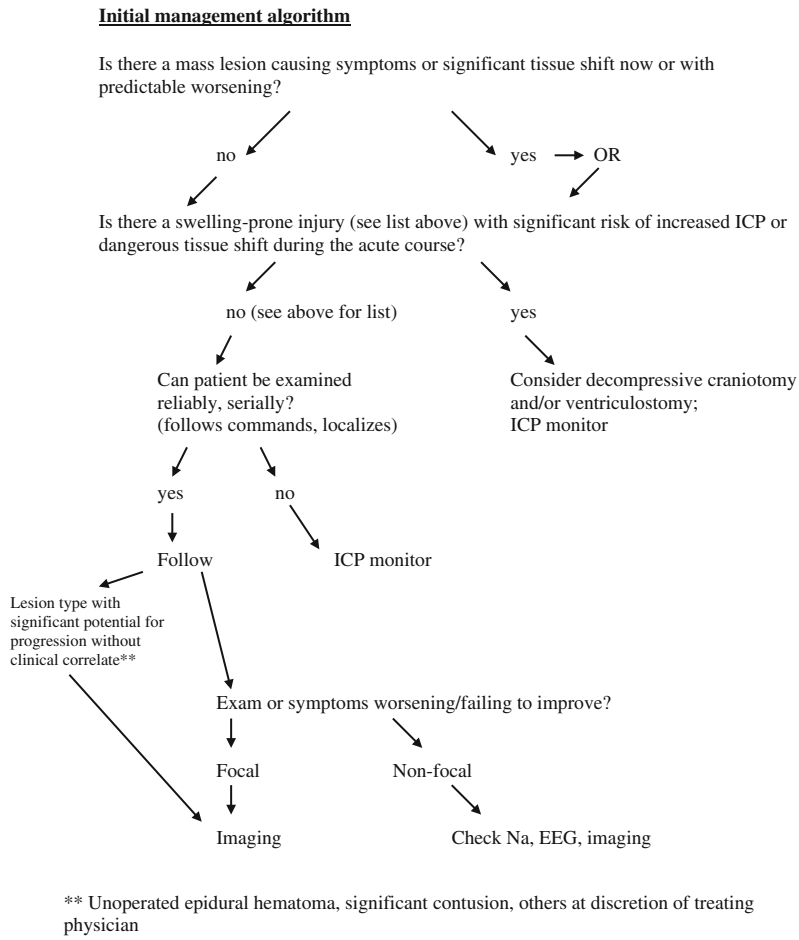

Fig. 29.1 Injury characterization is used in an algorithm designed to prevent specific types of complications, and to match the tools needed to monitor these changes with the specific clinical injury pattern. This approach was designed to be applicable to all ages of patients. Adapted from [1], with permission

charge" of what issues, and what are the planned next steps in evaluation and management. It can be helpful to address immediately typical concerns like the child's level of pain or anxiety, and what family members can do (or do not need to worry about doing) to be of help. Additionally, it can help to express explicitly that most families cannot fully remember or make sense of all they are told, and that the team expects them to have additional questions and will be available should questions or new information arise. Determining which family members will be the points of contact with the extended family can be useful at this initial meeting. Finally, it can be reassuring to explicitly plan a meeting for the next day, where the situation will be clearer, and family members will have a chance to ask more detailed questions.

Specific Injury Scenarios—Recognition, Acute Management, and Pitfalls

As there are a number of common scenarios involving specific mechanisms associated with pathoanatomic patterns of injury, we will outline some of the mechanism patterns and acute management concerns which may be helpful to recognize in children of different ages.

"Missile" motor vehicle occupants This injury scenario occurs when young children (infants, preschool, and early school age) are unrestrained inside a vehicle involved in a high-speed crash. Because they are mobile, they can become essentially airborne inside the vehicle, often

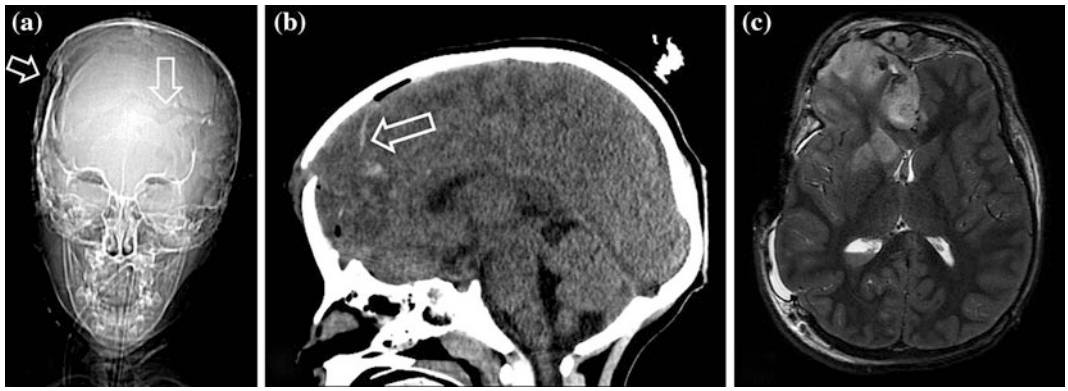

Fig. 29.2 CT scout image (**a**) and sagittal reconstruction (**b**) of a 4-year-old unrestrained child in a high-speed motor vehicle crash. She had major scalp avulsion, open depressed and widely diastatic skull fracture (*arrows*), and frontal dural rupture with cerebral hernia (*arrow*, **b**), and required aggressive fluid resuscitation. **c** Postoperative T2-weighted MRI (postinjury day 1) showing multifocal surface contusions, epidural collection at site of frontal diastatic fracture and dural rupture, and damage to the deep gray matter

moving head first, and can sustain major contact injuries to the head as it strikes an unyielding surface (Fig. 29.2). Because of significant scalp and skull injuries, the ability to expand the elastic scalp with subgaleal hematoma, and a relatively low blood volume at baseline, young children may present with shock just from skull and subgaleal hemorrhage, even without major scalp laceration or concomitant somatic injury. This problem is exacerbated if there are accompanying lacerations, long bone fractures, or visceral hemorrhages. Because children have robust cardiovascular compensatory abilities, at initial presentation they may appear relatively well from a hemodynamic point of view, but are prone to "crashing" into instability as blood loss reaches a critical threshold, taking the unwary clinician by surprise. This scenario can be complicated by the fact that a motor vehicle crash involving young children may be associated with multiple patient/occupant arrivals simultaneously, and so can predispose to distractions for the care team from an initially relatively well-appearing child. Thus, the management mantra in this setting is to pay careful attention to volume replacement early, typically with isotonic fluids, and to continue close and frequent monitoring during the acute postinjury period.

