Cerebrovascular and Endovascular Neurosurgery

Complication Avoidance and Management

Chirag D. Gandhi
Charles J. Prestigiacomo
Editors

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I dedicate this book to all that have helped me become better:
To all the patients and families who have taught me how to become a better physician and surgeon.
To all my mentors, colleagues, and authors of this book who have instilled in me the profound desire to forever learn and never stop seeking what is best for my patients, thus making me a better student of medicine.
To my closest friends who have grounded me and helped me grow to become a better colleague and partner.
Most of all, to my parents and brother, my in-laws, my dears, Cindy, Rachel, Laura, Michelle, Julie, (and yes, our cats and guinea pigs), for the constant, unconditional support that makes me a better person.
All that I am is because of all that you are.

C.J. Prestigiacomo

Firstly, to my patients and their families for providing me with a clarity of purpose.
To my parents and grandparents for the life pearls and setting me on the path.
To my in-laws for their gentle wisdom and the most precious of gifts.
To my students, residents, fellows, and colleagues for helping me practice the art.
And of course to my dearest Sedna, Ronan, and Gita whom I hold above all things.

C.D. Gandhi

Preface

Physicians and surgeons are human. We make mistakes. Patients are harmed by what we do and by what we do not do. Unintentional as it may be, it nonetheless has its consequences to the patient, the family, and to you. The one element that everyone can find solace in is that, hopefully, every mistake is a one-time event. It happens, we learn from it, others learn from it, and it never happens again.

In the event of a complication, the proceduralist will review what happened, first and foremost internally. In most cases, the error is identified and the steps to avoid such an error again are defined. Sometimes this occurs with the aid of an external forum of colleagues and peers. On occasion, the proceduralist will reach out to a mentor or partner and discuss the case in broad terms to gain insight into the events or perhaps garner wisdom from the mentor's prior experiences. In so doing, the proceduralist not only learns from his or her own errors but also gains the wisdom of his or her mentor in an attempt to avoid making similar errors in the future.

This is how this book was born.

We see this book as a venue for members of the cerebrovascular community to share their experience and expertise. Most importantly, it is a venue for the dissemination of the many nuances in complication avoidance and complication management for some of the most difficult procedures that are performed for cerebrovascular disease.

The book is divided into four major parts, each with a specific focus. The first part provides the reader a detailed view of what a complication is, what it is not, and the general principles in formally assessing and reviewing complications, adverse outcomes, and errors. It is meant to provide a fertile landscape for each reader to begin a formal approach to analyze complications within their respective institutions and within their own practice. The second, third, and fourth parts of the textbook respectively describe the technical nuances of specific surgical, endovascular, and radiosurgical procedures for vascular diseases of the central nervous system and head and neck. These chapters serve as the central focal point for the book. Each chapter discusses the methods for complication avoidance and complication management. The reader thus is able to gain valuable knowledge and experience from experts in the field and in so doing reduce the frequency of poor outcomes in his or her practice.

Complication avoidance and complication management requires teamwork and communication. A very unique and helpful feature of this textbook is the presence of checklists for procedures and for complication management in the "techniques"

chapters. These checklists are made to be freely duplicated or modified and incorporated into an emergency procedures binder for the operating room, the endovascular suite, or the radiosurgery center. By turning to the specific checklists and reviewing them with the team prior to the procedure, the team gets "prepped and primed" for anything that may happen. The presence of a Table of Complication Avoidance and Management Principles also provides a necessary summary that enhances the team's preparation.

We should never forget our complications or those to whom it happened. We should use the experience to strengthen us and make us better. It is our hope that this textbook will help the reader improve patient outcomes through a greater understanding of the nuances of all neurovascular procedures. It is our hope that the checklists and tables will become a living document for each institution, dedicated to improving communication and teamwork among the many disciplines that care for these complex patients. It is our hope that this textbook will help all of us to decrease complications in our patients and help us to continue striving to do no harm.

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Part I

General Aspects

What Is a Complication? The Philosophical and Psychological Aspects

1

Neil Majmundar, Celina Crisman, and Charles J. Prestigiacomo

Introduction

A 56-year-old female patient with a past medical history of hypertension and type II diabetes mellitus undergoes a diagnostic aneurysm at 1 year after coil embolization of an anterior communicating artery aneurysm. Fortunately, the aneurysm had been coiled prior to rupture, and the patient had not suffered any neurological deficits. Other than some difficulty in gaining access to the right common carotid artery, the angiogram went without any particular setback. In the post-procedure recovery unit, the patient complained of left arm weakness. Upon examination, the patient was unable to move her left arm, and it had no tone. She was rushed back to the angiography suite, where she was discovered to have a thrombus in a distal MCA branch, unable to be treated. MRI showed an MCA territory infarction. She was sent back to the recovery unit, where the attending physician explained the undesired outcome and the steps which would be taken to optimize her long-term outcome with hope of regaining some function in the left arm. Was this a medical error resulting in neurological deficit, or was this a complication of the procedure?

With the many advances in medicine comes the need to render the medical lexicon more precise and accurate. The environment in which modern medicine is practiced makes this need all the more important when discussing complications or adverse events. A complication is unplanned, uncommon, and unwanted. The difficulty lies in that defining a complication in general and defining a complication for a specific illness or procedure is a moving target. So many variables affect its characterization and its perception that it is difficult to develop a cohesive, standard

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definition for which all will agree. It is a definition that needs to resonate with patients, families, all health-care workers, clinician-scientists, and lawyers.

In its broadest sense, a complication is the result of unexpected events that result in an unwanted and uncommon outcome. Importantly, some of these events are directly the result of the disease process, genetics, or some other events that are beyond an individual's current control, whereas others can, indeed, be modified. Though this is instinctively obvious, historically there has been great difficulty in establishing a clear delineation between that which can and cannot be modified when discussing complications. This challenge has been the principal reason why there is a lack of consensus in the medical lexicon when discussing complications.

Historical Perspective

For as long as there has been the practice of medicine, there has been the potential for an unexpected, unwanted, and uncommon outcome. Mostly focused on surgical, or procedural, treatments, the concept of the complication was recognized since the days of Hammurabi, describing, for example, cutting the hand of the surgeon whose patient (of high status) would die after treatment (such as lancing a lesion) [1]. This concept of technical ineptitude as the only cause of a complication is carried through to the days of Hippocratic medicine in Greece. Adverse outcomes that could not be directly and concretely attached to an intervention were relegated to the whims of the supernatural and thus out of human control or blame.

Interestingly, though the Egyptian, Hippocratic, and Galenic writings demonstrated the fatalistic aspects of medical and surgical care, they also sowed the seeds of scientific inquiry. The numerous observations and subsequent care plans suggested "lessons learned" in the care of prior patients. With regard to the procedures themselves, it is clear that specific "instructions" on techniques for wound care, fracture management and splinting and, of course, trephining emanate from recognizing and modifying (more specifically, correcting) the missteps (hence, "complication management"). Most notably, as the physicians and surgeons began to discuss post-procedural care, discussion of complication management or avoidance required that the event be *recognized* as a complication in the first place. Galen's concept of laudable pus, for example, clearly a complication of any wound, was considered the normal course of healing (and thus not a complication). Indeed until the eighteenth century, carotid ligation with the use of a suture protruding from the skin *depended* on inflammation and infection to help definitively occlude the vessel. This observational docket of information, aligned with the birth of scientific anatomy and dissection, became the seeds of identifying the complication as we try to define it today [2].

There was some growth in our collective understanding of what physicians and surgeons could do to improve outcomes during the Renaissance. The focus of this improvement was fundamentally based on the surge in knowledge that came with human dissection combined with the beauty and accuracy that came with the rise of

Renaissance art. Thus, improved, accurate knowledge of human anatomy helped in reducing technical complications.

The greatest growth in the prevention of the complication occurred in the eighteenth and nineteenth centuries, and as expected, this growth focused on surgical procedures. Indeed, such growth paralleled the improved fund of knowledge in physiology and anatomy. Additionally, the introduction of anesthesia, the understanding of germ theory and infection, Listerian techniques, and the fundamental lessons of Florence Nightingale in the Crimean War are but a few of the many events that synergistically helped to improve complication avoidance, detection, and management. However, defining a complication remained elusive.

What Is a Complication?

Medical complications are difficult to define, making them challenging to differentiate from medical errors and at times leaving a medical outcome up to one's interpretation. The term "complication" has had a broad definition. As was discussed above, it reflected any event or outcome that was unwanted or unexpected, whether within or outside of the physician's control. More recently, *Collins Dictionary of Medicine* defines a complication as "an additional disorder, or new feature, arising in the course of, or as a result of a disease, injury, or abnormality" [3]. Again, the definition presented herein is broad and accounts for "natural" causes as well as iatrogenic causes. However, determining what is a complication in the course of treatment for a disease process from a medical error is of extreme importance. This distinction gains in amplitude when the outcome of complication or error significantly alters the long-term outcome of the patient. A more granular lexicon was necessary.

In 1991, Brennan et al. published an analysis in *The New England Journal of Medicine* investigating more than 30,000 records of hospitalized patients. They defined an *adverse event* as "an injury that was caused by medical management (rather than the underlying disease) and that prolonged the hospitalization, produced a disability at the time of discharge, or both," and *negligence* as "care that fell below the standard expected of physicians in their community" [4]. They estimated an adverse event rate of 3.7% and adverse events due to negligence to be 1% [4]. This landmark series of papers played a role in defining adverse outcomes due to physician negligence for medical malpractice. More recently, in 2016 Makary and Daniel published an analysis in the *BMJ* stating that medical error is the third leading cause of death in the USA, resulting in approximately 250,000 deaths per year [5]. This places death from medical error behind heart disease and cancer and ahead of respiratory disease as causes of death in the USA. Although the exact number of deaths from medical error is difficult to determine, the number itself is alarming when placed in the context of deaths due to other causes.

Medical complications and errors carry significant medical, ethical, and legal ramifications. In the scenario provided, stroke and neurological deficit are known complications when undergoing an angiogram. Nonetheless, one can always

wonder when the embolic event occurred, whether a different catheter could have been used, and whether the attending physician and fellow carefully studied the arch and vessels from the prior intervention to prepare for the anticipated difficult access. All these post-procedure complications can cloud the picture and change what was thought to have been a complication into a medical error, especially when there are legal ramifications involved.

Complications change with time and even technology. Hearing loss and facial palsy (partial or complete, temporary or permanent) after the resection of an acoustic neuroma of any size were common and expected though still unwanted. Today, hearing loss or, more importantly, facial palsy for an acoustic neuroma less than 1.5 cm in size is *neither* common *nor* expected as well as unwanted. Thus, it is now considered an *avoidable* adverse event. Sokol et al. emphasized this point by enhancing the definition, stating that a surgical complication (adverse event) is undesirable, unintended, and a *direct result* of surgery that, if it had gone well, would not have occurred [6].

What Is a Complication? The Philosophical Aspects

A medical complication is an undesired outcome which may not be under the control of the physician. Complications are results which were not desired but within the scope of potential outcomes. Medical errors and mistakes, in contrast, occur because of negligence or misguided action. For example, a complication would be a postoperative hematoma despite achieving hemostasis prior to closure. What if the hematoma occurred after the surgeon failed to practice proper hemostatic technique? Then the same outcome would constitute an error. As another example, an error (in this case, negligence) is closing a surgical wound with a foreign body remaining inside, consequently, having to take the patient back to the operating room to remove the foreign body. At times the line between complications is cut and dry, but it is often obscure.

Complications and adverse events often vary between different specialties. In general surgery, complications include surgical site infections despite the use of prophylactic antibiotics and sterile technique or the failure of an end-to-end bowel anastomosis. In many cases, the patient may require an increased length of stay, is subjected to the risk of intravenous antibiotics, or may undergo another operative intervention to relieve the risk. In obstetrics and gynecology, pregnancy and labor carry the risk of significant complications to both the mother and baby and can often result in the loss of both lives. In internal medicine or in the outpatient settings, patients with certain illnesses can deteriorate as a complication of their illness. Examples include acute respiratory failure after community-acquired pneumonia or an anaphylactic reaction to a medication which the patient was unknown to have an allergy resulting in a hospitalization. These complications vary in both scale and type, as some are part of a disease process and others resulting from an attempt at treatment.

As mentioned earlier, the line between complication and error is not always clear, and many times what one may believe is a complication may be seen by others as an error. For example, outcomes can range across the spectrum between a complication of the disease and gross negligence resulting in error. Referring back to the acoustic neuroma operation in the field of neurosurgery, for example, the outcomes of facial nerve deficit and hearing loss are possible following a craniotomy for resection of acoustic neuromas. Acoustic neuromas may vary in size, presentation, and radiographic features with some obviously being much larger than others. Patients who present with symptoms of headache, nausea, gait disturbance, hearing loss, and hydrocephalus secondary to the tumor may be more likely to accept an outcome resulting in unilateral hearing loss or mild facial nerve palsy than those who present without any symptoms. This does not mean that the hearing loss or facial nerve palsy is not a complication, but that the surgeon and patient may agree that the benefits of a complication such as hearing loss or facial palsy are acceptable over the life-long risks the tumor may carry.

A patient without many medical comorbidities who develops a postoperative myocardial infarction following a 5-hour elective surgery is a complication which was not under the direct control of the physician. This is true if the preoperative evaluation was complete, the surgery was indicated, and the length of surgery was reasonable. This event would be considered a complication as the event occurred despite all necessary steps taken to avoid it. In contrast, a post-interventional angiography procedure resulting in a groin hematoma or pseudoaneurysm due to improper technique for closure is a medical error because the error occurred as a consequence of poor technique.

In *Complications: A Surgeon's Notes on an Imperfect Science*, Atul Gawande discusses problematic encounters and outcomes which he learned from as he progressed through his residency training [7]. He writes, "The way that things go wrong in medicine is normally unseen and, consequently, often misunderstood. Mistakes do happen. We tend to think of them as aberrant. They are, however, anything but" [7]. While error is impossible to avoid in medicine, physicians of today, as our predecessors, must constantly work toward ways to decrease the rate.

As Gawande states, medical complications and errors will occur as long as humans continue to practice medicine. Physicians must continue to strive to achieve the best possible outcomes for each patient, doing no harm to the patient and staying true to the oath which they all promised to abide before entering medicine.

Psychological Aspects

Medical complications play a significant role at times in changing both the patient's and the doctor's lives. Physicians can struggle, at times, with the outcomes of their complication for their entire medical careers. In a 2010 study in *Surgery*, Patel et al. demonstrated the impacts complications have upon a surgeon [8]. Of the 123 surgeons who responded to the questionnaire for the study, 92 (76%) experienced their first complication during residency. The study promoted the idea that additional

support after residency should be in place for physicians to avoid burnout. Many times, physicians take the poor outcomes following a complication upon themselves. This can result in difficulties which the physician suffers in his/her personal life. In addition, it can result in decreased confidence, belief that one cannot adequately perform his/her job, and other alterations in practice. While complications change patients' lives, we must also remember the importance of constructively learning from the complication, studying the cause, and preventing it in the future.

Conclusion

All can agree that complications, adverse events, and medical errors are unwanted, rare, and unexpected. Defining each precisely is extremely important yet very difficult. In many ways, they are defined based on the surrounding environment and the need. The reader will appreciate that the scenario presented at the beginning of the chapter lacks a clear-cut answer; it can be debated as more details about the case are presented. Medical complications are inevitable. Adverse events will occur. Medical errors can happen. The goal of physicians should be to work toward developing a system in which the occurrences of these events are at a minimum. They should acknowledge the errors that are made, identify the causes, strive to understand them, take ownership of that which they can modify, and derive ways to avoid them in the future. Most important of all, the physician must never forget the complications in which he/she was involved, for in remembering them, the physician shall become stronger, safer, better for medicine, and better for the patients.

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Medicolegal Aspects of Complications

2

Michael P. Marks

Introduction

Adverse events or outcomes are unwelcome occurrences. Unfortunately, adverse events will likely occur sometime during the physician's lifetime in the practice of medicine. The possibility of such an event should be taken into account when planning and discussing treatment. Patients should be advised about the possibility of adverse events during the process of informed consent. An adverse event may occur despite all appropriate precautions being taken by the treating physician, but some adverse events are clearly preventable. An adverse event may trigger a malpractice action by a patient or patient's family. This chapter will discuss the informed consent process, adverse events, malpractice claims, and the physician's role in documentation and disclosure. The information that has been provided in this chapter is based on a review of publications on the subject. It should not be construed as legal advice. If as a healthcare provider you are involved in a legal case, get the direct advice of a risk manager or a lawyer.

Informed Consent

In general, the elective procedures described in this textbook are performed only following a doctor-patient discussion about that treatment and the associated complications that might ensue. Every adult patient has the right to make decisions about his or her healthcare. That decision must be an informed decision.

The concept of informed consent is a relatively new idea in the history of Western medicine. As far back as the time of the writing of the Hippocratic Corpus

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in Greece during the fifth and fourth century BC, physicians were instructed to "attend to the patient with cheerfulness and serenity … revealing nothing of the patient's future or present condition" [1]. It was not until the twentieth century that the concept of informed consent was formulated and developed into a widely recognized and applied conversation between the doctor and patient that recognized the patient's need to know [2].

Much of the discussion about the more recent evolution of informed consent is based on legal case history, which has framed current thinking of informed consent as a right of patients based on ethical principles. This is understood as a principle that is based on the autonomy of the individual and of individual freedom of choice [3]. These ethical principles have been codified by many professional medical organizations. A code of ethics adopted by the American Board of Neurologic Surgery called for "open communication with the patient" and requires that "medical or surgical procedures shall be preceded by the appropriate informed consent of the patient" [4]. Informed consent has also come to be viewed as an obligation which may enhance the doctor-patient relationship. The recently adopted code of medical ethics outlined by the American Medical Association describes informed consent in this way: "Informed consent to medical treatment is fundamental in both ethics and the law. Patients have the right to receive information and ask questions about recommended treatment … Successful communication in the patient-physician relationship fosters trust and supports shared decision making" [5].

What are the elements of informed consent? Informed consent should include an adequate discussion of what is involved in the procedure, in other words, what will happen during treatment. It should include a discussion of the expected benefits and the risks or complications that can occur with that treatment. Finally, it should also include a discussion of alternative treatments, including the alternative of no treatment and the risks and benefits of these other options.

A key early case, often cited as a cornerstone in the development of the legal concept of informed consent, is a 1914 New York Supreme Court decision, Schloendorff *v. Society of New York Hospital* [6]. Mary Schloendorff was admitted to the hospital with a "stomach disorder." The treating physician diagnosed a fibroid tumor and recommended surgery. She consented to an examination under ether which she was told would be needed to better characterize the tumor, but she refused surgery to remove the tumor. While she was unconscious, the tumor was removed, and she suffered a complication of the surgery. The court found that "Every human being of adult years and sound mind has a right to determine what shall be done with his own body; and a surgeon who performs an operation without his patient's consent commits an assault for which he is liable in damages." Subsequent cases involving consent were often brought as assault and battery cases and focused more exclusively on the idea that the patient had to consent to the procedure not whether they were well informed. Today cases based on battery are generally limited to situations where there was no consent obtained, a different physician performs the procedure than the patient was led to believe was going to perform the procedure, or the procedure performed is substantially different than the one the patient consented to [7].

The idea of informed consent was first used in a landmark 1957 case *Salgo v. Leland Stanford Jr. Univ. Board of Trustees* [8]. The patient in this case, Martin Salgo, agreed to aortography, and the procedure was complicated by permanent lower extremity paralysis. Mr. Salgo, his wife, and his son all testified that they were not given any information about the nature of the procedure, and the treating physicians admitted that the patient had not been apprised of any risks of the procedure [9]. Among the instructions given to the jury, the judge specified that a physician had a duty to disclose to a patient "all the facts which mutually affect his rights and interests and of the surgical risk, hazard and danger, if any" [9].

Informed consent generally moved from cases considered under the legal delineation of battery to that of negligence. The legal definition of negligence is "a failure to behave with the level of care that someone of ordinary prudence would have exercised under the same circumstances. The behavior usually consists of actions, but can also consist of omissions when there is some duty to act" [10].

A defining case in the move to considering lack of adequate informed consent as a matter of negligence is a case decided in 1972 by the US Court of Appeals for the District of Columbia Circuit, *Canterbury v Spence* [8]. Jerry Canterbury was a minor who suffered from back pain and saw a neurosurgeon working at the Washington Hospital Center, Dr. William Spence. Dr. Spence recommended that Canterbury undergo a laminectomy for a suspected ruptured disk. He did not disclose that there was risk of permanent neurologic deficit from the operation to the patient or his mother. He was asked by the patient's mother if the surgery was dangerous and chose merely to say "not any more than any other operation" [11]. The patient suffered a complication and had permanent difficulty walking, urinary incontinence, and bowel paralysis. The appellate court found that Dr. Spence had been negligent and that the physician was required to divulge risks that a "reasonable person" would "attach significance to" [11].