In addition, young children with this trauma scenario typically sustain surface contact injuries with epidural hemorrhages and multifocal contusions, and only rarely sustain "bland" diffuse axonal injuries, likely related to the predominance of contact mechanisms, the predominantly translational (rather than rotational) nature of the motion, and smaller brain volume. If patients arrive at the hospital from the scene, and have small epidural collections that do not warrant immediate surgery, it should be kept in mind that both (needed) volume replacement and relative coagulopathy increase the chance for continued or delayed hemorrhage. Expanding venous epidural hemorrhage or bleeding into contused or lacerated cortex are the most common causes of delayed hemorrhages in this setting. For this reason, follow-up imaging, often with rapid MRI techniques when available in order to minimize brain irradiation and to increase the sensitivity for parenchymal contusion detection, should be performed at least once, and then serially as needed. At the author's institution this is done with rapid T2 imaging in three planes and a susceptibility-weighted sequence, which in total take less than 5 min to complete (Fig. 28.2).

A final caution is that some children in this setting, typically those in a slightly older age group (e.g., school age), may present with impressive facial lacerations or other facial trauma impeding communication or eye opening, but relatively less intracranial injury due to

increased skull strength and the absorption of impact in the facial skeleton. The caution here is that such children may be completely awake and alert in spite of a superficially frightening appearance, and should be handled with sensitivity during the initial trauma evaluation and management.

Children struck by motor vehicles The injury patterns vary in this scenario depending on the details of the mechanism and the size of the child. Older children and adolescent pedestrians present similarly to adults, and may have lower extremity long bone fractures, visceral injuries, and both contact and deceleration injuries such as subdural hemorrhages and diffuse axonal injury. Younger children can have a variety of injuries, but their lower center of gravity sometimes helps minimize the force of the impact. Children riding bicycles, skateboards, or other wheeled conveyances may have an initial height and velocity that can exacerbate the magnitude of the forces experienced. There is some preclinical evidence and anecdotal clinical evidence that adolescents may have a longer time course of brain swelling after contusional injury; thus, adolescents may require extra observation when recovering from significant contusions to avoid premature withdrawal of treatments such as electrolyte management and anticonvulsants [33].

"Face first" injuries While some of these considerations are covered in the specific mechanism scenarios above, some children have falls, sports (such as skiing), or other mechanisms that result in high-force facial injuries along with intracranial injuries. A few points can be kept in mind in this setting. One is that forces may travel through the frontal lobe, across the anterior skull base, and into the midbrain. Such patients occasionally present with dilated pupils because of focal midbrain involvement, rather than having this clinical pattern reflect herniation. Recovery of function may be possible, and this should not be taken as a sign of necessarily poor prognosis. Second, pituitary stalk injury often occurs in this setting, and needs to be monitored with endocrinology assessments over time and a detailed high-resolution (typically T2) MRI to look for stalk integrity, which can help predict whether diabetes insipidus is likely to be transient or permanent, and whether an intermediate phase of excessive antidiuretic hormone secretion is likely to occur. Finally, bifrontal swelling is sometimes extreme, and decompression may be warranted. Involvement of the sagittal sinus if fractures have occurred in this area needs to be anticipated.

Pediatric passengers with restraints Properly used vehicle restraints can decrease injury burden to an amazing degree. Restraints coupled with appropriate airbags and other safety engineering advances are the main reasons for decreased mortality over the past decades. However, a few situations require special consideration. First, older children with lap belts can sustain Chance or other spine fractures, in addition to visceral and soft tissue injuries related to the restraint itself [34, 35]. For this reason, it is imperative that emergency responders and the team at the initial trauma hospital follow rules for immobilization and for a complete neurologic assessment. This must include an efficient but thorough exam of the sensorimotor findings of the upper and lower extremities and sacral dermatomes. If a child has been sedated or given pharmacologic paralysis at the scene, the handoff at the receiving center must include clear indication of the movement status at the scene of all four extremities, and their strength. Children who are unable to be examined and for whom there was no clear exam at the scene should be treated as though a spine injury is present.

While most Chance-type fractures of the thoracolumbar or lumbar spine involve obvious bony injury which is visible on plain films or CT scan, on occasion spine injuries will arise from transient displacement followed by subsequent relative realignment. For this reason, an MRI may be needed to fully assess the spine in a very young child.

Another diagnostic and acute management pitfall in children in restraints is cervical distraction injury. Because of the relative size of the head in infants and toddlers restrained in car seats and because of the relative immobility of the shoulders and torso in a typical carseat harness design, in a high-speed crash, the head may be

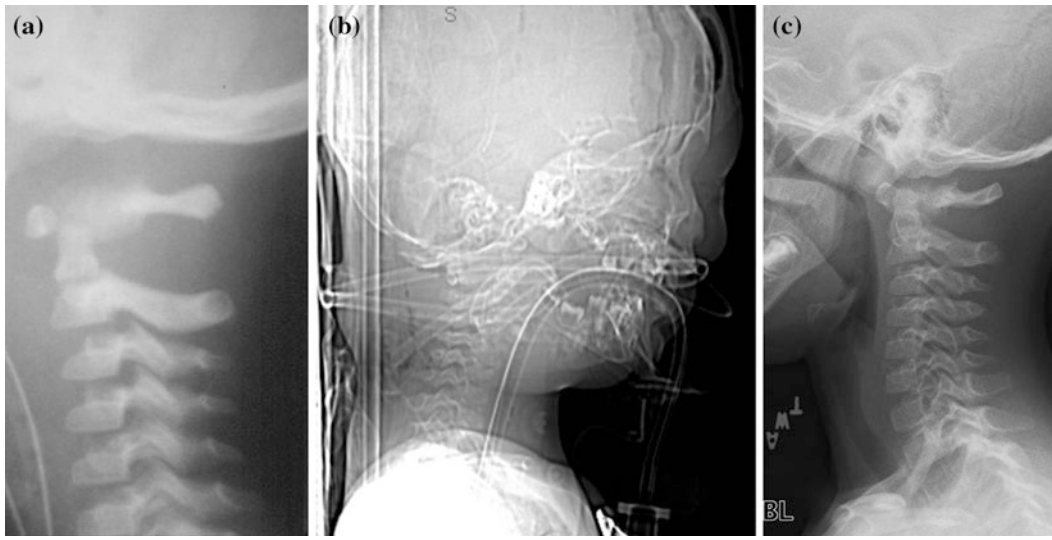

Fig. 29.3 Cervical spine injuries in toddlers. **a** Distraction injury. Lateral cervical spine X-ray in a toddler restrained in a child seat in a high-speed motor vehicle crash. Patient was neurologically intact; MRI showed extensive subarachnoid hemorrhage at the cervicomedullary junction and ligamentous injury treated with prolonged immobilization. **b** Fatal injury of toddler run over by truck in driveway. He had no vital signs, multiple skull fractures, and cervical vessel disruption along with cervical spine injury. **c** Lateral spine film of 13-month-old struck by garage door. He had linear occipital skull fracture and resistance to full neck extension. MRI showed posterior interspinous soft tissue edema only, with normal cervicomedullary junction ligaments and no hemorrhage. He was treated with nonsteroidal analgesics and gradual increase in activities

subjected to distraction force which is transmitted to the cervical spine. This can result in atlanto-occipital and/or atlanto-axial ligamentous distraction injuries; additional levels may be involved as well (Fig. 29.3) [24]. The distraction can be exacerbated if early responders attempt to immobilize the spine by applying a cervical collar which is too big for a young child, thus causing even more distraction. Thus, young children are best immobilized with sandbags or intravenous bags on either side of the head, held with tape, in neutral position (which sometimes requires elevation of the trunk to compensate for the prominent occiput) if a suitably small collar is not readily available. As in all transported trauma patients, having a clear understanding of what the child was doing at the scene with respect to movement of each upper and lower extremity is invaluable. In distraction injuries, brachial plexus stretch injury also may occur, as can pupillary and/or eyelid asymmetries due to Horner's syndrome, which requires assessment of each pupil's ability to dilate in dim light, as well as assessing for ptosis. MRI should note any retroclival hemorrhage or other evidence of ligamentous injury.

Two additional points should be kept in mind in these related scenarios. First, while vascular injuries can occur in many situations, any time there is a significant distraction mechanism, consideration should be given to a vessel assessment (often obtained via MRA at the time of the evaluation of the spinal soft tissues or brain). Vertebral artery injuries can occur with cervical distraction whether a vertebral fracture is present or not. The second point to be made is that children whose injury mechanism has resulted in seatbelt injuries also have experienced forces which may increase the risk of cervical distraction injuries and vascular injuries, and this should be assessed even if the main focus is on the more local effects of the seatbelt. Thus, a child with a lower extremity neurologic deficit from a lap belt injury should undergo a complete upper extremity examination, including assessing for cervical tenderness in the distribution of the

large cervical vessels. Any report of transient neurologic deficits should prompt immediate evaluation.

"Ping-pong" fractures These are smooth, focal indentations of the skull in infants and toddler-aged children which result from the application of focal force to the calvarium. A common scenario is a fall from standing height into the corner of a coffee table or other protuberant object, but these can occur from focal impacts during polytrauma scenarios as well. Ping-pong fractures also can occur from birth. They are almost never associated with significant intracranial trauma underlying the indentation, and the bone itself typically is incompletely fractured. Scalp swelling is variable, and sometimes the lesion will come to light only after a few days have passed when the indentation becomes visible. In young infants these usually will remodel spontaneously; larger lesions of those in a visible location such as the forehead can be readily elevated through a small burr hole at the edge of the indentation using a curved instrument, although if the fracture is more than about 1-week old, more extensive removal and reshaping of the bone may be needed, as healing may have progressed to the point that the bone is stiffer and so not easily "popped" back into shape. There is little evidence that conservative management is associated with worse outcome with respect to neurologic deficits or seizures, both of which are extremely rare in this setting.

Brain laceration with linear skull fracture in infants/toddlers While brain laceration can occur from depressed skull fractures and penetrating injuries in all ages, it can be more difficult to recognize in infants and toddlers when it occurs in a specific pattern which depends on a malleable skull, which is not seen in older children and adults. This pattern typically occurs from a mechanism involving significant force, such as a fall from a window or a motor vehicle collision, when a focal force beyond the tolerance of the skull causes a linear skull fracture which "bends in" transiently, tearing the dura and lacerating the underlying cortex and sometimes subcortical white matter. After this brief, transient displacement, the skull may resume its more typical convex configuration. While the fracture edges may appear a bit offset or diastatic, the key to diagnosis of this injury is the associated line of edema and/or hemorrhage seen in the laceration cavity of the brain parenchyma. This may be subtle on CT and sometimes is better seen with edema or blood-product-sensitive MRI sequences (Fig. 29.4). The importance of recognizing this injury is threefold, first because cortical injury in young children increases the risk for seizures, which may be subtle or even subclinical in this age, and second, because of the high associated with dural and arachnoid tears which may predispose to formation of the so-called "growing skull fracture" which usually requires surgical repair. Some authors have advocated early exploration/repair when this pattern is identified. Finally, it may be helpful to counsel families that this is a more significant focal injury than may be apparent initially, and that swelling followed by encephalomalacia is the typical evolution of injuries of this type. In infants, clinical deficits may not be apparent for injuries very early in life, but may become more apparent with subsequent maturation of motor control networks. Thus, a child with a brain laceration in motor cortex may not show a major deficit until months or years after the injury, and it may be prudent to follow children to see whether rehabilitative interventions may be helpful in minimizing late effects.