Failure to obtain informed consent prior to a procedure can be the basis of a malpractice action. The cornerstone of this claim is that the physician withheld information that would have led the patient, acting as a reasonable person, to not consent to the procedure. What is the standard that physicians are held to in order to decide that they have withheld crucial information? States are essentially split between a "physician-based" standard and a "patient-based" standard. In a jurisdiction that applies the physician-based standard, there is a requirement that physician disclose information which a reasonable physician would disclose. When a state uses a patient-based standard (also known as material risk standard), the physician's disclosure should include the information that an objective patient would consider material.

Who should obtain the informed consent? The simple answer is the physician or member of the physician's team that is considering performing the procedure for which the consent is being obtained. In complex procedures, if other physicians are performing portions of the procedure, those individuals should obtain separate consent. For instance, in an anterior approach spine surgery, when the general or vascular surgeon is performing the exposure procedure, that physician should consider the need to obtain informed consent regarding his/her portion of the procedure.

There are certainly circumstances which the law recognizes are exceptions to the obligation a physician has to obtain informed consent. These include an emergency situation, a circumstance which would dictate that there is common knowledge about the risk, and when the physician is aware the patient has prior knowledge of that risk [8]. In an emergency situation, the physician may act without the expressed consent of the patient if the patient is unable to consent. In general, it is preferable to obtain consent from family members if possible, but if there is no time, to proceed with treatment [8]. The two criteria that should be met to have a medical emergency preclude the need for informed consent are that the patient is incapacitated and that a life-threatening situation requires urgent treatment [7].

Adverse Events and Malpractice

An adverse event has been defined as "an injury that was caused by medical management, rather than the underlying disease" [12]. An adverse event or injury does not in and of itself constitute grounds for malpractice. Clearly some complications occur despite the physician performing and managing an indicated procedure in an acceptable fashion with proper safeguards in place. These events are known to occur and are discussed at the time of informed consent as recognized risks. In essence, they are not preventable. For example, aneurysm rupture is a known complication of surgical clipping and endovascular coiling and may occur even in the best managed circumstance. When an adverse event is however due to an error, it is a "preventable adverse event" [13]. Errors have been classified as "active" when they are due to the direct actions of a healthcare worker or "latent" when there is a systemic problem causing the error which may be related to issues arising from the facility, equipment, or organization [14].

In order for an adverse event that has caused an injury to meet the legal definition of malpractice, four criteria must be met which come under the broad terms of *duty*, *breach*, *causation*, and *damages* [15]. The physician has to be shown to have a *duty* to care for the patient, in other words that there is a physician-patient relationship. Assuming that relationship exists, the physician's *duty* is to "possess and bring to bear on the patient's behalf that degree of knowledge, skill and care that would be exercised by a reasonable and prudent physician under similar circumstances" [15]. The second criterion to be met is that there was a *breach* of that duty. Most malpractice cases are brought for negligence. Negligence is often evaluated as a standard of care question. In a malpractice case, the issue of what a reasonable and prudent physician would have done under similar circumstances or what was the standard of care would be decided with expert opinion. The third criterion that must be satisfied is *causation*, in that the physician's negligence was the cause of the injury. This relationship has the legal term "legal cause" or "proximate cause" [16]. It requires that the negligence be a "substantial factor" causing the injury, not necessarily the only or major cause of the injury [16]. Finally, the physician breach needs to result in *damages* or a loss to the patient which generally results in recovery of damages through a monetary award. Damages can be awarded for physical, emotional, or financial loss. Damages are classified as "general" when they are for issues like pain

and suffering or grief. They are classified as "special" damages when they are related to medical costs of current and future care and loss of income.

Malpractice claims are unfortunately quite common in the United States. A survey of claims against physicians through a single large nationwide insurance carrier during a 14-year period ending in 2005 showed that in any given year, 7.4% of physicians had a claim against them [17]. There was a marked variation in that percentage depending on subspecialty, with high-risk specialties generally being the procedure-based surgical specialties. Neurosurgeons had the highest rate, with 19.4% having a claim in any given year, and psychiatrists having the lowest rate at 2.6%. Estimates of cumulative risk suggested that by the age of 65 years, 75% of physicians in low-risk specialties would be sued, while in high-risk specialties, 99% of physicians would be sued [17]. Although there are a large number of claims filed, the same study showed that 78% of claims did not result in payment to the claimant. Additional recent data does suggest that the rate of claims being paid has generally declined from 1994 to 2013 [18].

Documentation

In tangible terms, when there is a litigation, the question is not if something occurred but if it can be proved that something occurred. Documentation of the informed consent discussion with the patient should be part of the medical record. Most hospitals require that there be a signed consent form in the medical record before a procedure is performed. Hospital licensing organizations and state licensing agencies require hospitals to have informed consent policies, and hospitals can share in the liability if the physician has not obtained informed consent [19]. However, getting the consent form signed is not a substitute for obtaining informed consent. Some consent forms will only include a description of the proposed procedure and the physicians performing that procedure. Often the signed consent form will only contain a nonspecific comment about risks, benefits, and alternatives being discussed. In some legal jurisdictions, the form is presumptive evidence that a full discussion occurred, and the burden of proof lies with the plaintiff to prove that adequate consent did not occur [8]. However, it is often recommended that the physician enters a separate note into the medical record that documents a full discussion occurred with the patient [16]. It is also suggested that this note should include a discussion of the major risks and those that are the most serious [16]. Commentators suggest, depending on the nature of the procedure, the note would look something like: "Risks discussed with patient included but were not limited to, infection, bleeding, nerve/nervous system damage, damage to adjacent organs, paralysis, stroke and death."

Disclosure

At the core of any discussion about disclosure lies the ethical obligation that physicians have to their patients. Modern medical ethicists have routinely called for physicians to disclose errors to patients [20, 21], and major medical societies have

strongly supported this policy. The Principles of Medical Ethics of the American Medical Association calls truthful and open communication between doctor and patient "essential for trust in the relationship and respect for autonomy" [5]. It specifically tells physicians they should "disclose medical errors if they have occurred in the patient's care." The Joint Commission also advocates that accredited hospitals inform patients when an adverse event has occurred, endorsing that "the licensed independent practitioner responsible for the patient's care, or his or her designee, discloses to the patient and family any unanticipated outcomes of care, treatment, and services" [22].

Despite these entreaties, there appears to have been a mixed reaction in the physician community to the actual reporting of errors. This is highlighted by a relatively recent study which queried a large number of US and Canadian physicians by survey [23]. It found that 98% of physicians agreed that a serious medical error should be disclosed but that number dropped to 74% when a minor error was involved. The study also found that 74% of the physicians felt that disclosure of a serious error would be very difficult. In addition, 21% said that if the patient was unaware that the error happened, they would be less likely to disclose the error, and 19% said they would be less likely to disclose an error if they thought the patient was going to sue.

At the crux of the physician, concern about disclosure is the exposure to legal risk. Some organizations, generally smaller self-insured hospital systems, have adopted a full disclosure policy which includes an apology and remediation for an error [24–26]. These organizations have suggested that a full disclosure policy with an accompanying apology can actually result in reduction of claims and have shown this within their hospital systems. A clear connection between disclosure and the increased likelihood of a legal action has not been established [27]. However, potential concerns still exist and are reflected in the legal arguments against offering an apology [28]. The possible hazards to apologizing include a concern that the apology could actually trigger a legal action by painting the picture that there is an easily winnable case. Perhaps, more important is the argument that in most jurisdictions an apology can be entered into evidence and may be used as an admission of guilt [28]. In addition, a conflict with the insurance company could exist from either disclosure or apology since malpractice policies often have a clause requiring the insured entity to cooperate with efforts to defend against a legal action [28].

The conflict between the need to disclose errors and the possible hazards of disclosing those errors is far from resolved. As some authors have suggested, the current malpractice model which names physicians as targets of fault may have to be replaced with a system based on no fault or the liability of the entire healthcare organization [29]. Perhaps as physicians move into a model of employment by a healthcare entity and away from private or small group practice, this will become an easier goal to achieve. At the present time, however, recommendations like that of the American College of Obstetricians and Gynecologists for disclosure are being made: "It is important to understand the difference between expressions of sympathy (acknowledgement of suffering) and apology (accountability for suffering).

Expressions of sympathy are always appropriate. The appropriateness of an apology, however, will vary from case to case. When considering whether an apology is appropriate, the physician should seek advice from the hospital's risk manager and the physician's liability carrier" [30].

Conclusion

Every adult patient has the right to make decisions about his or her healthcare. That decision must be an informed decision. Obtaining informed consent is vital to the physician–patient relationship. Informed consent should discuss the expected benefits and the risks or complications that can occur with treatment. It should also discuss alternative treatments, including the alternative of no treatment and the risks and benefits of these other options. With an open and clear discussion, physicians can help to minimize misunderstandings and potential legal action should an adverse event or complication occur. Finally, if an adverse event occurs, the physician should consider consulting risk management for support and advice.

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Residency/Fellowship Training and the Complication

3

Celina Crisman, Raghav Gupta, Neil Majmundar, and Chirag D. Gandhi

Introduction

Complications occur in medicine and lead to myriad losses, ranging from years of independent living to economic productivity and ultimately also including insurance and hospital costs. Hospitals and practitioners endeavor to minimize complications with strategies such as preoperative checklists, "hard stops" built into electronic medical records, and conferences devoted to the discussion of complications. Teaching hospitals embrace challenges beyond providing quality care and effectively avoiding complications; they also bear responsibility for training future physicians and surgeons. The need to effectively train residents and fellows introduces new challenges into complication prevention schemes. Greater experience understandably may lead to fewer complications; however, the experience necessary for complication avoidance and safe practice must be acquired during residency. Thus, training programs and teaching hospitals grapple with the challenge of providing minimally experienced residents with the experience necessary for independent practice while not exposing patients to undue complication risks. This chapter examines the connection between physicians in training and complications, the impact of hour restrictions and burnout on complications, as well as the resident liability in malpractice cases.

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Trainees and the Impact on Complication Rates

The relationship between resident/fellow participation and complications has long been a topic of speculation and investigation. A study specifically considering the impact of experience on complications and adverse outcomes compared error rates in June, the end of the medical year when residents are considered most experienced in their given roles, with error rates in July, the month when residents are newly promoted and thus least experienced in a particular function [1]. The study was prospective and identified errors through routine patient encounters, rounds, and daily patient chart audits; errors included any instance where incorrect medical care was administered, whether an incorrect action was performed, or if there is a failure to act. Errors involving a resident were specially categorized. The incidence of errors, calculated as a percentage of total patient days, did not differ significantly between June and July, months in which resident experience ostensibly maximally diverges. In June, the error rate was 7.1%, slightly but not significantly lower than the error rate of 7.5% identified in the preceding month of July. However, residents were involved in 52.5% of errors in June, compared with only 39.7% in July, a statistically insignificant difference. Furthermore, in the aforementioned study, 80–90% of errors did not result in adverse outcomes [1]. This study thus suggests that less experienced residents do not make significantly more errors than their more experienced counterparts. Furthermore, the finding that most errors do not adversely impact outcomes suggests that various system checks effectively identify initial errors and prevent their escalation.

Subsequent studies considered the impact of resident participation on surgical outcomes, an especially relevant inquiry given that the experience of the surgeon is widely understood to directly correlate with the probability of a positive outcome. Thus, the direct surgical experience obtained in residency is essential to later successful practice, but one must question whether its acquisition has ever had a negative impact on patient outcomes. A recent study considered this question in the context of one of neurosurgery's most intricate and technically demanding procedures, aneurysm surgery. The study specifically deliberated upon the impact of resident involvement on outcomes in patients undergoing surgical treatment of aneurysms and retrospectively contrasted outcomes of procedures featuring resident participation with those of surgeries involving only an attending. Notably, the study restricted its focus to aneurysms less than 1 cm in size and located in the internal carotid artery, with the understanding that these are simpler aneurysms more likely to permit substantial contributions from an assisting resident [2]. Indeed, authors noted that advanced participating residents were expected to perform critical maneuvers within the case, including dissection of the Sylvian fissure and aneurysm neck, along with clip placement. After the authors reviewed 355 operative cases, 196 involving residents and the remaining 159 performed without residents, they identified no statistically significant difference in the incidence of permanent adverse outcomes [2]. This study supports the idea that resident education, for the benefit of future patients, and effective care of current patients may be pursued in tandem.

A larger, recent retrospective review of resident impact echoed earlier studies in finding no significant risk associated with the presence and participation of training residents in surgical care. This study compared patients who had undergone neurosurgical procedures with only an attending to those operated on by a team

including a resident and an attending with regard to 30-day postoperative morbidity and mortality. Notably, patients whose team included residents experienced both a significantly higher complication rate and mortality rate, at 20.12% and 2.07%, respectively. These rates unfavorably contrast with the attending-only rates of 11.70% and 1.22%. However, upon multivariate analysis, there was no significant difference in either 30-day morbidity or mortality between the groups [3]. Thus, resident participation, as an independent variable, did not correlate with an increased risk of complications or death; rather residents may have been more likely to play a role in the care of patients with more significant comorbidities or those patients who were undergoing riskier procedures [3].

Fatigue, Burnout, and Restricted Work Hours

Despite no strong evidence that resident participation directly leads to more complications and worse outcomes, residents are indeed in training and thus lack the experience and procedural memory that often enable practiced attendings to deftly perform complex procedures. Where experience is necessarily lacking and cannot itself protect against complications, supervisors and mentors must look to other strategies for preventing complications in care administered by residents. Thus, burnout and fatigue due to long hours and sleep deprivation have emerged as rectifiable potential contributors to complications.

Burnout has been characterized as a chronic stress-induced syndrome resulting in depersonalization, emotional exhaustion, and perceived incompetence in the workplace [4, 5]. Medical and surgical residents are particularly at risk for burnout due to the demanding nature of their job, lack of autonomy, and long irregular hours that they often work [5, 6]. In a study published in 2002, which surveyed residents in an internal medicine residency program, nearly 76% were found to have met the criteria for burnout [7]. These rates can, however, vary from one study to another based on the matrices used in the evaluation of burnout.

Performance deficits are a serious consequence of emotional exhaustion and can result from sleep deprivation and long working hours. Friedman et al. reported that interns were less likely to detect arrhythmias on electrocardiograms when sleep deprived as compared with well rested [8]. Grantcharov and colleagues further demonstrated that a single night on call had profound effects on psychomotor performance during laparoscopic surgery (as assessed via a simulator), resulting in decreased accuracy and increased error rates [9]. Among neurosurgical residents, Ganju and colleagues reported a 13.1% average decrease in performance after a call shift. Variables these authors collected and factored into their analysis included elapsed time for procedures, incidence of cognitive errors, and tool handling/smoothness [10].

Seeking to mitigate the effects of long work hours on residents' performance in the clinical setting, the Accreditation Council for Graduate Medical Education (ACGME) mandated an 80-h work week for residents in 2003. The ACGME also established that residents were to work for no longer than 24 h at a time with an additional 6 h allotted for educational activities and continuity of patient care [11, 12]. In a prospective study evaluating the effects of these changes on surgical residents' job satisfaction, motivation, and quality of life, the researchers found decreased

rates of burnout and an increased motivation to work; however, they identified no statistically significant differences in the quality of patient care administered [11]. Similar results were observed in a study surveying internal medicine residents at the University of Colorado before and after implementation of the ACGME's work hour restrictions [13]. A prospective study conducted by Dumont et al. [14] contrasted outcomes before and after implementation of the ACGME work hour restrictions on a neurosurgical service and obtained results similar to the previously cited studies [15]. Their study focused upon both morbidity and mortality and subdivided complications within each category into preventable and unpreventable complications. They report a statically significant increase in both overall morbidity and morbidity deemed preventable by the researchers and collaborating attendings. However, the mortality rate was decreased, albeit not significantly, and there was no notable change in preventable mortalities. Furthermore, notable changes in the case mix occurred during the study, with significantly more atraumatic subarachnoid hemorrhages presenting in the years following implementation of work restrictions, and these changes may have had an impact on experienced morbidities and mortalities. The authors cite increased sign-outs and an inferred lack of familiarity with each patient as a possible explanation for the increased morbidity. While this study indicates that hour restrictions are no panacea in the realm of complication prevention, it demonstrates a need for more in-depth and lengthy review.

While addressing burnout in medical residency training programs is of paramount importance, the effects of a reduction in working hours across different medical and surgical specialties remain poorly understood. Proponents of policy changes argue that enhanced resident satisfaction and decreased fatigue will lead to improved performance within the clinical setting. Furthermore, residents working a maximum of 80 h may find themselves with more time to both maintain familiarity with the literature and become academically productive, both of which may improve the quality of patient care delivered in the near future. Critics counter that these policies may affect the quality of education at training programs and can disrupt the continuum of patient care. A common criticism holds that residents will gain exposure to fewer cases under work hour restrictions and thus forfeit the expertise that follows from multiple, repeated exposures. Results from the few early available studies on work hour restrictions are inconsistent, with some supporting a reduction in working hours, others associating such a restriction with an unexpectedly negative impact on patient care, and many finding no significant difference in outcomes. There exists a real need for further investigation, particularly long-term investigation, into the effects of various interventions aimed at reducing physician burnout and avoiding the complications potentially accruing from burnout.

Legal Implications of Trainee-Associated Complications

The manner in which the legal system deals with complications incurred through care delivered by residents is also of relevance, given that legal rulings often alter practice patterns as physicians endeavor to avoid unfavorable rulings. Notably,

in-training status does not afford residents' protection from malpractice claims, and estimates hold that approximately 22% of lawsuits name a resident among other possible defendants [15]. Malpractice claims must incorporate four key elements for success before a court; there must exist a duty to provide care, the duty must be breached, there must be a poor outcome, and finally the poor outcome inspiring the suit must be attributable to the breach of duty [16]. The breach of duty represents the most frequently contested element of a malpractice claim and typically requires a deviation from the accepted standard of care. However, the standard of care becomes especially difficult to identify in the case of residents, and courts have grappled with whether to compare residents to their resident peers, to licensed general practitioners, or to attendings within the relevant specialty. Although courts have remained cognizant of the societal value of medical training and aware that experience occurs on a continuum, recent decisions have tended to move from holding residents to a standard of care expected of residents to measuring residents' work against the standards applicable to fully trained specialists [17]. Courts and scholars justify the gradual shift on several grounds: residents may present themselves as physicians to patients who in turn reasonably assume that the standard of care associated with a fully trained specialist physician will be met. Furthermore, residents operate under the supervision of experienced specialists, and this supervision functions to ensure that a higher standard of care is attainable [17]. It follows that residents may improve their position before a court by fully disclosing their resident status to patients; however, even such disclosure does not mollify expectations that a specialist standard of care will be satisfied given the expectation of supervision.

Liability for complications incurred by residents generally extends to their immediate designated supervisors and also to the employing facility. The theory of vicarious liability finds application and permits claims of negligence or of failure to meet a given standard of care to be filed against supervising attendings even when those claims are reference actions of resident physicians [17]. Attendings become liable due to an implied failure to provide adequate supervision. Notably, supervising attendings assume the duty necessary for application of vicarious liability through contracts, on-call schedules, and discussions pertaining to consults and plans for care. Similarly, hospitals necessarily assume a duty to provide care for patients, and upon operating as teaching hospitals, they undertake a responsibility to implement and ensure adequate supervision. Thus, residents may be, and often are, named in claims of medical malpractice and can generally expect to be held to the standard of care associated with a fully trained specialist. However, accountability often extends to specialist supervisors and even teaching hospitals via vicarious liability.

Conclusion

In applied specialties such as neurosurgery and neurointerventional surgery, experience is of paramount importance. However, it is precisely experience that resident physicians lack. Several studies have queried a connection between resident care and complications and discovered no definite evidence that resident involvement causes more complications. Efforts to reduce complications,

however, are always relevant and warranted. Work hour restrictions have emerged as a means of preventing complications, yet the necessarily short-term studies available suggest that restrictions have had little impact on complications. When complications do occur, residents' in-training status does not exempt them from legal action. Rather courts generally hold residents to the standard of care expected of a fully trained specialist. Furthermore, vicarious liability extends to supervising specialists and teaching hospitals, given the duty to provide adequate supervision.

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Analyzing Complications

4

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Introduction

Analysis of complications, errors, and adverse events is part and parcel of healthcare delivery. Surgical complications result in increased morbidity, mortality, length of stay, readmissions, reoperations, defensive medicine, malpractice claims, and unnecessary costs. In the last two decades, surgical performance improvement has accelerated in response to clinical, financial, and legislative pressures.

In the 1999 landmark report *To Err is Human*, the Institute of Medicine (IOM) studied medical errors in the United States and found an annual rate of one million preventable adverse events, including 44,000–98,000 preventable deaths and $17–29 billion added costs [1]. In response to both medical errors and rising costs of healthcare, the Institute for Healthcare Improvement (IHI) formulated the Triple Aim: patient experience of care, population health, and per capita cost of health [2]. In 2010, in the *New England Journal of Medicine*, Porter defined value-based healthcare as outcomes divided by cost, challenging health systems and providers to become value rather than volume centered [3–5]. Spurred by the Affordable Care Act, Congress passed the Medicare Access and CHIP Reauthorization Act (MACRA) of 2015, establishing the future of medical reimbursement as merit-based incentive payment systems (MIPS) and alternative payment models (APMs) [6, 7]. In addition, public scrutiny of surgical complications continues to increase, as evidenced by the recently released and highly controversial ProPublica surgeon report card of provider-level performance based on Medicare data [8].

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History of Quality Improvement in Surgery

In the early twentieth century, Ernest Amory Codman laid the foundation for modern surgical performance improvement [9]. As a surgeon at the Massachusetts General Hospital, Codman developed a longitudinal system for tracking errors termed "end results" [9–11]. Codman meticulously recorded patient outcomes and systematically reviewed adverse events [11]. He created a classification system for complications as technical errors related to the procedure, as errors in medical management, or as manifestations of the severity of the patient's disease [12]. Codman's work proved controversial for profiling surgeons at the individual level, and the debate on public reporting continues today. However, Codman's early work led to the development of the hospital standardization program and subsequently the Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) [11]. In 1919, the minimum standards required hospitals to track and analyze complications; in 1983, the "Accreditation Council of Graduate Medical Education [ACGME] made it a requirement for departments with surgical training programs to hold 'a weekly review of all current complications and deaths, including radiologic and pathologic correlation of surgical specimens and autopsies'" [11]. Present-day surgical morbidity and mortality (M&M) conferences grew out of Codman's work.

Morbidity and Mortality Conferences

Surgeons, in particular academic surgeons, adopted M&M conferences as the medium for analyzing complications. Although M&M conferences are regular meetings explicitly focused on improving outcomes, they have several shortcomings. M&M conferences are not standardized across institutions. Ideally, conferences include a multidisciplinary audience, explore both technical and structural causes of complications, draw a representative sample of cases from the overall pool of complications, provide takeaways for preventing future complications, and assess longitudinal complication trends [13–16]. However, M&M conferences often fail to meet these goals. For example, complication discussion can derail into individual blame and excessive focus on technical details rather than overall structural assessment of contributing causes [17]. Anderson et al. reviewed 152 cases presented at M&M conferences and found that failure to "deliver disciplined treatment strategies, to recognize structural failures, and to achieve situational awareness" was among the most crucial causes of adverse events [17]. Bilimoria et al. developed an online morbidity, mortality, and near-miss reporting system to track patterns of adverse events for 15,524 patients with 957 complications [18]. The automated system analyzed weekly M&M reports and found underreporting of adverse events and skewed attribution of the cause of complications. M&M conferences reported 25% of complications and 42% of inpatient deaths; of reported adverse events, 75.2% were attributed to the nature of disease [18].

Antonacci et al. modified the traditional M&M conference over a period of 4 years by prospectively collecting data from 29,237 procedures, 1618 adverse

events, and 219 deaths to create a provider-level report card for 60 surgeons [12]. There was a 40% reduction in mortality and 43% reduction in age-adjusted mortality [12]. McVeigh et al. implemented a validated paper-based complication proforma on M&M conference reporting for 2093 cases and found 73% increase in morbidities reporting using the proforma compared to standard M&M reporting [19]. Mitchell et al. standardized the M&M by using a validated communication tool—situation, background, assessment, recommendations (SBAR)—and found improved quality of resident presentation and attendees' educational outcomes [19].

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) is a national, risk-adjusted, internally audited, and prospectively collected database of 30-day complications with 3.7 million cases from 517 institutions [20]. Studies of NSQIP have demonstrated reductions in complications of participating institutions. Hutter et al. compared data collected by M&M conferences to NSQIP and found considerable underreporting of in-hospital and postdischarge complications and deaths by M&M conferences in comparison to NSQIP [11]. The authors found that 50% of deaths and 75% of complications were not reported in M&M conferences [11].

Manufacturing Quality Improvement Methodologies

Performance improvement in surgery can be enhanced by the study of quality improvement methodologies and business intelligence strategies used in industries such as manufacturing, aviation, financial services, nuclear power, and computer science. For example, Sedlack et al. considered the Six Sigma methodology and compared complications in laparoscopic cholecystectomy to those in the aviation industry [21]. Bile duct injury occurs at a rate of 1 in 1500 cases, "equivalent to 95 defects per million opportunities … thus operating at 5.25 sigma. If the aviation industry operated at 5.25 sigma, there would be roughly 20 commercial airplane crashes everyday in the USA alone" [21].

In 2011, Nicolay et al. performed a systematic review of MEDLINE, the Cochrane Database, Allied and Complementary Medicine Database, British Nursing Index, Cumulative Index to Nursing and Allied Health Literature, Embase, Health Business Elite, Health Management Information Consortium, and PsycINFO databases to identify manufacturing quality improvement methodologies applied to surgery [21]. They found that (1) continuous quality improvement (CQI), (2) Six Sigma, (3) total quality management (TQM), (4) plan-do-study-act (PDSA) or plan-do-check-act (PDCA) cycles, (5) statistical process control (SPC) or statistical quality control (SQC), (6) Lean, and (7) Lean Six Sigma were used to reduce complications, reduce infections, reduce operative delays, improve antibiotic usage, reduce pain, reduce length of hospital stay, and reduce cost.

Shortell et al. defined the five principles of continuous quality improvement (CQI) and total quality management (TQM) as "(1) a focus on underlying organizational processes and systems as causes of failure rather than blaming individuals; (2) the use of structured problem-solving approaches based on statistical analysis;

(3) the use of cross-functional employee teams; (4) employee empowerment to identify problems and opportunities for improved care and to take the necessary action; and (5) an explicit focus on both internal and external customers" [22]. Ferguson et al. conducted a randomized control trial (RCT) of 267, 917 patients with CQI or no intervention for improving beta-blockade and internal mammary artery grafting for coronary artery bypass grafting; CQI improved beta-blockade from 3.6% (control sites) to 7.3% in the intervention sites [23]. Stanford et al. implemented TQM in the form of a cardiac surgery checklist, a European system for cardiac operative risk evaluation (EuroSCORE), monthly morbidity meeting, and daily progress reports in a pre- and post-intervention to reduce complications for cardiac surgery patients [24]. The 30-day mortality rate for 685 patients in the pre-intervention group decreased from 3.5 to 1.25% for 400 patients in the post-intervention group.

Moen et al. defined PDSA and PDCA cycles, also known as the "Deming, Shewhart, or control cycle[s], circle[s], or wheel[s]" as "four step cycle[s] for problem solving include planning (definition of a problem and a hypothesis about possible causes and solutions), doing (implementing), checking (evaluating the results), and action (back to plan if the results are unsatisfactory or standardization if the results are satisfactory)" [25]. Zack et al. implemented PDCA cycles in a surgical ICU and found that central-line-associated bacteremia decreased "from 3.7 to 2.8 per 1000 CVC line days" [26]. Goodney et al. implemented a PDSA cycle and a vascular surgery closure protocol in pre-intervention group of 140 patients and a post-intervention group of 112 patients; the intervention decreased minor complications from 17 to 7% and decreased closure device use from 57 to 32% [27].

Dr. Walter Shewhart developed the theory of statistical process control (SPC) or statistical quality control (SQC) while working at AT&T Bell Laboratories; Benneyan et al. wrote that SPC "tease[s] out the variability inherent within any process so that both researchers and practitioners of quality improvement can better understand whether interventions have had the desired impact and, if so, whether the improvement is sustainable beyond the time period under study" [28]. SPC maps processes by using Pareto and control charts in order to identify the sources of special cause variation amenable to intervention. Duclos et al. studied "control charts to monitor post-operative recurrent laryngeal nerve palsy and hypocalcaemia" over 2 years in 1114 thyroid procedures and found a 35.3% reduction in hypocalcaemia [29]. Ryckman et al. implemented monthly reports and control charts in pediatric surgery over 3 years to reduce postoperative surgical site infections (SSI). SSI decreased from 1.5 to 0.54 per 100 days [30].

While working at Motorola in the 1980s, Bill Smith built on the principles of Deming's TQM and created Six Sigma [Brady et al.]. The purpose of Six Sigma is to reduce variance; the term "Sigma" refers to the deviation from the median in the Gaussian normal distribution [31]. Six Sigma considers the number of steps that may lead to complications rather than unilaterally focusing on complications [31]; for surgery, this means analysis of required steps for any given process that may lead to complications. Six Sigma's phases for improving existing processes are define, measure, analyze, improve, and control (DMAIC) with

the ultimate goal of achieving 99.99966% error-free processes or less than 3.4 defects per million operations (DPMO) [Brady et al.]. Aboelmaged et al. reviewed 417 articles in the Six Sigma literature from 1992 to 2008 and reported that "examples of Six Sigma tools include Pareto analysis, root cause analysis, process mapping or process flow chart, Gantt chart, affinity diagrams, run charts, histograms, quality function deployment (QFD), Kano model, brainstorming … [and] examples of Six Sigma techniques include statistical process control (SPC), process capability analysis, suppliers-input-process-output-customer (SIPOC), SERVQUAL, benchmarking" [31]. Adams et al. implemented process mapping, cause and effect mapping, feedback and progress reports, and DMAIC cycles to reduce turnaround times between cases and found decreases in patient and surgeon out-to-in time by 32%, improvement in sigma for the process from 1.53 to 2.13 and savings of $617,000 [32]. Frankel et al. implemented cause and effect mapping, standard operative procedures, training videos, and clinical management algorithm guidelines and found a decrease in catheter-related bloodstream infections from 11 per 1000 to 1.7 per 1000 [33].

Originally labeled as the "Toyota Production System," Lean was developed in the mid-twentieth century as a manufacturing quality improvement methodology. Dellifrane et al. drew a distinction between Lean and Six Sigma as focus on "doing the right things (value-added activities)" versus "focus on doing things right (with no errors)," respectively. The basic steps of Lean quality improvement methodology are defining "an inefficient process, [identifying] waste within the process by delineating value-added and non-value-added activities, [improving] the process by creating standardized work, and [using] standardized metrics to guide the work." Muder et al. implemented Lean methodology to identify colonized patients, improve surveillance of swab cultures, isolate supplies, redesign isolation rooms, and improve use of alcohol-based hand sanitizer to study the rate of methicillin-resistant *Staphylococcus aureus* (MRSA) in surgical ICU patients over 4 years [34]. The MRSA infection rate decreased by 68%. Niemeijer et al. used a twofold Lean and Six Sigma approach to implement mapping using supplier-input-process-output-client (SIPOC) analysis, DMAIC cycles, Dutch version of appropriateness evaluation protocol (D-AEP), and dashboard feedback for 747 trauma surgery patients in the pre-intervention group and 946 patients in the post-intervention group. The length of stay for trauma patients decreased by 2.9 days [35].

Crew Resource Management

Morey et al. studied aviation crew resource management (CRM) and developed the Emergency Team Coordination Course as the intervention arm of a prospective quasi-case-control study of emergency department (ED) errors [36]. Crew resource management is mandated for all "military and commercial U.S. aviation crews and air carriers operating internationally … the basic principle of CRM is that crew communication and coordination behaviors are identifiable, teachable, and applicable to high-stakes environments" [36]. The rationale for the study was the data

from Risser et al. demonstrating lack of teamwork behaviors as responsible for 43% of ED closed claims post-adverse event indemnity payments [37]. Furthermore, Levin et al. reported that 80% of anesthesia errors are due to human error, and Taggart et al. reported that 70% of commercial aviation accidents are due to crew errors [36, 38]. Briefly, Morey et al. implemented the Emergency Team Coordination Course by organizing "around five team dimensions (maintain team structure and climate, apply problem-solving strategies, communicate with the team, execute plans and manage workload, and improve team skills)" [36]. Nine academic and community institutions with 684 clinical staff in the experimental group and 374 staff in the control group were evaluated on seven outcome measures [36]. Assessments were conducted before training and 4 and 8 months after training [36]. Overall, the clinical error rate decreased from 30.9 to 4.4% in the experimental group [36]. The major limitations of the study were the quasi-experimental nature as the interventional groups self-selected for the intervention; however, when Morey et al. compared hospital characteristics, there were no significant differences between the control and intervention arms [36].

McCulloch et al. implemented a 9-h nontechnical crew resource management (CRM) course to study 26 laparoscopic cholecystectomy and 22 carotid endarterectomy pre-interventions and 32 laparoscopic cholecystectomy and 23 carotid endarterectomy post-interventions [39]. They found a significant decrease in operative errors from 1.73 to 0.98 per operation and a significant decrease in nonoperative procedural errors from 8.48 to 5.16 per operation [39]. Though nontechnical skills improved technical performance, teams had variable responses to the intervention, and there was considerable culture resistance [39].

Checklists

Hales and Pronovost reviewed the use of checklists, inspired by error management tools in aviation, aeronautics, and product manufacturing, in medicine [40]. Hales and Pronovost defined a checklist as "a list of action items or criteria arranged in a systematic manner, allowing the user to record the presence/absence of the individual items listed to ensure that all are considered or completed" [40]. The authors cited the example of "the Boeing 777 Electronic Checklist … [which] decreased errors by an additional 46% as compared to paper-based checklists alone" [40]. Wolff et al. "used daily checklists and reminders in clinical care pathways for inpatients admitted for acute myocardial infarction or stroke" and found up to 55% improvement in primary outcomes such as "administration of aspirin in the emergency department, receipt of beta-blockers within 24 h of admission, dysphagia screening within 24 h of admission, and administration of aspirin or clopidogrel to ischemic stroke patients within 24 h of admission" [41]. Using checklists to prevent catheter-related bloodstream infections, the authors found a "decrease in the catheter-related bloodstream infection rate from 11.3/1000 to 0/1000" [40, 42]. In a separate study, Pronovost et al. demonstrated "a 50% decrease in ICU length of stay" with the implementation of a

checklist of daily clinical goals [43]. Early work with checklists in surgery led to the development of the World Health Organization (WHO) surgical safety checklist (SSC). The SSC "consists of 19 items and is used at three critical perioperative moments: induction, incision and before the patient leaves the operating theatre. The items contain an oral confirmation by the surgical team of the completion of some key steps for ensuring safe delivery of anesthesia, antibiotic prophylaxis, effective teamwork and other essential practices in surgery" [44]. In 2013, Bergs et al. conducted a systematic review and meta-analysis of the WHO SSC [44]. The authors performed a meta-analysis for any complication, surgical site infection, and mortality and found risk ratios of 0.59 (95% CI 0.47–0.74), 0.57 (95% CI 0.41–0.79), and 0.77 (95% CI 0.60–0.98) for the impact of the WHO SSC on postoperative outcomes [44].

Formula 1 Pit Stops

Catchpole et al. used a prospective interventional design to study Formula 1 pit stops and aviation models as tools for improving patient handoffs from complex congenital heart surgery to the postoperative ICU [45]. The research team met with the Ferrari F1 Formula 1 racing team and studied practice pit stops to design analogues to surgery. The new handover protocol was a triple-phase process with changes to leadership, task sequence, task allocation, predicting and planning, discipline and composure, checklists, involvement, briefing, situation awareness, training, and review meetings [45]. In 23 pre- and 27 post-intervention patient handoffs, the authors found a reduction in technical errors from 5.42 to 3.15, reduction in mean number of information handover omission from 2.09 to 1.07, and reduction of more than one error in technical and information handover from 39 to 11.5% [45].

Conclusion

While this review evaluated several approaches to surgical quality improvement, cultural attitudes are part of the challenge to analyzing complications in surgery. Sexton et al. conducted a survey of attitudes toward error, stress, and teamwork in medicine and aviation in 1033 surgeons, nurses, fellows, and residents from the United States, Israel, Germany, Switzerland, and Italy and 30,000 airline captains, first officers, and second officers from major global airlines [46]. Surgeons denied the effects of fatigue on performance at a rate of 70% in stark contrast to 26% of pilots [46]. Only a third of medical staff "reported that errors are handled appropriately at their hospital, a third of intensive care staff did not acknowledge that they make errors [and] over half of intensive care staff reported that they find it difficult to discuss mistakes" [46].

Overall, multiple business intelligence strategies have been applied to the analysis of complications, adverse events, and errors in surgery. Surgical morbidity and mortality (M&M) conferences are the most commonly used format for quality improvement but have several shortcomings. In the past two decades,

several studies have demonstrated significant improvements in care delivery and surgical outcomes with the application of manufacturing quality improvement tools, crew resource management, and checklists.

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Quality Assurance

5

Alon Orlev and Ketan R. Bulsara

Introduction

Technological advancements in medicine have resulted in complex systems for diagnosis and treatment. In the past, a few tertiary medical centers offered advanced medical treatments through highly trained practitioners. In recent years, more rural hospitals have gained experience using these technically demanding systems. An example of this is cardiac catheterization which evolved from primarily being utilized only in large medical centers in the 1980s to later diffusion of treatment capabilities into smaller, remote hospitals. As technology and expertise spread from selected few large medical centers to numerous smaller centers, procedural guidelines and quality assurance protocols were required in order to standardize treatment and evaluate results.

In vascular neurosurgery, many neurologic conditions that were until recently either untreatable or treated solely by microsurgical techniques have now become amendable to the rapidly evolving endovascular techniques. With this evolution, a growing number of practitioners from various medical backgrounds became involved in endovascular treatments. Given the heterogeneous background of the endovascular therapists, it is essential that there be procedural guidelines/standards that all the stakeholders accept. This is an essential first step to ensure quality care is uniformly delivered [1, 2].

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Quality Assurance Rational

Quality assurance involves clarifying procedure indications, treatment guidelines, results, and spectrum of acceptable complications. This process therefore involves all stakeholders ranging from patients to practitioners to hospitals and policy makers. Quality assurance measures are initiated at the specific medical society level by specifying training requirements. Treatment efficacy and safety then need to be measured. These results ultimately should guide hospitals and governing agencies in policy making and budgeting decisions [3].

In recent years, numerous patient- and peer-based reviews of practitioner performance have also been initiated outside the confines of the medical field. These are often nonformal publications that are published either in popular magazines or online. They rate physician performance based on patient reviews. Patients and families are becoming increasingly reliant on these nonformal quality measurement publications both for physician selection and even for deciding on what form of treatment to choose. The ultimate result is physicians as well as medical establishments are attempting to increase patient satisfaction and achieve higher-performance reviews in both the formal and nonformal reviews. The results of these will ultimately have implications regarding reimbursement.

Quality Assurance Challenges

As in many other medical fields, devising general quality assurance measures is a challenging task. Quality measures must take into account an extensive variability in patient population, hospital and country medical resources, physician reimbursement system, treating practitioner experience, and other factors. Often, these variables have an extensive role in diagnosis and treatment, therefore affecting quality indicators. A medical system which is reimbursed based on fee-for-service may perform more extensive diagnostic procedures than a medical system with quality-based reimbursement. Furthermore, it has often been argued that tertiary care centers treat more complex pathologies and therefore their complication profile may be different than that of community hospitals. Along these lines, training hospitals may have different outcomes than non-training facilities. Quality assurance measures must take into account the broad variability of setting, doctor, and patient population. Creating quality assurance measures accounting for this variability is no easy task and is an evolving process [4, 5].

Neurosurgical Quality Assurance

Studies comparing neurosurgical outcomes to other surgical fields have shown a trend toward increased morbidity in neurosurgical units. A large study published in 2016 on more than 48,000 neurosurgical patients showed that inpatient adverse events occur in neurosurgical patients at a higher frequency than non-neurosurgical

patients. This persisted even with risk adjudication for neurosurgical patients in safety indicators including pressure ulcers, iatrogenic pneumothorax, central line infection, postoperative hemorrhage or hematoma, postoperative respiratory failure, pulmonary embolism or deep vein thrombosis, and postoperative sepsis. This increased rate of complications and morbidity for neurosurgical patients has no clear explanation; however, it may imply that the measures utilized by other surgical specialties may not be applicable across all subspecialties.

In this same study from 2016, risk-adjusted rate for patient safety indicators was examined among neurosurgical patients undergoing procedures for different indications. The pathologies were broadly divided into four categories—neoplasm, epilepsy, trauma, and vascular lesions. The study found that the complex disease processes faced by neurosurgical patients predispose them to higher risk-adjusted rates and complications independently of other factors [4].

Breaking down the neurosurgical population further, there is a significantly higher rate of adverse events in vascular patients than in all other neurosurgical groups measured. Threefold higher complications in the common patient safety indicators were found in vascular patients when compared to neoplasm/seizure patients. Furthermore, this rate of complications was almost twice the rate in trauma patients. Interestingly, this study also showed higher rate of adverse events in large hospitals (>500 beds) compared to smaller hospitals (<200 beds). A higher rate of complications was also observed in high volume tertiary centers compared to lower volume neurosurgical units. A likely resulting interpretation from this is that even within neurosurgery, the complexity of the disease being treated is of paramount importance and needs to be adequately risk adjudicated [4].

Endovascular Quality Assurance

The multiple stakeholder medical societies ranging from neurosurgery, neurology, and neuroradiology have devised training requirements for medical professionals in order to ensure that physicians of diverse background acquire adequate training to safely perform endovascular procedures. Agreeing on a uniform set of training guidelines and outcome standards among all the stakeholders will be critical to ensuring quality care [6].