Periorbital, orofacial, and vertex penetrating injuries Because the bone is very thin in certain locations around the facial and periorbital skeleton in children, and even over the vertex in infants, penetrating injuries in these locations can be missed unless care is taken to identify them. Sometimes objects penetrate transiently, and a dot of air and/or a small skin laceration is the only clue that a foreign body has entered the intracranial compartment. Penetration through the roof of the orbit or nasal cavity with sharp, pointed objects such as sticks, metal, or glass can occur with minimal surface stigmata. Unless an injury is very superficial and "clean," management usually involves surgical debridement, intraoperative culture, and repair, with broad-spectrum antibiotics for a variable interval

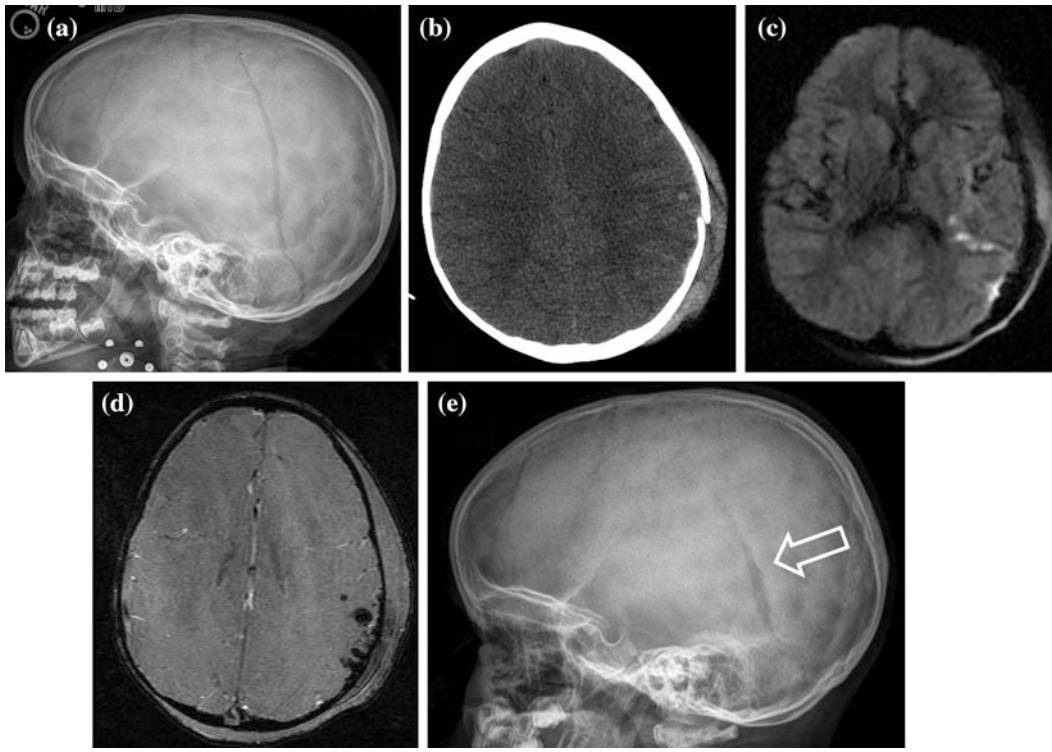

Fig. 29.4 A 3-year-old with fall from second story window. Note large diastatic left temperoparietal fracture in CT scout film and axial image (**a**, **b**). **c** and **d** FLAIR and susceptibility-weighted imaging show linear cortical laceration at site of transient in bending of malleable skull. **e** "Growing skull fracture" could be seen at 2 months after injury (*arrow*)

depending on the circumstances and judgement of the treating team as well as culture results. Unrecognized penetration can present with a delayed infection or sometimes with a vascular injury. MRI may be more sensitive than CT for the parenchymal changes, while CT is better at detecting subtle breaches in the bony anatomy. MRA or CTA may be a useful consideration in these cases depending on the location of the injury.

Crush injuries A crush injury is a static injury, meaning it occurs from relatively slow application of force. Because of their "engineering," children are surprisingly resistant to slow application of force, which assists with avoiding injury during birth. Thus, the interdigitation of the cranial sutures, the malleability of the subarachnoid space, and the high water content of the unmyelinated brain all allow for gradual deformation without tissue failure until forces are extreme. This is the reason that many children can survive toppling furniture or television sets and having their heads run over by motor vehicles, and many can do quite well from a cognitive point of view [36, 37].

Fatal crush injuries typically occur when the forces are extreme, when they are not relieved promptly, when there is a cervical-cranial distraction, or when the crushing object prevents breathing (Fig. 29.3). When not fatal, children may present with multiple calvarial and/or basal skull fractures, marked subgaleal hematoma, and variable strain injuries to cranial nerves, vessels, and brain parenchyma. Because victims are usually toddler or preschool age, they may present with shock from blood loss into the scalp. Children with crush injuries often have a frightening appearance on presentation, with

marked facial and scalp swelling, and sometimes with airway compromise. However, the brain may be relatively spared, and a good recovery is often possible with appropriate management. Pituitary stalk injury can result in delayed diabetes insipidus so careful attention to all details needs to ensue for optimal outcome.

Gunshot wounds Children with gunshot and explosives wounds are managed similarly to adults, with the caveats mentioned above regarding blood volume, and with their superior plasticity kept in mind. Thus, the rules that predict mortality do not always apply to young children, who may do better than expected, both with mortality as well as with morbidity. For these reasons, an aggressive approach is generally undertaken, but children with significant injury to the midbrain, brainstem, and other vital deep eloquent areas are unlikely to overcome the effects of injury, and early discussions about level of care are appropriate.

Suspected nonaccidental injuries Children with brain injury from nonaccidental mechanisms may have polytrauma including skeletal and visceral injuries, and require a full evaluation by a comprehensive trauma team, even when the brain injury appears to be the predominant clinical feature. Likewise, children with inflicted injury who come to attention because of extracranial injury may benefit from brain imaging, particularly if the clinical exam is limited because of age or other injuries [38, 39]. The most common intracranial imaging findings include subdural/subarachnoid hemorrhage with or without additional brain parenchymal damage. The most severe form of injury is unilateral or bilateral hemispheric hypodensity, or "big black brain" (so-called because of its extensiveness and appearance on CT scan), which carries a high rate of mortality and long-term morbidity [40, 41]. It should be kept in mind that this same injury pattern can be seen in accidental trauma, although less frequently than it is seen in nonaccidental injuries.