The published guidelines set various complication threshold levels and call for review of policies and implementation of changes within a practice if the procedure thresholds are not met. As an example, a 1% incidence of permanent neurologic deficit was set for cervicocerebral angiography, and higher levels call for investigation and specific action measures. Additionally, 16 specific indications for diagnostic angiography as well as relative contraindications have been outlined by the SNIS quality improvement guidelines. Procedural success rate defined as establishment or exclusion of pathologic condition was also defined. This procedural success rate was set by SNIS at 98% [5, 7].

In a different publication in 2013, international multisociety consensus quality improvement guidelines for endovascular treatment of stroke was published. These

guidelines were designed for individual practitioners result assessment. They aimed to establish minimum mandatory performance standards for treating physicians. Among the many guidelines, time interval from patient arrival at the hospital to specific diagnostic and therapeutic measures was established. Next, measures regarding revascularization results were defined. The clinical outcome threshold was defined by measuring patients' neurological outcome 3 months after stroke intervention. Finally, the desired rate of adverse events was also defined. These guidelines were set for physicians to monitor and compare their performance to the desired standard of care. Training and mentoring was suggested for physicians who failed to meet the published thresholds [8].

Conclusion

Quality assurance guidelines are created in order to set desired goals for all participants of the medical process. They serve as safety outlines and are crucial in an evolving medical field to ensure safe and quality medical care. Quality assurance assists patients as well as doctors and medical centers through some standardization to diagnose accurately, decide upon optimal treatment, ensure that the treatment is of maximum benefit, and finally ensure patient safety. Some informal published and online quality measurements assist patients in selecting a specific medical center or practitioner. Using quality assurance methods, various treatments can be compared for efficacy and safety. Quality assurance measures for neurosurgical patients indicate higher rates of adverse events than in other surgical fields. Within neurosurgery, vascular patients suffer more adverse events than patients undergoing other neurosurgical treatments. Finally, the evolving endovascular treatment shows promise in enhanced treatment safety but must also adhere to and undergo constant monitoring by quality assurance methods. What is clear, however, is that quality assurance is a mandatory and integral part of advancing endovascular surgery in particular and all of neurological surgery in general. For it to be effective, all its stakeholders have to agree on training and outcome measures and then adhere to them.

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Quality Improvement

6

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Introduction

Consumers of healthcare have poor access to data on neurosurgeons that is directly relevant to the service they provide. Unlike statistics and rankings available for professional athletes, there is little data available for neurosurgeons that specifically reflects the quality of their performance in the operating room and their patient outcomes. Neurosurgeons, and in this particular case cerebrovascular neurosurgeons, are not measured directly by their surgical skill and strategy but rather indirectly on metrics such as the number of urinary tract infections their patients get, days spent in the hospital, 30-day readmission rates independent of intent, and all-cause 30-day mortality rates.

What about the quality of the neurosurgeon in preoperative decision-making strategies, surgical aptitude, technical prowess, or postoperative clinical acumen? Further, how experienced is the neurosurgeon? How many equivalent cases have been performed, and what are the particular success rates relative to the level of complexity of cases? Very little is available on these specific factors. Rather, the field of quality improvement has attempted to quantify and qualify nonspecific data, package it into simple rankings relative to other programs, and have it available for the general public.

In the current society, consumers of healthcare rely on more familiar forms of quality measures that are easily accessible and digestible. We see rankings on all kinds of services and goods consumed. Ubiquitously available through the Internet, restaurants are ranked based on the quality of the food, the service they provide, and their price (e.g., Yelp, Google, Amazon). Technical services provided by plumbers, electricians, and carpenters are being ranked (e.g., Angies list). And more recently, professionals such as dentists and physicians are also being rank.

Their metrics and how a "5-star" rating is calculated are not always clear. More concerning and ever more very popular is the number of votes received on social

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media websites, the number of "likes" or "followers," or how many "hits" on YouTube cases or videos are posted by a neurosurgeon. In this landscape, is it ethical as a physician to spend more time self-marketing rather than improve on the technical and clinical nuances of their craft? Neurosurgeons have to acknowledge the reality that consumer-based metrics continue to gain more weight as surrogates for quality. Their livelihood depends on it.

Is it fair for a specialized group of professionals to be judged by consumers with only a superficial knowledge of the field? Is the field of cerebrovascular neurosurgery too complicated to be broken down into specific quality measures that can be appropriately interpreted by the general consumer? In gymnastics, the nuance of a perfect "10" has been carefully crafted and worked out by the governing body of the sport and is judiciously applied to each case by a panel of judges. Should it be up to the governing body of neurosurgery to develop specific criteria for what makes up the "perfect cerebrovascular case" and provide the consumer with an easy one through ten measure of each performance?

Further, do cerebrovascular neurosurgeons want this type of scrutiny? Do they want to be stratified against their peers? How will this "objective" data affect the current nonspecific rankings? How will this affect the consumer in choosing a local neurosurgeon versus seeking out the "best" neurosurgeon in the field?

Since cerebrovascular neurosurgeons are not doing this as a specialized field, the ranking process is being taken over by those outside the field: consumers, US News and World Report, the federal government, and insurance companies. As the decision-making capacity and autonomy among consumers of healthcare increases, the demand for accessible higher-quality data on cerebrovascular neurosurgeons will only continue to rise. Here we describe the origins of quality improvement, its current state, and applicability to cerebrovascular neurosurgery.

Peer Review: Origins

Expert physicians started to set the standard and critique the quality of their respective field in the first century, as documented by Dr. Ali Al Rahwi (CE 854-931). He stated that it was the duty of a visiting physician to make duplicate notes on the condition of a patient. When the patient had been cured or died, the notes of the visiting physician should be examined by a local council of physicians, who would adjudicate whether the practicing physician performed according to the standards of the profession [1, 2].

Considered the pioneer of quality improvement in medicine, Dr. Ernest Codman, a general surgeon at Massachusetts General Hospital, kept track of his patient's demographics, surgery, and outcomes on a notecard. He followed them over a year, and made the outcomes public so that patients could use this data to guide which surgeon they would choose. This idea of making medical outcomes data public was controversial, and he was ultimately fired for developing and advocating an outcome-based measure for evaluating surgeon competency [3]. Evaluation was to remain internal and based on criteria measured internally rather than by a public that would not be educated enough to interpret the relative significance of medical outcome data.

Internal Live Discussion: M&M

Morbidity and mortality conference (M&M) also originated in the early 1900s at the Massachusetts General Hospital. There, the patient's clinical course and complication was described and peer critiqued. Measures were taken internally in an attempt to prevent these errors from occurring in the future [4, 5]. This M&M conference occurs behind closed doors today within respective medical specialties. The information discussed is considered privileged, protected, and non-discoverable in the case of litigation.

Public Demand: Quality Improvement

Popular demand for improvements in the quality of healthcare developed after a revolutionary paper "To Err is Human" was published by the Institute of Medicine in 1999 [6]. It reported 2–4% of deaths in the United States occurring secondary to preventable medical errors—a total of 44,000–98,000 people dying, with most occurring secondary to systemic healthcare errors and not just the individual provider [7].

Public Data: US News and World Report

In 1990, the first list of hospital rankings was made public in the US News and World Report and has since expanded to include rankings of different diseases and specialties including neurology and neurosurgery. Based on composite data from other organizations, such as the American Hospital Association Annual Survey of Hospitals, its determination of their rankings appears and has been consolidated by an independent organization RTI International (Research Triangle Park, NC) since 2005. Neurology and neurosurgery are bundled together in one of the 16 main specialties evaluated. Scores are given for factors such as "success in preventing pressure ulcers," "nursing intensity," and whether a hospital is a designated Alzheimer's center. These factors fit under the umbrella of four major indexes of hospital quality: structure, process, outcomes, and patient safety (Avedis Donabedian 1966 model) that are weighed into their final score [8].

This ranking has become important to the consumer in making decisions about which hospital to go to. Hospitals recognize this ranking is important to maintain their reputation and business and differentiate themselves against other local and national institutions. But is this cost-effective? In the setting of rising healthcare costs, hospitals with more than 400 beds spend an average of over $2 million dollars a year on advertisements [9]. Utilizing a high US News and World Report ranking is important in the advertising process. No direct difference in reimbursement from payers is based on this ranking.

Public Data: University Health Systems Consortium

The University Health System Consortium (UHC) provides rankings of specialties such as neurosurgery/neurology based on three main factors: length of stay (LOS), cost, and mortality. Complications are risk adjusted through four steps: (1) assign a

severity of illness and risk of mortality to each case, (2) select a patient population as the basis for the model of norms, (3) perform a regression model to predict the probability of the above three factors, and (4) assign an expected probability [10]. For the cerebrovascular field, a risk model calculation is performed for each patient with an acute ischemic stroke and intracranial hemorrhage.

Government and Insurance Companies

Whereas the determination of the standard and quality of care in medicine was historically limited to a select group of individuals determined to be experts in the field, it has evolved to be a public critique of easily measurable outcomes determined by nonexperts driven by the bottom line—reimbursement for services.

Quality improvement governing and regulatory systems evolved with the development of the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) in 1952, which has worked closely with the Centers for Medicare and Medicaid Services (CMS) since 1965 [11]. Hospitals need to meet certain quality criteria determined by JCAHO to receive reimbursement for Medicaid/Medicare patients [12].

Affordable Care Act of 2010

After the financial crisis of 2007, and the realization that up to 20% of the US gross domestic product (GDP) is spent in healthcare, there was a new wave in healthcare, switching from volume-driven reimbursement to one based on value. Value was defined as the outcomes obtained per dollars spent. The Affordable Care Act of 2010 was introduced with the goal "to reduce the cost of health care providing quality health care for individuals, families, employers, and government" [13]. In order to determine outcomes, it is necessary to have metrics. Outcomes need to be risk adjusted to the particular population that is being studied. Having outcomes is necessary in order to interpret, compare, and improve different interventions or procedures.

Reimbursements are now tied to outcomes through value-based purchasing, pay for performance, and accountable care organizations. Specifically, CMS has required all physicians and physician extenders (e.g., PAs, NPs, CRNAs) to participate in the Physician Quality Reporting System (PQRS). Incentives were available for those practitioners who registered by December 31, 2015. Those that did not report or inadequately reported their data are subject to penalties up to 4% in payments in 2018. CMS uses PQRS data to calculate a "value-based modifier" (VM).

Starting in 2017 (payments will occur in 2018), a VM is added to a physician and their group which tiers the payment for services provided to a Medicare/Medicaid on a composite scores of quality and cost [14].

The first preview of this data was released April 2016 to groups and individual practitioners and serves as a starting place to prepare for the initiation of the new value-based modifier system in 2017. THE American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS) have criticized this VM program of having no specific or relevant neurosurgical outcomes data with a "one-size-fits-all" approach.

Cerebrovascular neurosurgery-specific PQRS are limited to the use of prophylactic antibiotics, percentage of patients where prophylactic measures to prevent DVTs were taken, the use of aspirin to prevent thrombotic events, proper screening and counseling for smokers, and the percentage of patients that have strokes after CEA or CAS for both symptomatic and asymptomatic patients [14].

Cerebrovascular Quality Initiatives: Qualities Outcomes Database

In an effort to provide more relevant and specific outcomes, the National Neurosurgery Quality and Outcomes Database (N2QOD) was developed at Vanderbilt University in 2013. Now reorganized as the Qualities Outcomes Database (QOD) , it is considered a Qualified Clinical Data Registry since 2015. Initial data was limited to spine but has now broadened to include the following cerebrovascular pathologies: intracranial aneurysms, arteriovenous malformation, ischemic stroke, carotid disease, and intracerebral hemorrhages [15].

The goals of the QOD are to (1) establish risk-adjusted morbidity and health-related quality of life outcomes for the most common cerebrovascular surgical procedures performed by cerebrovascular surgeons; (2) generate national benchmarks for morbidity, mortality, and quality data specific to individualized CV patient populations and practice settings; (3) provide quality data in real time, allowing measurements of health services' initiatives or practice paradigm shifts; (4) report on surgeon- and practice-specific quality and outcomes measures for supporting claims submitted by private payers; and (5) demonstrate the comparative effectiveness of different cerebrovascular surgery procedures.

Cerebrovascular Quality Initiatives: Neurovascular Quality Initiative (NVQI)

The Patient Safety and Quality Act (PSO) was developed in 2005 to allow physicians to share and analyze data anonymously, protected from legal discovery, without the barriers of patient consent and IRB approval, as long as the data remained HIPAA compliant. The Society of NeuroInterventional Surgery (SNIS) partnered with a clinical registry provider (MS2) to develop a web-based platform where physicians can enter data into a community database for acute ischemic stroke, arteriovenous malformation, and cerebral aneurysms [16]. Data collected include patient demographics, history, procedure, postoperative outcomes, and follow-up. Physicians, hospitals, and manufacturing device companies can access real-time analyses of this pooled data. Physicians can use this to compare their own data with others anonymously. Hospitals can use this to set benchmarks for quality improvement. Device companies can assess trends in device complications and improve their engineering and development.

The NVQI is limited by selection bias. Do physicians who submit data to the NVQI differ from others in practice? Do they tend to submit only interesting cases,

those with good or poor outcomes? Is it fair for hospitals to set benchmarks for quality improvement based on selected cases?

Cerebrovascular Quality Initiatives: Comprehensive Stroke Center Status

The Joint Commission, previously known as JACHO, created a three-tiered system for stroke centers: (1) Acute Stroke Ready Hospital, (2) Primary Stroke Center, and (3) Comprehensive Stroke Center. These tiers are based on specific criteria, such as the 24/7 availability of neuro-intensive care beds for stroke patients and the percentage of emergency department practitioners educated on an acute stroke protocol.

To help centers improve upon stroke care, the Joint Commission has joined the American Heart Association to develop a program called "Get with the Guidelines" for Stroke [17]. Performance measures such as the "nimodipine treatment is administered" for subarachnoid hemorrhage patients are set by the Joint Commission. The "Get with the Guidelines" program provides a "training program" with specific performance measures (e.g., door to needle time, TICI scores) as well as educational materials and checklist for the individual hospitals and group to help meet these standards.

It is interactive and can be customized to help facilitate discovery of areas of improvement that an interdisciplinary team can target. It provides ongoing data to provide feedback of improvement so that a program can continue to adapt to new data and improving targets. The program awards those that do well with bronze, silver, and gold levels for the amount of consecutive time that the hospitals demonstrate performance (3, 12, and 24 months, respectively) as well as different levels of Stroke Honor Rolls.

To complicate this even more, hospitals can receive a "comprehensive stroke center" certification not only through the Joint Commission but based on a different set of criteria and process by DNV-GL. Eligibility criteria include high-volume centers that treat more than 20 subarachnoid hemorrhage patients a year, perform ten coilings or clippings of aneurysms, and administer IV-tPA administration to more than 25 patients over 2 years. They need a dedicated neuroscience ICU with CT/MRI capabilities 24/7365 days a year (DNV-GL) and have similar outcome measures based on the American Heart Association and American Stroke Association measures [18].

Despite these efforts, are these measures and goals relevant? In ischemic stroke, the onset of symptoms to hospital door time is not included and has not changed recently. The goal of 60 min from hospital door to IV-tPA in 1 h is only met by ~1/4 of hospitals with this capacity. Are these goals realistic? Are they missing the point [19, 20]?

Medicare Government Data: Hospital Compare

Most recently in July 2016, the federal government released the Medicare Hospital Compare website that gives stars to hospitals based on death rates, readmissions, safety indicators, and patient satisfaction scores. This was an attempt to simplify the over 100 separate measures that the government reports on healthcare.

Providing a simple ranking of hospitals and specialties comes at a cost. Is it accurate? The Hospital Compare gave better ratings to hospitals with more missing data from nonacademic institutions with less complicated patients. Further, a modification in the statistical methodology of this same dataset changed the rankings of over 35% of the hospitals from the preliminary release in April versus the final release in July [21]. The large discordance between different ranking systems of the same hospital has also been heavily criticized [9]. The integrity and inconsistency of the data collection and analysis brings into question the ability of consumer-available rankings to accurately reflect the quality of specific hospitals and healthcare programs. On the other hand, do the measures that have developed specifically for cerebrovascular pathologies accurately reflect our goals of care and stratify the different centers appropriately?

Conclusion

The landscape of quality improvement in neurosurgery has evolved. We started from an era where patient outcomes were scrutinized in private among a group of physicians with a shared common knowledge base. Now quality improvement has turned to the hands of the consumer through social media, the government through Hospital Compare, private organizations such as US News and World Report, insurance companies through UnitedHealthCare, and mixed organizations such as the Joint Commission. Each with a complicated rating methodology that takes into account criteria that may not be relevant to our specialty, who uses statistical analysis that have little internal or external reliability.

In the current landscape, individual neurosurgeons and hospitals have to acknowledge and respect these criteria since their reimbursement and professional livelihood and integrity are inextricably linked to these [7]. All of this is occurring as ever-increasing healthcare dollars are spent on improving the appearance of quality measured by external sources and less effort spent on improving and evolving their individual craft of neurosurgery.

In preparation for the Olympics, we expected Michael Phelps to focus on his specialized task—swimming. He had dedicated time practicing, refining his technique, building his strength, concentration, and prowess to optimize his critical performances. The statistics were simple and clear—he was the fastest swimmer. Do neurosurgeons have this type of protection and space to refine their craft? With clear data showing that surgical skill varies widely among surgeons and that technical prowess is significantly associated with fewer complications, lower mortality, and shorter surgeries [22], we may be side-tracking the progress of the field of cerebrovascular neurosurgery with quality goals that are driven by outsiders with little expertise or understanding of the field.

We hope the insight provided here will guide leaders in our field to be innovative and unassuming in improving the direction of quality improvement in cerebrovascular and endovascular neurosurgery.

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Training and Standards

7

Ephraim W. Church and Kevin M. Cockroft

Introduction

Between the 1960s and 2000s, neuroendovascular surgery has extensively and dramatically evolved [1, 2]. Initial efforts were aimed at high-risk "inoperable" vascular malformations. The 1970s saw microspheres and detachable coils introduced. Microcatheters, microwires, and liquid adhesives appeared in the 1980s. As recently as 1990, Guglielmi pioneered the electrolytically detachable coil. This remarkable story continues to unfold as technology and techniques continue to advance, most recently in the area of ischemic stroke.

Training programs appeared rapidly as neuroendovascular surgery progressed. Occasionally these programs were formed and fellows graduated with limited oversight [3]. Additionally, there has been considerable discussion regarding the steep learning curve of many neuroendovascular operations [4]. For example, Singh et al. reported a steep learning curve in their elective aneurysm embolization practice over a 7-year period. The complication rate dropped from 53 to 10% [5].

Both neuroendovascular and open cerebrovascular surgery may carry high morbidity. The risk of stroke from diagnostic cerebral angiography is 0.3–5.7%, and risk is increased in patients with cerebrovascular disease [6]. Surgeon competence increases in a linear fashion up to 100 cases, and up to 200 cases may be necessary for the trainee [7]. Neurological complication rates for coiling of cerebral aneurysms range from 5 to 14%. Morbidity may be as high as 11% for clipping of unruptured aneurysms [8]. Like neuroendovascular surgery, there is clearly a learning curve for open cerebrovascular surgery. It is evident that guidelines and oversight for training and granting of hospital privilege are essential for the continued success of vascular neurosurgery.

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Neuroendovascular Training

Early Training Guideline Efforts

Although angiography was developed by neurologists and neurosurgeons, to a large extent, neurosurgeons left the field to develop open cerebrovascular surgery skills, harnessing the power of the operating microscope and microsurgical techniques. Meanwhile, radiologists developed new technologies and techniques in cerebral angiography. As neuroendovascular therapies become a reality, it was recognized that this new field would flourish only with close collaboration between neurosurgery and neuroradiology. Both fields bring essential knowledge and skill, and the greatest advances occurred at centers where teams of neuroradiologists and neurosurgeons worked together [9].

In 1994 there were more than 15 training programs in neuroendovascular surgery, but there was no formal process to ensure that both clinical skill and technique of trainees were thoroughly developed [9]. Initially, there was little opportunity for neuroendovascular training during residency. Significant modification of training programs would be necessary to incorporate new knowledge and skill. Early visionaries rejected the option of developing neuroendovascular and open cerebrovascular approaches in separate specialties because it is too easy to develop and propagate biased views about patient management. A hybrid form of training was needed.

The American Society of Neuroradiology (ASNR), the American Society of Interventional and Therapeutic Neuroradiology (ASITN), the American Association of Neurological Surgeons (AANS), and the Congress of Neurological Surgeons (CNS) developed informal recommendations for training guidelines as early as the 1990s [9]. This statement described paths for a physician with a radiology background and for a physician with a neurosurgical background. Both completed their respective residencies followed by 1–2 years of neuroendovascular surgery training (80–120 cases). For the radiologist, "a significant amount of time should be devoted to clinical neurosurgery with direct experience in neurointensive care management." Similarly the neurosurgeon "must receive formal instruction in radiation physics and radiation protection." Laboratory training should be incorporated into both pathways [9]. This early recommendation was followed by publication of a training program syllabus listing anatomic and physiologic knowledge, procedural aspects, pharmacology, and knowledge of cerebrovascular disease [9].

Joint Society Guidelines and Accreditation Council for Graduate Medical Education Program Requirements

The ASNR, ASITN, and the AANS/CNS Cerebrovascular Section developed and formally endorsed guidelines for training physicians in neuroendovascular surgery in 2000 [1, 10]. This document was remarkable in that it was 14 years in preparation and required considerable negotiations between governing bodies during a time when the field was still very young. Key features included training in the

management of cerebrovascular disease, understanding of treatment options, performance of neuroendovascular surgery, and perioperative management. Other specified features were as follows:

1. Duration of training was 1 year.
2. The program director was certified by a governing body and had expertise in neuroendovascular surgery, concentrating at least 50% of his/her practice in this area.
3. There was at least one full-time faculty member per two residents.
4. There were at least 12 months of preparatory trainings, including theoretical and clinical training as well as at least 100 catheter-based diagnostic angiographic procedures. Following this, there were 12 continuous months of clinical training. Specific areas of training were delineated. There were daily ward rounds and regular conferences including morbidity and mortality. Residents were encouraged to attend at least one national conference or course.
5. The program performed at least 100 therapeutic neuroendovascular cases per year, which were of sufficient variety. The trainee maintained a case log.
6. Appropriate equipment and facilities were available.
7. There was an environment of inquiry and scholarship, and residents engaged in scholarly activities including research.
8. Residents were encouraged to interact with related specialties through conferences/teaching.
9. There were reasonable duty hours and work accommodations.
10. There was semiannual evaluation.

This document was well received by the specialties, although some commented that the training period should be lengthened. Although the guidelines represented a standard, there was no enforcing body. Individual programs were responsible for the quality of training.

Based on the joint society guidelines, the Accreditation Council for Graduate Medical Education (ACGME) published program requirements for graduate medical education in "endovascular surgical neuroradiology" in 2007 (revised as recently as 2016) [11, 12]. ACGME guidelines indicate that a fellowship in interventional neuroradiology, endovascular neurosurgery, or endovascular surgical neuroradiology should be jointly administered by ACGME-accredited programs in neurological surgery and neuroradiology at the same institution. The length of training should be 1 year. There is a prerequisite of exposure to catheter techniques (100 angiograms) along with exposure to neurointensive care and neurosurgical techniques. Training should include exposure to the full spectrum of cerebrovascular disease (specific areas are listed). Up-to-date equipment and space must be available. The program should foster an environment of knowledge development, and there should be a program director who regularly evaluates trainees.

Similar neurosurgery/neuroradiology collaborative efforts also occurred in Europe in the early 2000s. The Union of European Medical Specialists Section of Neurosurgery and the European Board of Neuroradiology proposed training

standards and prescribed a training period of 2–3 years [13]. Prior to this, training standards in Europe often required prerequisite fellowship exams in radiology, making it difficult for neurosurgeons to enter the field [14]. There were similar efforts in Korea [15].

Current Training Guideline and Accreditation Efforts

Up to this point, training guidelines prescribed a hybrid of neurosurgical and radiological training. As the field matured, some argued successfully that this was no longer practical [16, 17]. While acknowledging the unique contributions of both neurosurgery and neuroradiology, many called for incorporation of neuroendovascular training into standard neurosurgery residency training. Neuroendovascular training was to be integrated into the neurosurgery residency, and residents with a particular interest would be free to pursue full training and certification during residency. Harbaugh argued that every ACGME requirement for training programs was currently fulfilled in neurosurgery residency, with the exception of performance of endovascular procedures and training in radiation physics, radiation biology, and radiation safety. These items could be added to the residency syllabus. In order for neurosurgeons to maintain a leadership role in the treatment of cerebrovascular disease, it was argued that neuroendovascular techniques must become part of the neurosurgery core curriculum. As an added benefit, mastery of angiogram interpretation would make neurosurgeons better at open cerebrovascular approaches. Moreover, patients will probably prefer surgeons who can perform all approaches and recommend whichever is best in their individual case.

An AANS Endovascular Task Force was asked to determine what might be done to ensure neuroendovascular surgery became the mainstream within neurosurgery. They offered several recommendations: first, an accelerated training pathway allowing neurosurgeons to perform a limited number of endovascular operations might be considered; second, neurosurgery programs should be required to introduce residents to endovascular techniques; and, third, they advocated continued close collaboration with interventional neuroradiology [16]. This effort led to incorporation of neuroendovascular knowledge and techniques in the ACGME/American Board of Neurological Surgery Milestone Project. A clear path for neuroendovascular training and certification of neurosurgical residents (and others) was delineated by the Committee on Advanced Subspecialty Training (CAST).

CAST is the most recent and most rigorous outline for training and certification in neuroendovascular surgery in the United States. This comprehensive program was agreed to by all the major societies involved in neuroendovascular work, including the Cerebrovascular Section of the AANS/CNS, the Society of Neurointerventional Surgery (SNIS), and the Society of Vascular Interventional Neurology (SVIN). CAST reports to the Council of the Society of Neurological Surgeons and is responsible for subspecialty training fellowships and certification in neurosurgical subspecialties. Recently published program requirements for neuroendovascular surgery include stipulations regarding setting, program director, faculty, and facilities/resources.

The fellowship training structure is outlined for neurosurgeons, neurologists, and radiologists. For the neurosurgeon, this includes completion of a 7-year ACGME residency. As a prerequisite, the candidate must perform at least 200 catheter-based diagnostic and/or interventional cerebral angiographic procedures. This is followed by 12 contiguous months of fellowship experience performed no sooner than PGY6. There must be a minimum of 250 interventional procedures, and minimum numbers of procedure types are specified. There are guidelines regarding documentation of clinical experience, conferences, and scholarly activity. Finally there are guidelines for supervision, duty hours, and evaluation [18, 19].

Individual Certification

In addition to program accreditation, in September of 2015, CAST began accepting applications for individual certification. All certificates are time-limited and will expire on December 31, 10 years after the date of issuance and/or concurrently with the timing of maintenance of certification renewal of the primary board certification (whichever comes first). General requirements for certification include completion of a neuroendovascular fellowship accredited by CAST and/or a fellowship with a similar structure as those accredited by CAST, board certification by the American Board of Neurological Surgery (ABNS) or the American Board of Medical Specialties (ABMS) of Radiology or Neurology, and a current, active, and unrestricted license to practice medicine in the United States. Of note, a "grandfather" system is currently in place until 2020. This "Practice Track" as it is known allows physicians who have already completed their primary board certification in neurosurgery, neurology, and/or radiology and have had additional training and/or experience in NES prior to the availability of CAST-accredited training programs to be eligible for CAST certification. To be considered for this program, applicants must have completed an ACGME-accredited residency training program in neurosurgery, neurology, or radiology with ABMS board certification. Applicants must also have completed a neuroendovascular fellowship or other equivalent trainings with a similar structure as those accredited by CAST and submit documentation of extensive neuroendovascular clinical practice experience. The entire application process can be completed online.

Other Training Initiatives

Spiotta et al. described a sequence of neuroendovascular milestones within neurosurgery residency training: core diagnostic angiography, advanced diagnostic angiography, guide catheter delivery, simple aneurysm embolization, and advanced aneurysm treatment [3]. They also made the case for simulation in neuroendovascular training. In one study, a group of residents performing angiography on a computer simulator were able to approximate fellows' performance over the course of the trial [20]. The authors also argued for inclusion of neuroendovascular simulator training in neurosurgical residency.

Others have advocated neuroendovascular simulation training, particularly at the resident level [21, 22]. Fargen et al. piloted a simulator-based curriculum aimed at neurosurgical residents [23]. After a 2-day simulator course, seven neurosurgery residents showed significantly higher written test scores, technical skills ratings, improved surgery times, and reduced fluoroscopic time. This group went on to confirm these findings in a larger cohort [24]. Rabbit, pig, and synthetic models have also been developed for training purposes [25–30]. One group discussed the possibility of virtual reality training in neuroendovascular surgery, drawing on concepts from aviation training [31].

Standards in Neuroendovascular Surgery

Guidelines for Specific Operations

Standards for some operations have been published. Neurosurgery and neuroradiology societies collaborated to produce guidelines for carotid artery stenting (CAS) [6, 32]. These guidelines specify operator prerequisites and number of CAS to be performed under supervision (4) and independently. More recently, guidelines for thrombectomy for acute stroke have been published. A collaboration between multiple societies including neurosurgeons, neuroradiologists, and neurologists (the NeuroVascular Coalition) first defined adequate training for neuroendovascular procedures for ischemic stroke in 2009 [33]. Recommendations included completion of an ACGME-approved residency training program in neurosurgery, neuroradiology, or neurology and 1 year of neuroendovascular training. They recommended prior experience including at least 100 cerebral angiograms, documented training in microcatheter techniques, and at least ten cases as primary operator. Further, it was felt that physicians should have outcomes that meet national standards. Physicians should have ongoing stroke-specific continuing medical education (CME), procedures should be performed at comprehensive stroke centers, and there should be around-the-clock access to neurologists and neurosurgeons in order to manage complications of treatment.

These guidelines were recently updated by an impressive worldwide collaboration of numerous societies [34]. Baseline training qualifications include residency training in radiology, neurology, or neurosurgery and dedicated training in neuroendovascular surgery. It is vital that physicians engage in ongoing stroke-specific CME. Physicians should also participate in a quality assurance program and demonstrate successful recanalization (TICI 2b or 3) in at least 60%, embolization to new territory in less than 15%, and symptomatic intracranial hemorrhage in <10% of cases. The statement also describes hospital requirements, including availability of vascular neurosurgery expertise.

Hospital Privileges

Although guidelines for hospital privileges in neuroendovascular surgery have yet to be published formally, we expect this type of effort to be forthcoming. CAST certification, involvement in the maintenance of certification (MOC) process, and

participation in a quality assurance program, such as a national registry, may well become required. Other related fields have published hospital privilege guidelines. For example, the Society for Vascular Surgery published guidelines for hospital privileges in vascular and endovascular surgery [35]. They suggest surgeons should have completed an ACGME-accredited vascular surgery residency. They provide guidelines for specific procedures. Lastly, they endorse both the Residency Review Committee for Surgery recommendations regarding open and endovascular case numbers in training and recommendations for credentialing in noninvasive vascular interpretation. Interventional radiology has likewise published statements regarding maintenance of privilege [36].

Maintenance of Certification

Hirsch et al. described the history and features of the MOC program in a publication for Society of NeuroInterventional Surgery (SNIS) members [37, 38]. Member boards of the American Board of Medical Specialties, including the American Board of Neurological Surgery (ABNS), received approval of MOC plans in 2006. MOC is based on six core competencies developed by the ACGME: professionalism, patient care and procedural skills, medical knowledge, practice-based learning and improvement, interpersonal and communication skills, and system-based practice. The four components of MOC are professional standing, lifelong learning, cognitive examination (every 7–10 years), and practice quality improvement. While the ABNS once granted lifetime certificates, time-limited certificates were granted starting in 1999. The MOC cycle consists of 3-year mini cycles. One must earn 150 h CME (at least 60 Category I in neurosurgery) and participate in the self-assessment in neurological surgery (SANS) examination each mini cycle. Practice quality improvement is assessed by submission of key cases and a tool for assessment, providing feedback about outcomes. Neuroendovascular is represented in this process with one of the recognized key cases being endovascular embolization of an anterior circulation aneurysm. The Quality Outcomes Database for Neurovascular (QOD-Neurovascular) a product of the NeuroPoint Alliance (NPA) an affiliate of the AANS is now operational and may aid in the practice quality improvement component of MOC. A similar quality database, the NeuroVascular Quality Initiative (NVQI) developed by the SNIS, is also available.

MOC efforts are occurring worldwide. The World Federation of Interventional and Therapeutic Neuroradiology published goals for maintenance of competence [39]. These include working in a comprehensive neuroscience center, completing at least 100 neuroendovascular cases in a 3-year period, maintenance of professional standing, satisfactory results of auditing, recertification every 5–10 years, and practice of continuous professional development (CPD). They define CPD “as the educative means of updating, developing and enhancing how doctors apply the knowledge, skills and attitudes required in their working lives.” Practitioners should also show a commitment to personal quality improvement.

Open Cerebrovascular Neurosurgery Training and Standards

A Changed Landscape: Fewer and More Complex Cases

While there are definite advantages to aneurysm clipping such as reliable occlusion, high rate of complete obliteration, and minimal chance of recurrence/hemorrhage, increasing numbers of aneurysms are being treated with neuroendovascular surgery [40]. The ISAT trial, published in 2002, probably did much to shift management toward endovascular treatment, but there were multiple contributing factors. Advantages of neuroendovascular surgery include shorter recovery and in many cases shorter operative time with lower short-term morbidity. Nevertheless, for the foreseeable future, there will remain many aneurysms for which clipping is the arguably most appropriate treatment modality. The presence of factors such as young patient age, hematoma, small size, and unfavorable branch relationships may continue to favor open surgical intervention. However, these can be difficult operations, requiring a degree of surgeon competence and resilience that can only be obtained with experience. Fewer training opportunities and more complex operations together form a significant challenge for the future of open cerebrovascular neurosurgery.

The reality of fewer open cerebrovascular training opportunities is well described. For example, Lai and Morgan reported a 53% reduction in microsurgical treatments of aneurysms in Australia between 2000 and 2008 [41], a time period spanning the publication of ISAT. The neurosurgical unit in Middlesborough, UK, reviewed all ruptured aneurysms treated in the pre-ISAT era from 1996 to 1999 [42]. They graded aneurysms for "ease of clipping" and "ease of coiling." If all aneurysms considered endovascularly easy or moderate were coiled, only 17 of 172 or 4 per year would have been available for clipping. These authors note such a problem is not unique to neurosurgery. A similar dilemma was seen in urology with the development of percutaneous lithotripsy. Vascular and cardiothoracic surgeries have faced similar training challenges. Strategies to overcome the loss of training opportunities include sub-specialization and fellowship training. The authors also warn that long-term follow-up of endovascular treatments may reveal problems and we may see an increase in open cerebrovascular volume in the future. To a certain extent, this warning continues to apply today, 13 years later.

Other authors have investigated the importance of experience in open cerebrovascular neurosurgery. Le Reste et al. performed a retrospective review of poor-grade subarachnoid hemorrhage patients treated with clipping by five surgeons with different levels of experience. Not surprisingly, they discovered an association between less experience and intraoperative rupture [43]. Also documented is the likelihood that clipped aneurysms are, on the whole, more complex than previously. Sanai et al. reviewed a series of 218 posterior communicating artery aneurysms treated over an 11-year period and found complex aneurysms (large/giant size, fetal posterior communicating artery, previous coiling, anterior clinoidectomy, adherence of the anterior choroidal artery, intraoperative rupture, complex clipping, and atherosclerotic calcification) were less likely to have favorable outcomes. They argue that, because the simple aneurysms are now treated with endovascular embolization, neurosurgeons should change their expectations and learn techniques for clipping complex aneurysms [44].

In 2002, Roberto Heros published an essay titled "Training the cerebrovascular surgeon for the 21st century," in which he traces the history of cerebrovascular neurosurgery and its present challenges [45]. He describes a golden era of cerebrovascular neurosurgery beginning in the 1970s with the operating microscope and the development of the EC-IC bypass. Many factors brought its decline including radiosurgery, less funding for research, and rapid progress in neuroendovascular surgery. He nevertheless argues that open cerebrovascular surgery is alive and well and should remain part of general neurosurgery training. Residents should be trained in a fully integrated open cerebrovascular/neuroendovascular service where they participate in the decision-making process regarding treatment methodology and care for both microsurgical and endovascular patients preoperatively and postoperatively. Heros points out that decision-making in vascular neurosurgery, best taught by example, is perhaps harder to master than the technical aspects, which are also complex. Fellowship training may help overcome loss of cases to neuroendovascular approaches, but exposure to a wide variety of cases will remain vital.

Others have advocated various different solutions for training in the setting of fewer but more complex cases. These include cadaveric and book study along with 3D preoperative planning [40] and surgical simulation [43, 46, 47]. Most agree that neurosurgery should maintain its leadership role in the treatment of cerebrovascular disease by training young neurosurgeons in both neuroendovascular and open cerebrovascular techniques. Neurosurgery residents seem to agree. Alshafai et al. sent a questionnaire regarding perceived competencies to residents from 45 countries who had completed their neurosurgical training recently. The vast majority thought that neuroendovascular and open management of aneurysms should be part of residency training (70.4% and 88.7%, respectively) [48].

Simulator Training and Fellowship Training

Much innovative work is being done in simulation training in open cerebrovascular neurosurgery [49]. Chugh et al. investigated the effect of a surgical rehearsal platform (SuRgical Planner) on aneurysm treatment with clip ligation. Their rehearsal platform offers the ability to practice a procedure prior to the operating room. In their study, time and number of clip attempts were improved following rehearsal [50]. Alaraj et al. created a real-time sensory haptic feedback virtual reality aneurysm clipping simulator (ImmersiveTouch). They tested the model on a group of residents who found it helpful overall [51]. Wong et al. devised a patient-specific virtual reality system for aneurysm clipping, as well as AVM resection (Dextroscope) [52, 53]. Future simulators will need to include representations of the brain surface and model brain and aneurysm deformation with retraction [49].

Aboud et al. created a model to simulate intraoperative aneurysm rupture, noting that rupture occurs in 9% of aneurysm surgeries [54]. Their "live" cadaver model includes artificial (sewn) and real (incidental) aneurysms, as well as artificial blood, which is irrigated through the cadaver head. Another group was able to 3D print patient-specific aneurysm models and implant them in human cadavers [55].

Surgery was then rehearsed. Others have described methods for the creation of hollow 3D aneurysm models [56, 57]. Even a human placenta model for microsurgical aneurysm clipping has been described [58].

Another potential solution for training of open cerebrovascular neurosurgery is support of fellowship training at high-volume cerebrovascular centers. The AANS/CNS Cerebrovascular Section maintains a database of both open cerebrovascular and neuroendovascular fellowships on their website. There are currently 11 open and 10 combined fellowships listed.

Guidelines for Competence

Neurosurgery residents graduating from an ACGME-accredited training program are considered competent in open cerebrovascular neurosurgery. Given the changing treatment patterns described above, this situation may change. Guidelines for competence may be needed in the near future if not already [41]. Here the CAST program may again play a role. Requirements for fellowship in cerebrovascular neurosurgery have been published [18, 19]. Prior to beginning the fellowship, the resident should have completed or be at a senior level in an ACGME-accredited neurosurgery training program. The standard length is 12 months. The experience should include participation in operative management of a wide range of cerebrovascular conditions, as well as study and research. At least 6 months must be spent in clinical activities. Expected characteristics, qualifications, or responsibilities of the sponsoring program, fellowship director, and faculty are outlined, but a volume of cases is not specified.

Recommendations

For Training Programs and Hospitals

- Take steps to further integrate neuroendovascular training into neurosurgery residency.
- Develop innovative strategies (potentially including virtual reality and simulation) for training future open cerebrovascular neurosurgeons in an era of fewer but more complex cases.
- Where appropriate, obtain CAST accreditation for training programs in neuroendovascular and open cerebrovascular surgery.
- Hire practitioners with CAST certification in neuroendovascular surgery.
- Acquire knowledge of credentialing guidelines for specific operations in order to ensure that physicians meet standards, recognizing that many operations have steep learning curves.
- Develop consensus standards for hospital privileges in neuroendovascular and open cerebrovascular surgery.

For Physicians

- Obtain CAST certification either through completion of a CAST-accredited fellowship or through the Practice Track pathway.

- Participate in MOC as outlined by the ABNS including CME, SANS, and practice quality improvement.
- Participate in a national registry (e.g., QOD-Neurovascular or NVQI) to advance knowledge and ensure outcomes meet national standards.

Conclusion

Dramatic changes in neuroendovascular and open cerebrovascular neurosurgery offer substantial challenges for neuroendovascular and open cerebrovascular neurosurgery. Significant progress has been made in training and certification in neuroendovascular surgery through the CAST program. Guidelines for hospital privileges and MOC remain important areas of effort in maintaining standards. There is a pressing need for innovation in training and maintenance of standards for open cerebrovascular techniques. We are confident that vascular neurosurgeons will rise to these challenges, ensuring the continued success of this exciting endeavor.