The most common histories in inflicted neurotrauma include a history of symptoms but no history of trauma (i.e., the child presents because of poor feeding, vomiting, lethargy, irritability, seizures, apnea, or unresponsiveness), or a history of a low-height accidental fall [42, 43]. It should be noted that accidental low-height falls can result in skull fractures in young children, and that thin venous epidural collections associated with fractures can be mistaken for subdural hematomas by radiologists unfamiliar with this appearance in children. This can occur because the collections can be thin and crescent-shaped, and also because in the setting of a skull fracture, the guideline that "epidurals do not cross suture lines" can be contradicted in the presence of a fracture. Thus the neurosurgeon needs to have a familiarity with which mechanisms typically are associated with which injury patterns at which age. MRI can be very useful for greater detail of extra-axial hemorrhages and parenchymal injuries, diffusion abnormalities, cervical spine evaluation, and prognostication when large-scale abnormalities are identified. It should be kept in mind that because of mixing of CSF and blood products in the setting of arachnoid tears, no imaging modality can reliably determine with certainty whether prior injury has occurred nor the exact timing of injury [27, 44, 45]. The neurosurgeon and patient are best served by calling on experts in child abuse injury patterns who can help make determinations about likely cause of injury and need for further evaluation, including skeletal survey, retinal examination, and bone scan.

Management of nonaccidental trauma follows general guidelines for brain trauma management, with the following additional considerations. Infants with brain injury in general, and those with inflicted injury in particular, are at high risk of seizures. Early prophylaxis (generally with levetiracetam or, sometimes, phenobarbital) is usually initiated, and continuous EEG can be helpful in early management. Evidence of cervical pathology is found in a high percentage of fatal cases, but a low percentage of clinical cases; nonetheless, MRI can be helpful in assessing for ligamentous injury if this is a concern [27]. Children with unilateral hemispheric hypodensity and incipient brain swelling can benefit from early hemicraniectomy, as the subfalcine herniation damage to the contralateral frontal lobe can

be avoided, thus preserving at least one functional frontal lobe for future learning and behavioral regulation. Children with bilateral hemispheric hypodensity (best seen as bilateral diffusion abnormality on MRI) have extremely poor outcomes [46–48]. When this diagnosis is certain, conversations about goals of care may be appropriate.

Brain Death in Children

As a general rule, brain death protocols for older children and adolescents are similar to those for adults. Protocols differ at different institutions, but some guidelines suggest longer periods of observation for infants and young children [49]. Adjunctive imaging findings such as nuclear medicine brain scans, in concert with a formal examination showing no clinical evidence of brain function, is considered definitive in defining brain death, and may be helpful for families wishing to consider organ donation after catastrophic injury.

Outcomes

For many injuries, children do better than adults, and adult predictions should not be used without modification for children. In particular, children with diffuse axonal injury almost always regain consciousness, and many have relative preservation of overall intellectual function, though with varying degrees of motor and cognitive deficits. Children with limited focal injuries also often exhibit surprising recoveries, even when the injury is in eloquent cortex. However, some studies show that the effects of injury may become more apparent with time, as cognitive demands increase with age, and as psychosocial and other behavioral processing becomes more important for normal functioning. For this reason, it is recommended that consideration of assessment along multiple domains be given after head injury in children [50, 51]. Early input from and follow-up by pediatric physiatrists and neuropsychogists may be extremely helpful in tracking progress and in making recommendations for specific therapies and school accommodations to maximize outcomes.

Finally, it can be helpful for the neurosurgeon to remain involved in long-term follow-up for pediatric trauma patients. This is helpful to the child and family, who often identify the neurosurgeon as a critical member of the acute care team. It is also helpful to the clinician, who builds long-term experience on which to base decisions for future patients. Trauma is increasing worldwide, and children deserve neurosurgeons who have an interest in their management and outcomes, and in improving the care of trauma in the future.

Summary

Infants, children, and adolescents have unique injury patterns and responses to injury. Understanding these patterns helps members of the polytrauma team to facilitate effective and coordinated functioning and to optimize patient outcomes and family experience. Outcomes from pediatric neurotrauma can be extremely gratifying. Even when disabilities persist, how a family experiences the care can improve or exacerbate their perception of the outcome indefinitely, so sensitivity and communication are the keys. Pediatric trauma is increasing across the world, and continuing efforts in research and implementation are warranted both to prevent injuries and to improve the care of injured children and their families.

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Care of Patients with Burns and Traumatic Brain Injury

30

Leopoldo C. Cancio and Basil A. Pruitt Jr.

Introduction

Patients with both severe thermal injury and traumatic brain injury (TBI) represent a small, but particularly challenging, population. Palmieri and colleagues recently analyzed the National Trauma Data Bank (2002–2009), finding that 711 of 8818 burn patients (8 %) had trauma, burns, and TBI. These multiply injured patients had much higher mortality (17 %) than burn patients without TBI or trauma (6 %) (T. Palmieri, personal communication, 2015). The purpose of this chapter is [1] to delineate patterns of injury that produce combined TBI and thermal injuries; [2] to deconflict the priorities in management of TBI, and those of severe thermal injury; and [3] to elucidate how the body's multisystem responses to severe thermal injury and to subsequent critical illness generate additional changes in central nervous system (CNS) function which further complicate recovery and rehabilitation.

Patterns of Injury

For many patients, the mechanism of injury which caused the patient's burns may also have caused mechanical trauma, and the initial assessment therefore must include evaluation for such nonthermal injuries. The following are examples of such high-risk mechanisms:

- Burns in the context of suspected child or elder abuse
- High-voltage electric injury
- Lightning injury
- Motor vehicle crashes
- Explosions
- Assaults
- Structural fires causing loss of consciousness

Each of these mechanisms merits a thorough workup for nonburn injuries. High-voltage electric injury places the patient at risk of tetanic muscle contractions, which may cause fractures of any portion of the spinal column, as well as internal injuries. Evaluation of these patients should proceed as if the patient had sustained a high-speed motor vehicle crash [1]. The same is

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true of lightning injury [2]. Burns associated with the operation or maintenance of motor vehicles range from those sustained in fires which take place while the vehicle is at rest (in which case the risk of nonthermal trauma is low), to those resulting from a high-speed collision. It is usually possible to risk-stratify these patients based on information obtained from Emergency Medical Services (EMS) personnel [3]. Explosive mechanisms of injury are frequently seen in casualties on the battlefield. Improvised Explosive Devices (IEDs) became the leading mechanism of thermal injury during recent conflicts in Iraq and Afghanistan. These events carry an elevated risk of both thermal injury and nonthermal trauma. A common scenario involves an IED detonated against a military vehicle. The initial explosion leads to mechanical injury, whereas secondary vehicular fires cause thermal and inhalation injury [4]. Structural fires causing loss of consciousness are common in civilian practice. The fire environment presents multiple inhalation hazards which may lead to loss of consciousness and brain injury. These include decreased ambient levels of oxygen, and increased ambient levels of carbon dioxide, carbon monoxide, and cyanide. The patient who is "found down" at the scene of a fire may have been exposed to a combination of these factors [5]. In summary, even extensive thermal injury need not produce an alteration in the neurologic examination during immediate postburn period. Rather, a decreased level of consciousness, or a focal neurological deficit, should prompt a thorough search for other problems.