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Complication Avoidance and Management Research

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Abbreviations

ARUBA	A Randomized trial of Unruptured Brain Arteriovenous malformations
COSS	Carotid Occlusion Surgery Study
CTA	Computed tomography angiography
DSA	Digital subtraction angiography
DVT	Deep vein thrombosis
EC-IC	Extracranial-intracranial
EEG	Electroencephalography
ICG	Indocyanine green
ICH	Intracerebral hemorrhage
ISUIA	The International Study of Unruptured Intracranial Aneurysms
MEP	Motor-evoked potential
PE	Pulmonary embolism
PET	Positron emission tomography
SEP	Sensory evoked potentials
TIA	Transient ischemic attack
TPA	Tissue plasminogen activator
VTE	Venous thromboembolism

Introduction

Research into complication avoidance and management begins with a clear definition of what constitutes a complication. This proves to be surprisingly difficult. An example is interpretation of the results of the CREST trial [1] for carotid stenosis in comparing the periprocedural stroke and myocardial infarction (MI) risk between the two treatment modalities studied—carotid endarterectomy (CEA) and carotid artery stenting (CAS). The trial reported higher stroke risk with CAS (4.1 vs. 2.3%; $p = 0.01$), which led proponents of CEA to propose that CEA was the preferable procedure of the two for stroke prevention. However, proponents of CAS argued that the vast majority of strokes were minor and non-disabling (81%) and pointed to the increased risk of MI with CEA (1.1 vs. 2.3%; $p = 0.03$). Counterarguments were that stroke was more impactful than MI on quality of life measures, while again pro-CAS experts noted that cranial neuropathy and/or MI were important enough to be considered as major complications of CEA. This preceding brief discussion is illustrative of the conundrum of defining a complication: what constitutes a complication to one group may be an acceptable side effect to the other and vice versa. Indeed this difference may be more disparate from the perspective of the patient. For instance, temporal muscle atrophy following pterional craniotomy for a complex incidental unruptured middle cerebral artery aneurysm requiring innovative clip reconstruction with bypass may be considered a minor expected trade-off for a highly involved procedure by the surgeon, whereas for the index patient, this may prove to be so irksome that it impacts daily social interactions. The latter may well be considered a complication of surgery in the patient's eyes. Similarly, aneurysm recurrence following coiling which necessitates further angiography, radiation, anesthesia, and intracranial arterial catheterization with its attendant risks may be considered expected "aneurysm maintenance" by the surgeon but a complication by the patient.

The elusiveness in defining a complication is expertly discussed in a thought-provoking paper by Sokol and Wilson in 2008. Through a stepwise development, they propose defining a surgical complication as "any undesirable, unintended, and direct result of an operation affecting the patient, which would not have occurred had the operation gone as well as could reasonably be hoped." This implies an error of *commission*. We however believe that there is also a distinct category of adverse health outcomes that result from errors of *omission* (Table 8.1). For example, the inability to detect an aneurysm that ultimately presents with fatal rupture could be construed as a complication resulting from non-diagnosis. Therefore research into complication avoidance could be organized into the following categories/phases of patient care:

1. Screening for disease detection and patient selection for treatment
2. Perioperative morbidity
3. Follow-up

Table 8.1 Illustrative examples of the role of research in aspects of neurovascular disease management

Disease	Challenge	Type of complication	Research focus	Proposed study method
Intracranial aneurysm	Fatal rupture after detection where treatment was withheld per ISUIA criteria	Omission	Hemodyanamic and morphologic factors predicting rupture (beyond size)	Natural history studies, prospective disease registry, prospective observational cohort studies incorporating flow dyanamics at different time points
	Intraoperative rupture	Commission	Safer anesthetic and surgical technique in operating room and endovascular suite	Patient-specific simulation
	Incomplete coil occlusion of wide-necked aneurysm or residual after clip reconstruction	Omission	Novel devices for aneurysm occlusion	Prospective device registry with long-term follow-up
Arteriovenous malformation (AVM)	Debilitating seizures from withholding definitive microsurgery for grade 1 AVM per ARUBA	Omission	Better assessment of treatment risks	Characterizing AVM hemodynamics with novel imaging such as NOVA at different time points in natural history and treatment
Carotid stenosis	Stroke during stent	Commission	Enhanced distal protection devices	Healthy collaboration with industry for innovation in device development
	Recurrent stenosis after CEA from progressive atherosclerosis	Omission	Optimization of risk factor management	Community-based behavioral intervention care paths
	Progressive cognitive decline due to hypoperfusion from carotid occlusion and withholding bypass per COSS	Omission	Cognitive assessment at different time points, with and without intervention	Randomized protocol-based study incorporating robust and reproducible scales

Table 8.1 (continued)

Disease	Challenge	Type of complication	Research focus	Proposed study method
Acute stroke	Hemorrhage from TPA in a patient who also underwent mechanical thrombectomy	Commission	Optimizing outcomes of endovascular recanalization independent of TPA	High-quality multicenter prospective cohort design compared to simultaneously collected controls matched as best as possible (randomization impossible given TPA is a standard of care currently)
	Continued aphasia from dominant M2 occlusion	Omission	Demonstration of feasibility of endovascular intervention	Prospective randomized trial design of outcomes after M2 recanalization
ICH	Progressive hematoma expansion and perihematoma brain injury	Omission	Minimally invasive clot evacuation and drugs delivered locally or systematically	Rapid phase 1/2 trials of novel clot stabilizing/ dissolution agents

Each in turn can focus on errors of omission or commission. In this chapter, we shall consider some relevant examples and scenarios where research on complications can improve patient outcomes in neurovascular surgery (defined as any technique involved in treating neurovascular diseases).

Types of Research

Several methods exist to study the above components:

1. Case reports
2. Case series
3. Epidemiologic studies
4. Database analysis or registry studies
5. Prospective observational studies
6. Clinical trials (matched cohorts and randomized)
7. Simulation studies and modeling
8. Surgical procedural protocol standardization studies [2]

Prospective clinical trials typically progress through Phases I to IV with Phase III trials constituting the benchmark randomized controlled trials (RCT) (with blinding) [2]. Data proven in RCTs are most robust since data is gathered prospectively in comparison with a control group and with well-defined endpoints while accounting and controlling for variability and bias. It must be realized that these are

very expensive, time consuming, and involve vast resources at each stage. Clinical trials may examine screening, prevention, diagnosis, treatment, and quality of life. Behavioral interventional studies that introduce and modify operational procedures in the operating room and angiography suite hold great promise toward quality initiatives [3]. A limitation of clinical trials is they are best suited for homogenous diseases where equipoise is clearly established for two treatments. This is problematic in neurosurgery where diseases are often highly heterogenous and equipoise is often lacking or controversial.

Screening and Patient Selection

Efficient screening that detects asymptomatic/preclinical disease can potentially reduce "omission"-related complications. General screening of entire populations has the best chance of detecting asymptomatic disease but has not been well defined for cerebrovascular diseases. Targeted screening has a role but defining the target population is not straightforward. A growing body of literature on familial aneurysms has made it easier to justify familial screening.

Intracranial Aneurysm

For cerebral aneurysms, screening of persons with two or more first-degree relatives has demonstrated increased incidence of aneurysms [4], but the perception on cost-effectiveness or impact on outcomes has not been uniform [5–7]. Even in diseases such as polycystic kidney disease, screening is deemed to be of utility if performed selectively [8]. Once detected, there is the issue of selecting appropriate patients for treatment since benefits despite therapy-related morbidity should outweigh the risks. The ISUIA trial, in two parts, attempted to answer this question for aneurysms, but several significant study limitations preclude blanket recommendations—the study had inherent serious selection bias, overestimates the prevalence of aneurysms, about 1/3 of patients in the prospective second part (2003) switched to treatment arms and were excluded from follow-up, and includes cavernous carotid aneurysms [7, 9]. The trials do highlight the relative lower rupture risks for small aneurysms less than 7 mm (during 5 years of follow-up) for anterior circulation but lend no credence to aneurysm morphology or hemodynamics which has been shown to potentially influence rupture risk [10–13]. The latter are ripe areas for research into enabling better patient selection for treating unruptured aneurysms detected following screening (or as an incidental finding). Selection bias related to enrolling low-risk aneurysms undoubtedly influenced results. A number of studies since ISUIA have suggested a higher rupture risk for small aneurysms [14].

AVM

The management of unruptured AVMs is challenging because of their variable hemorrhage risk and highly diverse morphologies and brain locations. Attempts have been

made to characterize this risk by incorporating individual AVM-related factors [15]. There are however pertinent AVM factors that are still inconsistently characterized in AVM scores. Comprehensive hemodynamic characterization of an AVM including the venous component coupled with prospective collaborative database analysis is an exciting possibility toward consistent and accurate prediction of rupture risk [16]. Patient selection for treatment of brain arteriovenous malformations (AVMs) is also not straightforward since similar issues plague the few available published trials. The best known (on some counts, infamous) AVM trial is ARUBA, but the study is markedly inadequate in that included were low-grade, surgically curable AVMs randomized to conservative management alone vs. any procedural therapy and studied for a short follow-up duration of 33 months (mean) [17]. This presents another exciting area of research—application of the knowledge gained from multiple studies of AVM treatment modalities (with surgery, embolization, radiosurgery, and combinations) into formulating a trial that combines AVM flow assessment (as opposed to only static morphological parameters) and comprehensive multidisciplinary team-based randomization with recognition of true equipoise. Machine learning algorithms hold promise in this area [18].

Carotid Stenosis

The utility of carotid endarterectomy in symptomatic (>50%) and asymptomatic (>60%) carotid stenosis was demonstrated by NASCET [19], ACAS [20], and ECAS studies [21]. However the increasing application of carotid artery stenting (CAS) has added an element of decision making that has been studied in RCT settings [22]. The concerns with increased periprocedural stroke in CAS are an area of research focus. Possible study designs include incorporating enhanced distal embolic protection devices and longer clinical follow-up to ascertain long-term benefit. Another area of research is the frequent argument that medical management of vascular risk factors has become more aggressive and standardized over the years to the degree that the number of asymptomatic patients with carotid stenosis needed to treat (NNT) with CEA/CAS in order to prevent one stroke may be increasingly higher [23] though improvements have occurred in parallel in surgical technique [24]. A direct comparison between CAS vs. best medical management *and* CEA vs. best medical treatment is being undertaken in the CREST-2 trial that should address this issue. There are also opportunities to incorporate physiological parameters such as carotid plaque morphology and/or flow velocities into similar studies [25, 26].

Occlusive Disease

Treatment for carotid occlusion by EC-IC bypass was deemed to be of no benefit in the recent COSS trial that selected patients based on PET determined hemodynamic (qualitative) flow reduction and randomized them to medical vs. bypass treatment [27]. Yet many flaws noted in that trial need to be addressed with further research [28]. Important among these is the application of rigorous cognitive assessment measures in patients with carotid occlusion given the known effect of hemispheric hypoperfusion in carotid stenosis and occlusion [29–31].

Cognitive status per standardized tools and stratification according to flow reduction (e.g., quantitative rather than qualitative, with use of NOVA measurements) and, thenceforth, comparison of best medical management vs. surgical treatment is a good research focus. Identifying and selecting appropriate candidates for treatment in patients with moyamoya disease based on cognitive assessment and cerebral blood flow measurements is a similar area for potential research [32, 33].

Acute Stroke

Acute ischemic stroke management was revolutionized by the demonstration in multiple randomized trials of the efficacy of endovascular thrombectomy in large intracranial artery occlusion after IV TPA administration [34]. Expanding the pool of eligible patients for IV thrombolysis can also impact the results of stroke therapy if exclusion criteria are narrowed. An example would be the inclusion of patients on novel anticoagulants and accumulating high-quality evidence supporting this [35]. On the other hand, there is an accumulating body of evidence that demonstrates similar outcomes in patients who are TPA ineligible that undergo endovascular clot retrieval [36, 37]. This is a fertile area of investigation because if demonstrated with level 1 evidence, intravenous thrombolysis-related complications might be eliminated in this patient population.

The benefit of endovascular recanalization in occlusion at the level of the M2 vessels remains to be demonstrated. Recanalization of a dominant M2 has the obvious potential of improving speech outcomes, for example, and should be aggressively evaluated [38].

Perioperative Morbidity Reduction

Periprocedural complications can be reduced with attention to pre-, intra-, and postoperative management. Interventions for reducing surgical complications begin in the preoperative phase. An example is smoking cessation before general anesthesia to reduce lung complications and improve wound healing [39]. Another area of research into periprocedural complications is VTE prophylaxis—a recent meta-analysis noted the relative risks and benefits of prophylactic anticoagulation in terms of number needed to treat to prevent DVT/PE/VTE at the expense of increased risk of ICH [40]. The specific indication for craniotomy has not been found to have any correlation with VTE risk [41] but research into the role of prophylactic anticoagulation in procedures such as aneurysm clipping and AVM resection will help understand risk-benefit ratios in vascular neurosurgery which are likely different from tumor or trauma surgery.

Prevention of ischemic complications in aneurysm clipping has relied on intraoperative monitoring with evoked potentials and/or EEG and vessel imaging with ICG [42]. However, no randomized study has established the utility of combined modalities and the stage of surgery when a particular modality may be more applicable. This lends itself to a potential multicenter study of how to best utilize SEP, MEP, ICG,

microvascular Doppler, EEG, and other simpler modalities such as near infrared spectroscopy (NIRS). Another important facet of improving safety of aneurysm clipping is improved visualization of arterial anatomy. Incorporating smaller and more flexible endoscopes is an area of research to minimize morbidity [43]. Another area of research is studying ways of broadening the indications for novel minimally invasive approaches for aneurysm occlusion such as endonasal endoscopic techniques [44].

Wide-necked aneurysms are traditionally treated with clip reconstruction or flow diversion. Newer devices such as the WEB (Sequent Medical, Aliso Viejo, California) or pCONUS device (Phenox, Bochum, Germany) are being introduced for treatment of wide-necked bifurcation aneurysms. Despite promising early results, sound long-term studies are paramount in ensuring continued aneurysm occlusion.

An area often relegated to the background in the "heat of battle" is intraoperative radiation exposure to the surgical team and the patient. This is of immediate relevance to the neurovascular team. Typical exposures vary from diagnostic angiography, Dose Area Product (DAP) 102.4/Kerma-Area Product (KAP) 142.10/0.8–19.6 (5.0) mSv, to higher doses for interventional procedures, DAP 160–172/KAP 382.80 [45]. Reduction of radiation doses requires appropriate use of protective equipment and change in machine settings [46]. Research into better and less cumbersome protection equipment with newer materials is required [47]. Another interesting avenue is the investigation and application of MR angiography as a substitute for diagnosis [48, 49] and ultimately for endovascular therapy [50].

Follow-Up

An important shortcoming of some recent trials has been the lack of adequate data both in terms of length and quality. When such studies end up denouncing therapy altogether or recommend one preferentially over the other, potentially fatal errors of omission and commission occur. The ARUBA trial followed AVMs for a mean duration of less than 3 years for a lifelong disease in patients whose mean age was only in the mid-40s [51]. The implication is denial of potentially curative therapy for seizure patients with grade 1 and 2 AVMs, some of whom may be battling toxic side effects of multiple drugs for seizure control. This clearly demonstrates the need for longer follow-up in studies and disease registries. The COSS trial also followed patients only for 2 years, while there have been reports of progressive hemodynamic insufficiency leading to poor outcomes [52]. In addition, cognitive outcomes were not documented as diligently as stroke/TIA events [53].

For the individual neurovascular patient, research into ensuring close and continued follow-up through behavioral intervention is important. For example, there is roughly 6–10% risk of restenosis 2–5 years after carotid intervention and an elevated stroke risk in these patients compared to those without restenosis [54, 55]. Similarly, there is a definite risk of long-term (10 years) recurrence of aneurysms after coiling requiring retreatment which mandates diligent follow-up [56, 57].

Complication Avoidance Through Simulation

A clear understanding of the positional relationship between various cerebral structures, cranial nerves, and blood vessels is difficult to appreciate on two-dimensional radiographic imaging. For example, the complexity of cerebral vasculature around an aneurysm requires both extensive and exhaustive mental visualization by the treating neurosurgeon. Any error in navigating this complex anatomy may result in potentially fatal consequences for the patient [58]. Also, some neurosurgical cases allow for only one neurosurgeon to operate at a given moment. This is especially true for skull base procedures which have a very small and narrow surgical field of access [58]. Therefore, it would be prudent to practice on anatomically tailored models using 3D printing technology to better understand the anatomic relationships between the lesion and the surrounding normal structures. Many reports on simulation have emerged which have evaluated the utility of 3D printing and virtual reality (VR) in the field of neurosurgery [59]. The use of 3D printer to construct patient-specific three-dimensional models based on actual surgical brain pathology is called rapid prototyping [60]. This technology uses processed 3D images (e.g., 3D-CTA, 3D-DSA) to fabricate patient-specific 3D models. This has been further possible with the digitalization of radiographic images which converts a normal two-dimensional image into 3D [60].

Simulation helps surgeons rehearse delicate surgical maneuvers prior to the actual surgery. In addition, simulation can enhance the training opportunities for neurosurgical trainees as the former have declined due to various factors. Recently, several reports have been published which have evaluated the role of a virtual reality (VR) neurosurgical simulator with haptic feedback in practicing and perfecting techniques [61]. Yet cost can be a barrier to widespread adoption of VR technology, at least at present. Consequently physical models in combination with pre- and posttest objective assessment hold great potential in technique simulation in vascular neurosurgery. Such simulation modules have been developed by the Congress of Neurological Surgeons (CNS) along with scales to assess the performance of students in different types of neurosurgical procedures. The NOMAT (Northwestern Objective Assessment Tool) is a practical example of such a scale that accompanies the CNS Microanastomosis module [62]. Validation studies of NOMAT scale have documented that the scale can reliably distinguish between various levels of performance exhibited by residents at different levels of training [62]. Limitations do exist. For example, it is difficult to 3D print the consistency of different types of aneurysms such as calcified, mycotic, or thrombotic components. Secondly, real-time complications like aneurysm rupture or tearing of friable tissues cannot be simulated effectively. Additionally, it is challenging to recreate the haptics and feedback of different microsurgical techniques. Progressive technological improvements in augmented reality and computing, including via high-end gaming platforms, is an area for active research.

Conclusion

Most complications can be viewed as errors of omission or commission that can impact a patient during disease screening, selection for treatment, surgical intervention, or follow-up. Multiple avenues may be exploited in the study of complications occurring in different stages of disease management in the cerebrovascular patient. Although no single research technique can guarantee a 100% avoidance in complications, the cumulative results of various techniques can provide trainees and surgeons a road map or a blueprint for improving patient outcomes in the field of neurovascular surgery.

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The Checklist

9

Charles J. Prestigiacomo

Introduction

In 2009, the World Health Organization (WHO) published an important monograph describing the status of surgical procedures and complications worldwide [1]. The authors reported an unexpected high incidence of surgery based on an international data of 56 countries. They estimated that between 187 and 281 million surgeries (one operation per every 25 humans) were performed in 2004, with a major complication rate of 3–22% and a mortality of 04–0.8% – amounting to almost, one million people. As they stratified the analysis, the WHO suggested that death rates in some countries after major surgery could be as high as 5–10%. Most importantly, the data suggest that approximately half of all complications in this report was preventable.

Measures to improve the safety of all types of surgery are imperative in this world whose global population ages and the utility of surgery increases with ever-increasing access and ever-improving technology. There have been many steps undertaken to help bring safety to surgery. Though appropriate access to experts, proper training, and technological developments seem to be the natural and obvious response to improving safety, history has shown this to carry only some effect.

In the complex environment that is the surgical theater, the need for a delicate balance exists between standardized approaches and techniques for any given procedure and the individualized, experientially – driven approach to any unexpected event. Certainly, in the midst of an unexpected or previously unseen event, there is great concern as to whether the course of action that will be chosen is "correct," i.e., will maximize the patient's outcome while minimizing any adverse events. Whether recognized or not, it is during these times that every surgeon will go through their

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own, sometimes private, sometimes not consciously recognized, checklist. It may be represented by a mentor's voice, a "flashback" to a similar event when they were a resident, or a sudden illumination and synthesis of various facts that surface at the most critical of moments. In all instances, the surgeon then proceeds to perform specific "steps" or "checks" to complete the procedure. In other words, checklists were never foreign to the medical field: they were just not outwardly recognized, organized, or studied.

Since its first, formal introduction into the world of medicine in 2006 [2], checklists and their use have penetrated many areas of medical and surgical science. Though outwardly proven to be of extreme benefit, the checklist is not a panacea. A direct benefit has been proven, yet there may be a greater effect in using the checklist from its collateral, or halo, effect. To understand how a checklist can be used, its benefits, its limitations, and most importantly what a checklist is not, a careful survey of the checklist is necessary.

Historical Aspects

Relatively new to the medical world in its current state, the checklist took its true form as a safety device in the aviation industry. As widely reported, in 1935 Boeing was presenting a new, four-engine bomber to the US Army Air Corps [3]. Known as the Model 299, its initial operations were near flawless such that it was assumed that the final phase of trials for approval was merely a formality. With approximately 200 aircraft to be ordered, Boeing ensured that their top test pilot, along with top pilots from the US Army Air Corps, would be conducting the flight. Though it was Pilot-in-Command (PIC) Major Ployer P. Hill's first time flying the Model 299, copilot Lieutenant Donald Putt had flown prior test flights on the Model 299. Of note, Boeing Chief Test Pilot Leslie Tower and Boeing Mechanic C.W. Benton were present on the flight as well. Upon takeoff, the craft proceeded to climb smoothly but suddenly stalled, turned onto its wing, and crashed onto the airfield, bursting into flames. Though all crew members (including Henry Igo, a representative from Pratt & Whitney, the engine manufacturer) initially survived the crash, Hill and Tower died of their injuries.

An investigation attributed the crash to pilot error as they noted that the elevator and rudder gust lock, the device that locks the airplanes control surfaces in neutral position, had not been released prior to takeoff (Fig. 9.1). The reason for this pilot error was attributed to the fact that pilot and copilot were required to trim each of the four engines' power individually to ensure normal flight attitude. In so doing, it was clear that the PIC forgot to remove the lock. Indeed, later investigations noted that this error was recognized, with the Boeing test pilot Tower attempting to release the lock, but too late. The plane, though clearly better than its competitors in all aspects, was deemed "too complex a plane for anyone to fly."

The army purchased a different bomber aircraft but decided to nonetheless purchase 12 Model 299s. It was clearly understood that another accident, however minor, would cancel the program permanently. Pilots, appreciating the benefits of

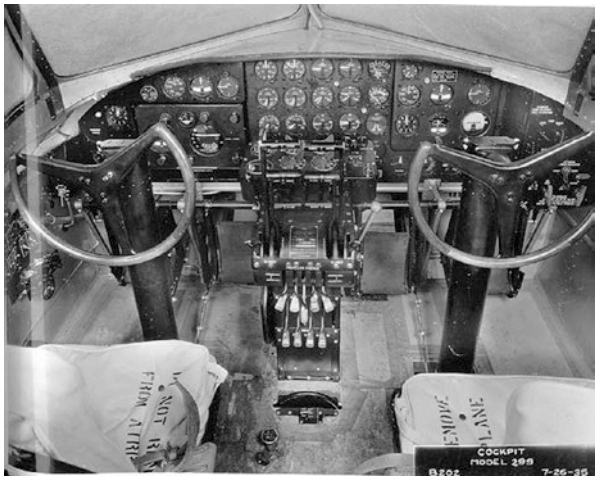


Fig. 9.1 Cockpit design of Boeing Model 299 demonstrating the complexity of a four-engine bomber, that will become the B-17 Flying Fortress

the plane and the fact that there was no room for error, began to collate a series of steps that would be sequentially performed such that critical elements would not be forgotten. Thus, four checklists were born: takeoff, flight, pre-landing, and after-landing. Simple in nature, and direct in content, these checklists became one of the foundational elements for aviation and space flight. The Model 299, with its trained pilots and checklists, flew without accident in the ensuing years accumulating over 1.8 million miles in the air. Of note, this impressive record resulted in the US Army Air Corps purchasing a total of 12,731 of these aircraft, which came to be officially named the now famous B-17 Flying Fortress.

The simplicity and beauty of the checklist allowed for the development of more complex systems. The incorporation of checklists in all aspects of complex technology was epitomized in the development of the numerous checklists for standard and emergency procedures seen in the Space Flight Program. Indeed, Apollo 11 Astronaut Michael Collins, pilot of the Columbia Capsule was quoted as stating that in the Apollo missions' three-man crew, the checklist served as the "Fourth crew-member" [4].

Checklists in medicine have existed for years, though not necessarily in the form we currently recognize. For instance, Cushing's introduction of the anesthesia record in 1894 to assess and record vital signs and their trends served as a checklist insofar as it standardized and organized the gathering of patient-specific information, such as heart rate, blood pressure, and respiratory rate [5]. Nurses embraced the idea of the checklist in the 1960s and thus created a method to chart vital signs as part of the routine.

In 2001, the checklist entered a new era in medicine. Firstly, the checklist turned its focus on a specific task. Secondly, it became focused on the physician. Finally, it was used as a tool to track and evaluate if quality in care could be improved. Pronovost et al. created a straightforward, simple list of steps required to avoid infections in central lines [6, 7]. This dramatic reduction in infections noted at the Johns Hopkins Hospital was then expanded to cover additional hospitals. In their publication of 2006, the authors reported a 66% reduction in central line infection

rate through the use of this simple, straightforward checklist in Michigan hospital ICUs [2]. Though the checklist was the focal point of the study, it was clear that many other aspects to conducting the study proved to be of benefit. Champions were chosen in each ICU to be responsible (and accountable) for that portion of the study. All members were educated in the evidenced-based data justifying the steps of the checklist (i.e., rationale and subsequent "buy-in"). Team members were given authority to "check" each other, eliminating some of the hierarchy and behaving more as a "crew."

Soon thereafter, multiple studies demonstrating the many benefits of checklists were published [8, 9]. Checklists for different procedures and evaluations in the inpatient and outpatient setting were created and evaluated. Though usually positive in the results that were reported, there seemed to be some studies where the effects were not as strong or neutral at best [10]. Consequently, checklists are being evaluated in the setting of additional tools and more complex environments.

Aspects to a Checklist

Checklists are deceptive. Their ability to exact change for the positive belies their ability to be created. The design of the checklist may have much to contribute to its ultimate success. Aviation checklists have an elegant simplicity, for example. Each checklist can fit on a small card for easy access, with large type font. Each item is summarized in a few words, and may include jargon. Jargon is an important aspect to the checklist, as it forces the user of the checklist to be familiar and even knowledgeable with the subject—an important aspect to ensuring success.

Weiser et al. discussed the methods by which one could design and launch a checklist in the medical field [11]. Taking example from the aviation industry, the authors noted that the implementation of the checklist should be performed in five steps: content and format, timing, trial and feedback, testing and evaluation, and local modification.

In designing a checklist, I consider the following acronym in order to help provide a functional checklist: A checklist should be "SIMPLE" (Table 9.1).

Table 9.1 "SIMPLE" aspects to the checklist

*S*tandardized	Must reflect a standardized protocol
*I*mmediate communication	Must be easily understood and communicated to all team members
*M*emorized elements	Must have key steps of the checklist memorized and executed almost reflexively
*P*ractical	Must have a practical cohesiveness and nature to the concept of the checklist (e.g. practical steps to achieve hemostasis)
*L*ogical	Must have a logical progression of steps that make sense
*E*asy to execute	Must "flow"

Standardized

The steps of the checklist should reflect a standardized protocol or a standardized portion of a protocol. It is thus important to first address whether the level of standardization exists.

Immediate Communication

The checklist must be easy and immediate to communicate to all members of the team. Whether the item of the list is designed to be executed or simply to be checked, it must be written so as to be easily understood.

Memorized Elements

Every checklist has certain elements that must be performed almost reflexively. They must be executed quickly and effectively without wasting the time to look at a checklist in the first place. In the particular case of emergency checklists, there will be elements (2 or 3) that must be memorized and executed in this reflexive manner.

Practical

Though checklists can be used for highly complex functions, there must be a practicality to it. The steps, process, and goal need to make sense.

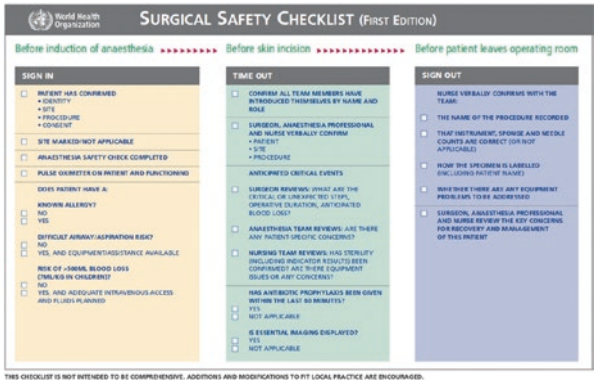
Logical

The checklist must contain a progression of steps. The more logical the steps are in the checklist, the easier it shall be to execute.

Easy to Execute

Finally, putting the aforementioned together, the checklist must be easy to execute. The synthesis of standardized, communicable, memorized elements that are practical and logical makes the checklist "flow."

Thus, the design of checklists in medicine should fulfill these criteria in order to maximize the likelihood of success. This alone, however, will not *ensure* success. The success of the checklist must also be well-integrated into the natural, existing


SURGICAL SAFETY CHECKLIST (FIRST EDITION)

World Health Organization

Before induction of anaesthesia | Before skin incision | Before patient leaves operating room

SIGN IN

- PATIENT HAS CONFIRMED
  - IDENTITY
  - SITE
  - PROCEDURE
  - CONSENT
- SITE MARKED/NOT APPLICABLE
- ANAESTHESIA SAFETY CHECK COMPLETED
- PULSE OXIMETER ON PATIENT AND FUNCTIONING

DOES PATIENT HAVE A:

KNOWN ALLERGY?
- NO
- YES

DIFFICULT AIRWAY/ASPIRATION RISK?
- NO
- YES, AND EQUIPMENT/ASSISTANCE AVAILABLE

RISK OF >500ML BLOOD LOSS (7ML/KG IN CHILDREN)?
- NO
- YES, AND ADEQUATE INTRAVENOUS ACCESS AND FLUIDS PLANNED

TIME OUT

- CONFIRM ALL TEAM MEMBERS HAVE INTRODUCED THEMSELVES BY NAME AND ROLE
- SURGEON, ANAESTHESIA PROFESSIONAL AND NURSE VERBALLY CONFIRM
  - PATIENT
  - SITE
  - PROCEDURE

ANTICIPATED CRITICAL EVENTS

- SURGEON REVIEWS: WHAT ARE THE CRITICAL OR UNEXPECTED STEPS, OPERATIVE DURATION, ANTICIPATED BLOOD LOSS?
- ANAESTHESIA TEAM REVIEWS: ARE THERE ANY PATIENT-SPECIFIC CONCERNS?
- NURSING TEAM REVIEWS: HAS STERILITY (INCLUDING INDICATOR RESULTS) BEEN CONFIRMED? ARE THERE EQUIPMENT ISSUES OR ANY CONCERNS?

HAS ANTIBIOTIC PROPHYLAXIS BEEN GIVEN WITHIN THE LAST 60 MINUTES?
- YES
- NOT APPLICABLE

IS ESSENTIAL IMAGING DISPLAYED?
- YES
- NOT APPLICABLE

SIGN OUT

- NURSE VERBALLY CONFIRMS WITH THE TEAM:
- THE NAME OF THE PROCEDURE RECORDED
- THAT INSTRUMENT, SPONGE AND NEEDLE COUNTS ARE CORRECT (OR NOT APPLICABLE)
- HOW THE SPECIMEN IS LABELLED (INCLUDING PATIENT NAME)
- WHETHER THERE ARE ANY EQUIPMENT PROBLEMS TO BE ADDRESSED
- SURGEON, ANAESTHESIA PROFESSIONAL AND NURSE REVIEW THE KEY CONCERNS FOR RECOVERY AND MANAGEMENT OF THIS PATIENT

THIS CHECKLIST IS NOT INTENDED TO BE COMPREHENSIVE. ADDITIONS AND MODIFICATIONS TO FIT LOCAL PRACTICE ARE ENCOURAGED.

Fig. 9.2 First edition of the WHO surgical safety checklist

workflow. For example, in implementing the WHO surgical safety checklist, it is required that members of nursing and anesthesia meet and discuss with the surgical team the patient's condition, surgical procedure, potential complications (such as airway and blood loss) and disposition (Fig. 9.2). Though intuitive and necessary, introducing a specific time where *all* members of the team were in one place to discuss the patient wasn't necessarily part of the existing workflow. The nurses and scrub technicians would be preparing the room for the surgery, while the resident and attending surgeon might be obtaining consent and the anesthesiologists might be reviewing the chart: all in different locations of the operating suites. However, once every member of the team was educated as to the potential benefits to the patient, every member of the team modified their personal workflow to incorporate this crucial step into the daily routine.

Once incorporated, each member of a small pilot team is encouraged to provide feedback during the trial phase. This equally crucial step serves several purposes: it quickly highlights the limitations of the checklist in its current form with regard to the SIMPLE criteria, and it gives all members of the team ownership. It also allows observers to note the amount of time it takes to execute the checklist, which becomes important when the list is then globally released to the entire team.

Once complete, the formal testing phase cannot begin without a mechanism of evaluating its effectiveness. Clearly, this step requires an understanding of what outcomes can and should be measured to reflect the true effects of the checklist. Additionally, it is evident that this phase will require personnel dedicated to gathering the data and ensuring compliance.

Finally, checklists are living documents. Though the major body of the checklist is the same, there should be room to modify it within each setting. In general, this should occur after a significant period of time has passed in using the initial version of the checklist. It is based on the data and feedback of this period of implementation that one can then reassess and make modifications in its form and use.

The Successful Checklist

As can be surmised, checklists do not achieve success in isolation. Though there are many important components to the successful checklist, some recently published data suggest that the checklist itself is not the key to success. There is evidence that the environment in which the checklist is practiced is just as critical as the usefulness of the checklist itself.

In order to achieve success with the checklist, all members of the team must be very familiar with the contents and terminology. As discussed previously, the use of jargon in the checklist ensures that the users of the checklist are more than mildly familiar with the procedures and issues involved during the use of the checklist. Not knowing the terminology included in the checklist forces all members of the team to become educated and facile on the topic well beyond the steps of the checklist.

Secondly, the use of the checklist requires training. Again, the benefit of this training is the subsequent cohesive nature of the team. Each member of the team now recognizes, understands, and acknowledges the contribution of all members in ensuring patient safety. Furthermore, each member of the team is trained in a standardized fashion to perform a specific function of or within the checklist. This likewise ensures that, as in the military whose soldiers train in the same fashion, any circulating nurse in an operating room, for example, will execute his/her duties in exactly the same way. Such interchangeability is *most* crucial when there is a need to execute an emergency checklist.

When used correctly, the checklist gives the team time to review. In the setting of less familiar events, such as emergencies, the checklist can quickly refamiliarize each team member of what would need to be done in case of emergency. It would provide all members the time and opportunity to ask questions and perhaps even discuss alternate solutions if events warrant it.

Checklists can be used as a point of departure for in-service education sessions with various members of the healthcare team. Though they should not serve as the focal point by any means, they would serve as an excellent summary and synthesis of what is important in the care of the patient for that specific medical or surgical problem.

What can be considered the *most* important aspects to a successful checklist are communication and teamwork (crew resource management). If one analyzes the aforementioned, it is clear that the common denominator for success is constant, transparent communication and teamwork. Each member of the team, though responsible for specific aspects of the checklist, is aware of all others and is attentive to the other members of the healthcare team. Communication is a continuous link among the members of the team in ensuring that all aspects of the list are adequately performed. Indeed, this communication is not performed and will not be successful if it is generated in a unidirectional "top-down" form. Success with communication allows for a free exchange of information and ideas without the restriction of hierarchy. Likewise, teamwork requires the ability for the leaders of the team to

recognize, acknowledge, and accept information, analysis, and solutions from all members of the team. Without communication and without teamwork, there is no education, training, review, or even smooth workflow. Without communication and teamwork, the checklist dies.

What a Checklist Is Not

It is as important to understand what a checklist "is not" as it is to know what a checklist "is." Checklists are not tools for teaching *de novo*, they are tools for emphasizing and enhancing knowledge that already exists in the armamentarium of a team. Checklists do not succeed if they are used as a primary source of knowledge. In other words, a checklist should address steps and techniques that are already familiar and facile to the group.

Checklists are not to be used as a means of introducing new protocols, techniques, or evaluations in isolation. Though helpful in those situations, they must be introduced after the very concepts have been taught and the team has become at least competent. As an example, the introduction of a checklist on embolization of an arteriovenous malformation and the emergency management of a vessel rupture will not be of any use if the team does not have a working knowledge of why the complication can occur and what needs to be done in this setting.

It is easy to use the checklist as a crutch, a means to not have to remember or even learn what should be done, especially in the rare instance of an emergency. It is this very attitude that will result in the failure of the checklist. The checklist will not supplant skill and experience: It is a guide to ensure that in the heat of the event, the team does not forget steps that they would otherwise know how to execute.

Checklists do not have the answers, and they do not bring insight. A checklist works when it is applied to the right circumstance. The team must first recognize the circumstance and apply a correct checklist to it in order to achieve success. Furthermore, it is important to recognize that the environment within which checklists in medicine are used is quite different from the environment of an aviation checklist. As discussed, the Model 299 bomber was built as a clone of the original model. Every craft is identical. When there is a failure (or emergency), the effects are reproducible and the subsequent approach to managing them are likewise identical. Checklists work well in that situation. Furthermore, there are laws of physics that come into play during emergencies that are of great import to the pilot and assist in performing some of the important emergency functions on a checklist (for example, during engine failure, the pilot must establish the appropriate pitch of the airplane to maximize gliding distance which is identical for every craft of that particular model). Humans, human illnesses, and their complications are not so. Only certain aspects of complications are consistent and reproducible from patient to patient (e.g., intraprocedural rupture of an aneurysm, embolus in a parent vessel). Thus, checklists cannot help in all situations.

A common downfall for the checklist is the regression to simple "box ticking" [12]. In a study by the National Health Service, the authors reported that though the

checklists were used 97% of the time, it was noted that only 67% of the checklists were complete [13]. In 40% of cases, at least one team member was absent. Again, this observation points to the importance of communication, inclusion, and buy-in from all members of the team and should begin well before the checklist is introduced into practice.

Emergency Checklists

Checklists are not only used to help prevent complications or adverse events. They are also employed to address the management of these adverse events, should they occur. The basic concepts underlying emergency checklists are no different than what has been discussed previously. The one major element to be focused on, however, is the need to frequently discuss and rehearse emergencies given the fact that they will (hopefully) seldom occur. Thus, the checklist serves as a focal point upon which the team can assemble and review the steps to any specific emergency. This is what is routinely performed on ships at sea in the modern Navy and what is performed in simulators for commercial airline pilots. During each instance, though the circumstances are modified or changed, there is particular focus on "executing the checklist." In these cases, the individuals are expected to perform the most critical maneuvers immediately and from memory, after which they can refer to the checklist to ensure that all steps were performed properly.

Emergency checklists require even more careful thought and planning, as there is no room for error, the stakes are very high, and the time required to execute them is very brief. In short, it must be executed perfectly and quickly each and every time.

Will the Checklist Save Medicine?

The rise of the checklist comes with some intriguing observations. As an example, though the WHO checklist has met with significant success, [9] there have been some studies reporting an inability to replicate the dramatic results reported in other publications [10, 14, 15]. As discussed, much goes into the success or failure of a checklist. This analysis has become a field of research in and of itself, known as implementation science. One of the key observations made by implementation scientists across all fields of medicine, education, and social work is the fact that success will in part depend on engaged leadership, local adaptation, and user buy-in [12].

The data strongly suggests that checklists have a beneficial effect to patient care if, and only if, it is truly embraced and executed as intended. The checklist in and of itself will not save medicine. It is what the checklist represents that may save medicine. As technology and complexity in medicine continue to grow at near-exponential pace, it is clear that the care of the patient is no longer under the proviso of one single physician. Multidisciplinary care that includes nursing, social work, physiatry, physical, occupational and speech therapy, nutrition, and pharmacy in

addition to the many physicians, requires excellent communication, input, and feedback. The properly executed checklist serves as the external evidence that such communication and integration of care is taking place. Improperly or shoddily performed, it will not be effective and indeed may become deleterious.

Conclusion

Checklists have been an excellent step in bringing safety to patient care and reducing error. An integrated approach to the checklist, with administrative support, graduated implementation, and staff buy-in helps to ensure success. It is important to recognize that the checklist is not the panacea to patient safety. Used intelligently, it can certainly help enhance human performance in the complex milieu of patient care and save lives.

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Alternatives to the Checklist

10

Stephan A. Munich and Michael Chen

Introduction

Checklists provide an organized, unambiguous means of monitoring one's progress and completion of tasks. The use of checklists in health care has been widely publicized. In 2006, the New England Journal of Medicine publication "An Intervention to Decrease Catheter-Related Bloodstream Infections in the ICU" [1] demonstrated a large, sustained reduction in infections in 103 intensive care units. These results were heralded as validation of the use of "simple checklists." A systematic review of the effects of safety checklists [2] concluded that safety checklists are effective in improving patient safety mostly by strengthening compliance with guidelines.

In 2007 and 2008, surgical staff at eight hospitals worldwide implemented a surgical safety checklist. The results, also published in the New England Journal of Medicine in 2009, demonstrated a reduction in mortality and complications. Given that the eight sites represented surgical teams in a wide variety of socioeconomic conditions, the World Health Organization recommended that all hospitals adopt the checklist or something similar. Checklists were heralded as a simple, inexpensive, generalizable, and effective means of saving lives. Checklist use has also been published in neuroendovascular surgery for both routine preprocedure "time outs" as well as for complications [3, 4].

A primary concern with a preoccupation with checklists is oversimplification. Many "checklist-championing" studies compare outcomes before and after the implementation of the checklist, rather than in a prospective two-armed, randomized fashion. They therefore do not account for the possibility of improved outcomes due to other influences, including the actual process of creating the checklist,

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improving technology, devices, enhanced communication, etc. Many of the reported successes of checklist implementation may have less to do with the checklist itself and more to do with the efforts needed for its development. Creating a checklist requires a critical evaluation of the current processes, effective and easily implementable improvements, and discussion among team members [5].

Checklists could be viewed as one of the three pillars to achieving an advanced patient safety culture, which includes not only the summarization and simplification of what to do but also measuring and providing feedback on outcomes and by improving a culture that has specific performance standards. In fact, some view a preoccupation with checklists to be not only a problem of omitting the other processes, but potentially counterproductive to a broader system that depends on synchronized function.