Primary Survey

The priorities of emergency management for patients with burns and neurotrauma (the "ABCs") are the same as those for other critically ill patients, with modifications based on the specific injury pattern encountered.

Airway Patients with severe thermal injury may require early endotracheal intubation for several reasons. Direct thermal effects and the indirect effects of generalized edema on oral, pharyngeal, and laryngeal structures may precipitate upper airway obstruction and rapid airway loss. Thus, early prophylactic intubation of patients with symptomatic inhalation injury or with extensive (e.g. >40 % TBSA) burns is prudent. Intubation of these patients should be performed by an experienced operator [6]. Lower airway and parenchymal inhalation injury causes abnormalities of ventilation–perfusion matching, and may mandate intubation in order to facilitate positive-pressure mechanical ventilation and pulmonary toilet. A depressed level of consciousness further increases the level of concern.

Breathing During the initial days after injury, it is unusual to fail to achieve oxygenation and ventilation goals appropriate for treatment of patients with TBI. Routine care of patients with inhalation injury includes provision of nebulized beta agonists, avoidance of injurious levels of tidal volume or of inspiratory pressure, and frequent suctioning of airway casts and other debris [6]. Our mechanical ventilator of choice for patients with inhalation injury is the VDR-4 (Percussionaire, Sandpoint, ID), which delivers high-frequency percussive ventilation and facilitates pulmonary toilet. It has been utilized in the care of patients with TBI and increased intracranial pressure. VDR ventilation may decrease ICP by improving PCO_2 clearance at lower inspiratory pressures [7, 8]. Patients with encircling thoracic burns (straightjacket-like) may develop decreased compliance, requiring emergent bedside escharotomy. Incision through the full thickness of the eschar (burned skin) along the lines indicated in the Figure restores compliance and gas exchange [9].

Circulation Burns of 20 % TBSA or greater cause loss of fluid, similar in composition to plasma, from the intravascular to the extravascular space, resulting in edema formation and hypovolemic shock. Overt hypotension may not be seen until significant volume loss has occurred, or until the patient receives a dose of narcotics or sedatives. Circulation management includes intravenous (i.v.) access (failing that,

intraosseous access as a temporizing measure). Fluid boluses are generally unnecessary and are avoided unless hypotension occurs. Hypotension despite fluid resuscitation should motivate a look for underlying causes, such as occult hemorrhage. Occasionally, institution of vasopressin and/or norepinephrine by continuous infusion is necessary in order to treat hypotension [10], while searching for underlying causes.

Disability A thorough neurological examination is an essential aspect of the initial evaluation of any thermally injured patient. Sedation and analgesia may make detection of neurologic deterioration difficult in patients with burns and TBI; liberal performance of computed tomographic (CT) scans of the head is therefore recommended. The combination of TBI and massive fluid resuscitation for burn shock argues in favor of ICP monitoring in patients with combined injury. At the same time, ICP monitors may cause meningitis, especially if they pass near or through burned skin. Thus, they should be placed through unburned skin if possible, and should be removed as soon as they are no longer needed [11, 12].

Treatment of pain is based on frequent, small i.v. doses of a narcotic. Ketamine at a starting dose of 0.25 mg/kg i.v. bolus is an ideal analgesic for patients in burn shock. Ketamine-based total i.v. anesthesia is commonly used in patients with major burns [13] and TBI [14, 15]. A recent meta-analysis did not show an association between ketamine use and increased ICP in patients with TBI [16]. In hypovolemic burn patients, ketamine rarely induces hypertension. Sedation can be provided by i.v. lorazepam at a dose of 0.5–1 mg, but benzodiazepine use is minimized if possible. Induction of general anesthesia is performed with great care during burn shock because of the risk of hemodynamic collapse.

Exposure and environmental control Nonthermal trauma must be sought and identified. Patients are at high risk of hypothermia because of the loss of the insulating properties of the skin. Great effort must be expended to keep these patients normothermic: warm fluids, warm room (>85 °F), heating lamps, forced-air warming blankets (e.g., 3 M Bair Hugger), and reflective blankets.

Fluid Resuscitation and Edema Management Burn-induced increase in capillary permeability results in edema formation and loss of blood volume over the first 24–30 h postburn. During this period, plasma-like fluid exits the microvasculature, and must be replaced. Intravenous infusion of a crystalloid solution, most commonly lactated Ringer's (LR) solution, is the cornerstone of therapy. The volume of crystalloid fluid infused during the first 24 h postburn can be initially predicted by the modified Brooke formula: volume in mL = 2 × TBSA × weight in kg. Half of this volume is scheduled for delivery over the first 8 h, and half over the second 16 h. This provides a starting rate for the infusion, which is then titrated every hour or 2, up or down, in order to achieve a target urine output of 30–50 ml/h for adults. Often, the rate has to be increased during the first 8–9 h, and then has to be decreased, in response to the urine output [17]. Other factors to consider when adjusting fluids include the base deficit or lactate; the central venous pressure or stroke-volume variability; the presence of hypotension or need for pressors; and the total volume infused [18].

The latter is a critical point. As plasma leaks from the vasculature and into the tissues, edema forms. Inside the confines of restricted compartments such as the abdomen and extremities, excessive edema formation leads to compartment syndromes. Experience with the abdominal compartment syndrome (ACS) identified a volume of 250 ml/kg over the first 24 h as a volume associated with increased risk of ACS [19]. Thus, we strive to avoid infusing >250 ml/kg during the first 24 h postburn.

Limited data exist on the effect of burn shock and resuscitation on cerebral edema (see below for details). In the absence of TBI, cerebral edema as a consequence of burn shock resuscitation is seldom diagnosed. Life-threatening cerebral edema is more commonly seen later in

the hospital course in burn patients who experience a rapid decrease in the serum sodium concentration, e.g., as a response to over-vigorous correction of hypernatremia [20]. On the other hand, a burn patient with TBI and extensive burns who requires i.v. fluid resuscitation merits strong consideration for ICP monitoring, with a goal of ICP < 20 mm Hg [12].

What strategies can be employed to restrict fluid infusion? First, careful monitoring and supervision of the fluid infusion rate is essential. Hourly titration, so as to keep the urine output within the target range, is performed. Tight control of fluid resuscitation is needed in order to minimize the risk of brain edema [12]. Second, awareness of the total volume infused (in ml/kg) allows one to identify those patients 'en-route' to a high-volume (>250 ml/kg) resuscitation. We recently fielded a computerized decision-support system that prompts hourly titration of fluid input and enhances provider awareness of excessive resuscitation; use of this device was associated with a lower incidence of abdominal compartment syndrome [21]. Third, volume-sparing strategies should be considered. Typically, the water and protein contents of burn-injured tissue are greatest at 24 h postburn and a new equilibrium is established across the capillaries, permitting a reduction in resuscitation fluid volume. During hours 24–48 postburn, 5 % albumin in normal saline is routinely infused and the patient is weaned from lactated Ringer's solution. The albumin dose is between 0.3–0.5 ml/kg/TBSA per day (see Table 30.1) [22]. In those patients whose LR infusion rate at 12 h postburn predicts a high-volume resuscitation, albumin can be started early [23]. The ability of albumin to reduce resuscitation volume in burn shock should be balanced against the finding of increased ICP and death in the TBI subgroup in the Saline vs. Albumin Fluid Evaluation (SAFE) trial [24].

In the setting of TBI, hypertonic saline (HTS) can be considered. In burn patients, HTS is controversial. A study involving historical controls demonstrated an increased risk of death and of acute renal failure in burn patients treated with HTS [25]. But in the setting of TBI, and with the required careful monitoring of sodium concentration, the benefits may outweigh the risks. High-dose i.v. ascorbic acid [26] is another 'rescue' strategy employed by some burn centers for patients in whom resuscitation is difficult. Continuous high-dose renal replacement therapy to offload fluid and reduce circulating levels of inflammatory mediators has also been employed by some, but long-term benefits remain undocumented [27].

Table 30.1 Albumin dose for burn resuscitation

Burn size (TBSA) (%)	Albumin dose[a] (mL*kg*TBSA)
30–49	0.3
50–69	0.4
70–100	0.5

[a]This volume is given by continuous i.v. infusion over a 24 h period. *TBSA* total body surface area burnt, percent. *kg* preburn body weight

There is considerable experience with the use of mannitol as an adjunct to the resuscitation of burn patients with high-voltage electric injury and myoglobinuria [1]. Here, the purpose of mannitol is to produce a brisk diuresis, to prevent pigment deposition in the tubules, and to act as a free-radical scavenger. In burn patients, careful monitoring of hemodynamic status (to include CVP monitoring and frequent measurement of the lactate level or arterial base deficit) is needed when mannitol is used.

Wound and Extremity Care

Wound debridement is not an emergency, but should be completed no later than 24 h after injury, and is usually performed within hours of admission to a burn center. Wound care should be performed in a dedicated hydrotherapy (shower) facility or in an operating room [28]. Initial wound care is directed at thorough cleansing of the patient using a surgical antiseptic solution, preferably chlorhexidine gluconate; aggressive removal of all foreign material and debris; debridement of blisters, exudate, etc. Burns are then dressed with an antimicrobial cream or dressing. The burn creams of choice are silver sulfadiazine (Silvadene, others) and mafenide acetate (Sulfamylon). An alternative is the use of silver-impregnated dressings.

The extremities are vulnerable to the effects of thermal injury and to the edema formation which subsequently occurs. Evaluation of a burned extremity includes a thorough neurovascular exam. Exercise and elevation combat edema formation and maintain range of motion. By decreasing the elasticity of the skin and by causing edema in the underlying tissue, a burn may exert a tourniquet-like effect and occlude venous outflow and arterial inflow. Progressive diminution in the Doppler signal in an extremity with circumferential deep burns is an indication for escharotomy, performed at the bedside with scalpel or electrocautery through the full thickness of the burned skin and into the subcutaneous tissue (Fig. 30.1). An unusual indication for cervical escharotomy is the patient with full thickness burns of the neck and increased ICP [11].

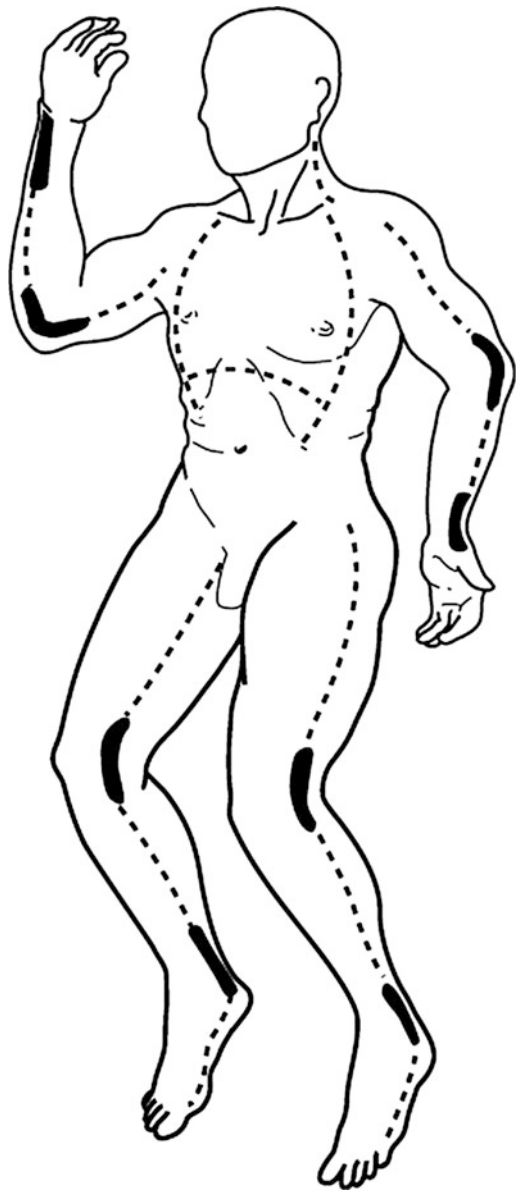

Fig. 30.1 Location of incisions for escharotomies. The bold lines indicate the importance of carrying the incisions across any involved joints

In patients who have sustained high-voltage electric injury, edema formation beneath the investing fascia typically produces a stony hardness to palpation of the involved muscle compartment, and may be associated with distal paresthesias. In the presence of such findings, fasciotomy, not just escharotomy, may be necessary. Spinal cord injury with either immediate or delayed onset of symptoms has been reported in patients with high-voltage electric injury. Immediate-onset symptoms often clear within 24 h. Those deficits of delayed onset are more apt to be permanent; they range from local paresis to quadriplegia, with motor deficits more common than sensory loss. Clinical presentation may include ascending paralysis or transverse myelitis, and can even resemble amyotrophic lateral sclerosis [29].

Effects of Thermal Injury on the Brain

Even in the absence of TBI, patients with extensive burns may sustain disruption of the blood–brain barrier (BBB) and consequent cerebral edema during the resuscitation period. Gueugniaud et al. placed epidural ICP monitors in 32 patients with TBSA > 60 % and no history of head injury. Peak ICP values of 31.4 ± 10.4 mm Hg were observed, on average, on day 2 postburn. Mean cerebral perfusion pressure (CPP) reached a nadir of 41.0 ± 10.2 mm Hg, also on day 2. Survival was associated with lower ICP and high CPP [30]. Shin and colleagues measured ICP and cerebral blood flow (CBF) in 8 sheep with 70 % TBSA burns. During the immediate postburn period,

CBF was maintained despite a decrease in cardiac output. At the end of the 6 h study, CBF decreased, ICP increased, and cerebrovascular resistance increased. Increased water content was observed in the brain at necropsy. The authors speculated that the mechanism for these changes could include impairment of the BBB, loss of cerebral autoregulatory function, and/or a decrease in the serum sodium concentration induced by large-volume resuscitation with lactated Ringer's solution [31].

Ding et al. conducted a series of experiments in a rat model directed at understanding the mechanism for postburn neurological complications. Thermal injury caused increased permeability of the BBB to labeled albumin [32]. In the same model, thermal injury caused increases in m-RNA expression of TNF alpha, IL-1 beta, and ICAM-1 in brain homogenates at 3 h, followed by increases in circulating levels at 7 h [33]. Brain edema and increased BBB permeability were associated with expression of matrix metalloproteinase 2 (MMP-2) and MMP-9 in the brain; these gelatinases act to degrade the basal lamina of the BBB [34, 35]. Inhibition of TNF alpha or of MMP-9 protected against the increase in BBB permeability and brain edema, while preserving the basal laminar proteins that comprise the BBB [36]. In another study, there was increased expression of tissue plasminogen activator (tPA) and of urokinase plasminogen activator (uPA) with BBB disruption and brain edema; tPA and uPA may upregulate MMP-9 [37].

Gatson and colleagues evaluated the role of estrogen in protecting against burn-induced brain inflammation in rats. Brain cytokine levels (TNF alpha, IL-1 beta, and IL-6) were much higher than systemic levels, suggesting increased local production. 17 beta-estradiol decreased cytokine levels in the brain, and exerted an anti-apoptotic effect. The possible clinical impact (e.g. on cognitive function) was not assessed [38].

Clinically, burnt patients present with both acute and chronic disturbances of CNS function. Acutely, delirium afflicts many critically ill burn patients and complicates their ICU management. Seventy-seven percent of mechanically ventilated burn patients were diagnosed with delirium using the Confusion Assessment Method in the ICU (CAM-ICU). Benzodiazepine use increased delirium risk [39]. Chronically, approximately one-third of patients admitted with serious burns develop posttraumatic stress disorder (PTSD). Improved pain control, manifested by increased use of opioids, helps reduce PTSD [40]. Studies from the recent wars in Iraq and Afghanistan showed that PTSD was more common in patients injured in explosions who had both TBI and burns [41]. The mechanism for this association is unknown.

Taken together, these clinical and basic science studies indicate the vulnerability of the CNS to cutaneous burns and burn-associated critical illness. Furthermore, they heighten the level of concern which should attend the patient with burns and TBI.

Aeromedical Evacuation

The hierarchical regionalization of burn care in both the civilian and military medical communities involves the transfer of burn patients with TBI to burn and trauma centers, if necessary by air. Johannigman and colleagues studied the effect of the stresses encountered during long-distance aeromedical transfer on ICP as monitored with intraventricular catheters in 11 critically ill combat casualties with TBI. ICP variability (±50 % of baseline) and instances of ICP > 20 mm Hg were observed throughout flight, but some patients experienced large increases in ICP related to takeoff and landing. ICP variability appeared to be patient-specific, that is, high in some and virtually absent in others. The authors attributed this to the adequacy of sedation and to the extent of previous surgical treatment. To minimize ICP fluctuation, they recommend loading casualties with the head towards the nose of the aircraft, with the head of the litter elevated by at least 30 degrees; adequate sedation; and venting of the intraventricular catheter as needed [42]. For patients with burns and TBI, the intensity of monitoring and the extent of intervention will be dictated by the time postburn and the fluid status of the patient.

In conclusion, the combination of extensive thermal injury and TBI is a particularly challenging scenario. Close collaboration between all members of the multidisciplinary burn and trauma teams is needed to achieve optimal outcomes. Emphasis must be placed on minimizing resuscitation volume, with assiduous monitoring of ICP to prevent cerebral ischemia and to reduce cerebral edema in the ICU and during aeromedical and other transfer procedures. Attention should also be directed toward control of pain and anxiety, maintenance of circulation in muscle compartments, adequate ventilation, early excision and grafting of the burn wound, and prompt institution of rehabilitation programs to maintain and restore function.

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Index

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