Neuroendovascular surgery involves the diagnosis and treatment of a relatively finite number of vascular pathologies. However, these procedures inherently involve great potential risk to the patient, consist of numerous technical details that are learned through experience, and also involve technologies and approaches that are continuously changing. Neurointerventionalists also operate as a part of a team, often working closely with colleagues from different specialties. As such, successful patient safety efforts necessarily involve something more comprehensive, dynamic, flexible, and inclusive.

In this chapter, we review alternatives to checklists in the neuroendovascular surgery. We discuss the other strategies to improve patient safety, including the advanced safety culture, the crew resource management, the Lean philosophy, and the "pit-crew model."

Advanced Safety Culture

Hudson et al. [6] elaborate on the critical features of an advanced safety culture, which highlights increasing informedness, vigilance, and an environment where feedback can be easily exchanged and increasing trust.

- Informed: managers know what is going on in their organization, and the workforce are willing to report their own errors and near misses.
- Wary: the organization and its constituent individuals are on the lookout for the unexpected, maintaining a high degree of vigilance.
- Just: the organization is normally a "no blame" culture, although some actions are agreed by all to be totally unacceptable, deserving some retribution.
- Flexible: such organizations reflect changes in demand and adapt rapidly to changes in circumstances, providing both high tempo and routine modes of operation.
- Learning: organizations expect to have to change, are ready to learn, and can do what needs to be done to improve.

Informedness is essential in that it builds trust and provides the substance by which team members can then be flexible and adaptable. Morbidity and mortality

conferences provide the mechanism for increasing patient safety informedness. The process could simply consist of reciting preselected data elements from a checklist and presenting the information in a nonconfrontational manner. Or, the conference could be designed to clearly communicate the underlying factors and system failings that led to the complication to really facilitate improvements. Focusing on underlying causes and systems failures helps direct attention away from the "sharp end" and may contribute to a more effective process. Near misses are also worthwhile to discuss as it reflects and showcases vigilance. Ideally, these conferences and an advanced safety culture overall build upon an organization that shares a common group goal of relentlessly pursuing better patient safety and can rise above reflexive competitive or defensive instincts that stem from individual self-interests.

Crew Resource Management

Crew resource management or cockpit resource management (CRM) is a set of training procedures for use in environments where human error can have devastating effects. Used primarily for improving air safety, CRM emphasizes optimizing interpersonal communication. The Joint Commission analyzed 2455 sentinel events and found that the primary root cause in over 70% was communication failure [7]. With these training techniques, the emphasis shifts from completing checklists to more dynamic, team-based approach that facilitates informedness and lateral, as opposed to hierarchical, communication.

Only since the late 1990s have elements of CRM been utilized in health care. The US Department of Health and Human Services also has recognized the utility of these methods, providing training to health-care teams. This training program, TeamSTEPPS (Team Strategies and Tools to Enhance Performance and Patient Safety), focuses on provider collaboration and interpersonal communication via huddles, debriefs, handoffs, and checkbacks. Every member of the team has the opportunity and is encouraged to communicate their concerns. Redundancy is viewed as positive.

One manifestation of patient safety practice using the CRM concepts is simulation-based training. In a pilot study from the Netherlands [8], simulation-based training was found to improve communication between health-care professionals and ultimately result in improvement in patient-reported quality of care. Cardiopulmonary resuscitation is a common requirement that is taught and reinforced with a combined classroom and simulation-based approach. Essential concepts include the clear feedback loop when giving orders and addressing team members in clearly and unambiguously. Simulation-based training in neuroendovascular surgery has been published primarily as it relates to basic angiographic skills [9, 10]. Stroke code simulations for neurology residents have been published with CRM principles that are more in line with building a team that functions on clear communication input on everyone's perception of patient safety [11].

Checklists are highly specific and often most useful when designed for particular situations. What may be a relevant checklist item for one procedure may not be

relevant for another. The skills learned in CRM often through simulation can inherently evolve over time. There is a recognition that all of us have flaws and everyone has the responsibility to become keenly focused on ways to reduce patient risks [12]. Therefore, emphasis on the greater system processes through simulation-based training exercises that practices lateral communication may be another effective approach.

Lean Management Philosophy

The Lean management philosophy embodies the elements of a broader safety culture that checklists are a part of. It highlights a more *efficient* use of resources to effectively meet the needs of patients. These goals are based upon the tenet that those doing the work should be the ones identifying the problems and designing the solutions [13]. Hence, all members are more thoroughly aware of concepts of patient safety, procedural efficacy, and speed. When focus and attention is taken away from the patient and procedure (e.g., when it is fixated on the checklist), efficiency may suffer. Gomez et al. described their experience in the application of the Lean management philosophy in the neuroendovascular suite [14]. The primary focus of this philosophy is "the creation of value for the customer through the relentless and iterative elimination of both waste and variation."

Although a complete description of their experience is beyond the scope of this chapter, in implementing the Lean methodology at their institution, Gomez et al. describe both didactic education and simulation exercises. They included staff across multiple roles—physicians, mid-level providers, technologists, and administrators. All providers were advised as to the sequence of and deadlines by which improvements would be made. Also critical to the implementation of this methodology was the input from providers, which occurred on a daily basis. The implementation of these principles meant that management had to dedicate time for employees to participate in this process without having to balance normal day-to-day job tasks. Employees need to be offered overtime, and this work had to be scheduled outside of normal business hours, reflecting the investment and sincerity of management. However, perhaps most critical is that the Lean management philosophy provides a framework of stability and processes that is inherently capable of responding to and accommodating the changing needs of delivering neuroendovascular care.

Pit Crew Model

Another means of improving efficiency in the neuroendovascular suite is the "pit-crew model," described by Rai et al. [15]; this model is based on the Six Sigma process developed in industry in the 1980s. It is based on the clear definition of team member roles to allow for "synchronized, parallel delivery of care." The reader is referred to the original article for a detailed description of the "pit-crew model."

Deliberate efforts are made with this model to decrease, if not eliminate, variability. Every critical step undergoes the DMAIC analysis of "define," "measure," "analyze," "improve," and "control."

In their application to the delivery of mechanical thrombectomy, they defined the time interval goals, each member was assigned an unambiguous role, time intervals were measured and discussed at team meetings, and new improved methods were instituted and further enhanced.

With implementation of the "pit-crew model," Rai et al. saw improvements in time in a variety of measured variables. During working hours, statistically significant improvements were seen in the following times: emergency room to CT scanner, CT scanner to endovascular suite, endovascular suite to groin puncture, CT scanner to groin puncture, and door to groin puncture. During off hours and weekends, statistically significant improvements were observed in all parameters except emergency room to CT scanner time, which had a nonsignificant trend toward improved time.

The "pit-crew" approach may be particularly valuable to optimize patient safety for time-sensitive cases such as mechanical thrombectomy that could benefit from clear definition of roles, parallel processing, and minimization of variability.

Conclusion

There has been significant recent enthusiasm in the use of checklists to improve quality of health care. However, as was seen in other industries, the health-care sector is now reevaluating the use of checklists. Rather, quality improvements focused on system processes, and providers may provide a more effective means to promoting safer health care that is both sustainable and adaptable.

As discussed in this chapter, crew resource management, a philosophy championed by the airline industry, focuses on open and lateral communication, adaptability, and accountability, among all team members. The Lean philosophy aims to eliminate waste and variability, and the "pit-crew model" emphasizes parallel delivery of care. Each of these strategies contributes in unique ways to patient safety in neuroendovascular surgery.

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Prepping the Environment

11

Ahmad M. Thabet and I. Paul Singh

Introduction

Noninvasive imaging studies to evaluate neurovascular anatomy/pathology such as computed tomographic angiography (CTA) and magnetic resonance angiography (MRA) have advanced significantly over the last few years; but interventional cerebral/spinal angiography is still the gold standard study for vascular imaging, achieving the best quality images, and assessing the blood flow dynamics within the brain and spinal cord. There are many indications of interventional cerebral/spinal angiography, including diagnosis and treatment of vascular stenosis/occlusion, cerebral aneurysms, arteriovenous malformations, dural arteriovenous fistulas, malignancy, and multiple other vascular anomalies. Using a systematic, evidence-based approach while preparing for cerebral/spinal angiography can help minimize the uncommon, yet potential risks of this procedure.

Preoperative Preparation

The first step to plan for an interventional cerebral/spinal angiography is to evaluate the potential benefits and risks of the procedure and evaluate for any potential contraindications such as allergy to contrast, kidney injury, and pregnancy. Obtaining medical clearance for the interventional cerebral/spinal angiogram

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from the patient's primary care provider may be essential if the patient has significant comorbid medical conditions. Additional clearance from cardiology or anesthesia may also be beneficial in select patients. At a minimum, the interventional team needs to acquire a detailed medical history, perform a thorough physical examination, and review laboratory values (particularly renal function and coagulation parameters). From a procedural standpoint, obtaining and reviewing neurovascular imaging studies, such as a CTA or MRA, are useful to learn the individualized patient's neurovascular anatomy, anticipate possible anatomical variants, understand the target pathology, and plan approaches. It is important to ensure that patients consume nothing by mouth for 8 h prior to the intervention to minimize the risk of aspiration because conscious sedation is commonly administered while patients are lying supine for an extended period of time. It is advised to avoid unnecessary deep sedation or general anesthesia to maintain the ability for a good neurologic assessment and vocal communication during the procedure in order to obtain a good quality study.

An informed consent should be obtained from the patient or his/her surrogate, stating the intervention, its indications, possible benefits, and risks. The potential complications should be discussed with the patient including puncture site complications (hematoma formation, pseudoaneurysm formation, retroperitoneal hemorrhage, vasospasm or dissection, and peripheral ischemia), neurologic complications (transient ischemic attacks, ischemic and hemorrhagic strokes, spinal cord infarction, and hemorrhage), and other complications (sedation/anesthesia-related complications and contrast-related complications).

To ensure the risks of angiography itself are low, practicing caution with the amount of contrast used, screening for, and pre-medicating acute/chronic kidney injury patients with N-acetylcysteine plus intravenous fluids may help reduce the incidence of contrast-induced nephropathy (CIN) though the incidence of this entity is now heavily debated. This also entails knowing the patient's weight and calculating the maximum volume of contrast that can be injected before starting the procedure (generally five times the patient's body weight when there is normal renal function). Also, reviewing the patient's allergy history and pre-medicating patients allergic to iodine contrast with diphenhydramine and steroids may help reduce the incidence of serious allergic reactions. In case of having such reaction, the medications and equipment to manage an airway obstruction/anaphylactic should be available in the angiography suite. With respect to CIN, it is prudent to review the patient's preoperative renal function tests. The incidence of CIN is higher in older patients with lower baseline glomerular filtration rates. Using the minimum amount of contrast and low concentrations in case of high-risk patients, along with preparing high-risk patients with good hydration, acetylcysteine, or sodium bicarbonate, and avoiding nephrotoxic medications may reduce the incidence of contrast-induced nephropathy [1].

Prior to the procedure, a time-out to confirm the patient's identity and the intervention should be done in the presence of the angiography suite team members. This ensures that all team members can provide checks and measures on these seemingly simple avoidance measures (Table 11.1).

Table 11.1 The equipment routinely used for diagnostic cerebral/spinal angiography

Haircut kit
Chlorhexidine pads
Full body drape
Radiation shields' covers
Heparinized saline bags (2000–4000 U/L) (weight based)
Contrast solution (high and low osmolarity) (low osmolarity in high-risk patients)
Extension tubes
Syringes (5, 10, 20, and 60 mL)
Angiocath tip
Heparinized saline basin
Towels
Gauze
Dressings (tegaderm)
Skin marker
Hemostat clamp
Scissors
Scalpel
Puncture needles (18, 21 g)
Needles' holder
J wire (0.035″)
Femoral sheath (4, 5 f)
Guide-wire (0.035″)
Diagnostic catheters (4, 5 f) (Terumo Glidecath, Cordis/Cook Vert or Davis, Simmons 2, Cobra 1/2)
Wire torque device
One-way and three-way stopcocks

Angiography Suite

The typical angiography suite includes a procedure room and a control room (Fig. 11.1). The size of the procedure room should be adequate to accommodate all team members and their equipment, including the operating team, anesthesia team, neuromonitoring team, and any other team members involved in the procedure. The equipment and medications used during cerebral/spinal angiography should all be available beforehand within the angiography suite, including catheters, guide-wires, and other endovascular devices/materials (Tables 11.2 and 11.3). It is also crucial that the anesthesia team has an easy access to all the necessary equipment and medications they may need during a routine or an emergency situation in the angiography suite. This involves communication prior to the start of the procedure so the anesthesiologist is aware of potential complications. Medications such as nicardipine or labetalol for acute lowering of blood pressures and intravenous vasopressors for rapid augmentation of mean arterial pressures should be readily available. Anticholinergics, such as glycopyrrolate are often used in cases where there will be manipulation of the carotid bulb. For interventional procedures, heparin and protamine sulfate

Fig. 11.1 Biplane angiography suite

Table 11.2 Medications commonly used in the angiography suite

Medication	Dose
Abciximab	0.25 mg/kg IV bolus, then 0.125 μg/kg/min IV drip
Aspirin	81 or 325 mg PO daily or 300 mg PR daily
Atropine	0.5–1 mg IV Q5M, max 3 mg
Clopidogrel	600 mg PO once, 75 mg PO daily
Dobutamine	0.5–1 μg/kg/min IV drip, then 2–20 μg/kg/min IV drip
Dopamine	5–15 μg/kg/min IV drip
Epinephrine	Cardiac arrest: 0.5–1 mg IV Q5M Hypotension: 0.05–2 μg/kg/min IV drip
Eptifibitide	180 μg/kg IV bolus, then 2 μg/kg/min IV drip, with another 180 μg/kg IV bolus 10 min after first one
Fentanyl	25–50 mg IV bolus
Flumazenil	0.2 mg IV bolus, may repeat Q1M, max 1 mg
Furosemide	0.5–1 mg/kg or 40 mg IV bolus, may repeat Q1H
Glycopyrrolate	0.1 mg IV bolus, may repeat Q2M
Heparin	50 units/kg IV bolus, target ACT 200–300 s
Labetalol	20 mg IV bolus, then 40–80 mg IV Q10M, max 300 mg
Lidocaine	Subcutaneous
Mannitol	1–2 g/kg IV drip over 30–60 min
Midazolam	0.5–1 mg IV bolus
Naloxone	0.4–4 mg IV bolus, may repeat Q2M, max 10 mg
Neuromuscular antagonists	
Nicardipine	5 mg/h IV drip; may increase by 2.5 mg/h Q15M; max 15 mg/h
Norepinephrine	8–12 μg/min IV drip, then 2–4 μg/min IV drip
Ondansetron	4 mg IV bolus immediately before anesthesia or 16 mg PO 1 h before anesthesia
Phenylephrine	100–180 μg IV bolus, then 40–60 μg/min IV drip
Propofol	20–40 mg IV bolus Q10S, then 0.05–0.2 mg/kg/min IV drip
Protamine	1–1.5 mg per 100 units of heparin, max 50 mg
Sodium nitroprusside	0.3 μg/kg/min IV drip, max 10 μg/kg/min
Ticagrelor	180 mg PO once, 90 mg PO BID, 60 mg BID
Tissue Plasminogen Activator (tPA)	0.9 mg/kg IV, 10% bolus and rest over 60 min, max 90 mg
Vasopressin	0.01–0.04 unit/min IV drip

Table 11.3 Checklist for prepping the environment prior to cerebral/spinal angiography

Indications, contraindications (contrast allergy, kidney injury, pregnancy), medical clearance if needed, medical history, medications, physical exam, labs (BUN/Cr, PT/PTT/INR, CBC), prior vascular imaging studies
NPO status, informed consent, time out
Other teams such as anesthesia and neuromonitoring if needed
Biplane system is preferred
Medications dosed and available (cart or with anesthesia)
Vital signs and pulse oximetry monitoring. Arterial line and intracranial pressure if needed
Sterile prep. of patient and equipment. Air free preparation of syringes and flush lines
Heparin and contrast concentration are weight based (low contrast conc. in kidney inj.)
Radiation protective outfits and shields
Minimum fluoroscopy dose needed: Reduce dose/pulse, pulse/sec, length and number of runs, and magnification; increase collimation; use straight AP/lat. Views, positions' presets, screen markers, previous runs for road maps, and low dose protocol for pediatrics
Arteriotomy: Confirm puncture site and arterial access, use 21 gauge needle and longer sheath if needed, connect to flush line, connect to BP transducer if needed, perform femoral angiography, use alternative access sites when needed
Catheter selection: Individualized to patient and intervention
Vessel selection: Guide-wire usage rather than puffing contrast in tortuous anatomy; select-catheter rather than exchanging over a guide-wire
Prevent air embolism by reexamining syringes and flush lines, double flushing technique, meniscus to meniscus technique, and using continuous flush lines whenever possible
Prevent, anticipate, and be ready to manage complications such as occlusive catheter, vasospasm, dissection, and thromboembolism
If using power injector, achieve a safe stable catheter position and individualize injection rates to blood vessels
Arteriotomy closure: Consider using vascular closure device in cases of coagulopathy or large sized sheath
Postoperative care: Lying supine for at least 6 h. Frequent puncture site checks, pulse checks, and neuro-checks. Clear discharge instructions

should also be prepared in the event of complications. In addition to the patient's table, a second table for preparation of equipment (Fig. 11.2) and a third table for preparation of embolic materials such as nBCA, Onyx, or particles should also be available. Biplane digital subtraction angiography systems are much more preferable than single plane systems for interventional cerebral/spinal angiography. They can help reduce operating time, radiation exposure, contrast dose, and procedural complications by allowing simultaneous imaging of the antero-posterior and lateral views. Rotational three-dimensional imaging can also help provide a more comprehensive and detailed view of the neurovascular anatomy/pathology.

Meticulous hemodynamic and neuromonitoring of the patient during interventional cerebral/spinal angiography is essential and the angiography suite should be equipped to provide such monitoring capacity. Continuous monitoring of vital signs and pulse oximetry is critical, and continuous monitoring of blood pressure through an arterial line or the femoral sheath should be considered in therapeutic cases. Comprehensive intraoperative electrophysiologic monitoring of patients under general anesthesia should be considered in more complex cases such as a balloon test occlusion, an eloquent vascular malformation treatment, or a tumor

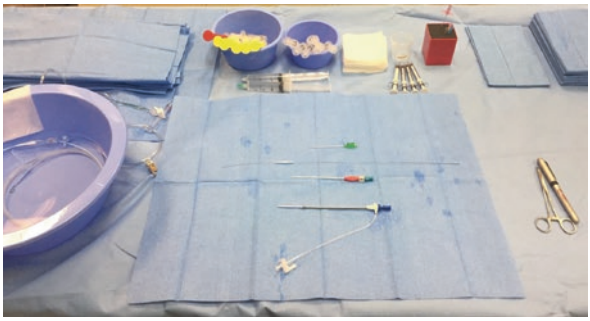

Fig. 11.2 Angiography suite equipment table

embolization. In cases of hemorrhage with elevated intracranial pressures, an existent intracranial pressure monitor should be transduced during the procedure whenever possible [2, 3].

Radiation Protection

Multiple epidemiologic studies of the effects of radiation exposure in doses much higher than those used in interventional cerebral/spinal angiography have demonstrated an association with higher incidence of delayed malignancy, cataract, atherosclerosis, and cognitive/growth impairment. Radiation protection can be achieved with the consistent application of simple safety precautions. Everybody in the angiography suite should practice radiation protection strategies to minimize radiation exposure. This includes neurointerventionalists, nursing staff, technologists, anesthesiologists, and other team members. All team members should wear radiation protective lead aprons, leaded thyroid shields, and lead-lined eyeglasses. Many facilities now use lead-lined skullcaps and arm protection as well. In addition to personal protective equipment, radiation protective shields should be used within the neuroangiography suite. Total radiation doses must be tracked with radiation badges for constant monitoring.

A focused attention to the cumulative fluoroscopy dose and a consistent effort to reduce it can cut down radiation exposure to the patient by 38–50% and to the angiography suite team by 80%. Fluoroscopy parameters such as dose per pulse and pulse second have more effect on the cumulative fluoroscopy dose than fluoroscopy time. Reducing these parameters along with reducing the length and number of angiographic runs can reduce the cumulative fluoroscopy dose significantly. Though increasing magnification reduces the size of the radiation beam, it also increases the skin dose, so keeping magnification as low as possible is recommended. Also, collimation reduces the size of the radiation beam and scatter effect to the patient and angiography suite team. Reducing the distance the radiation beam travels through the patient can also reduce the radiation dose. Therefore, using shorter projections with a narrow distance between transmitter and detector heads in addition to straight antero-posterior/lateral

views over oblique views is recommended whenever possible. Other techniques that can be used to minimize the cumulative fluoroscopy dose include using presets to store commonly used head positions instead of resetting them repeatedly, using screen markers to change positions instead of continuous fluoroscopy, and using previous runs to generate road maps instead of repeating them (when permitted by the software being used). Special populations, such as emergent pregnant patients and children should have a separate low dose protocol established. Using a low dose protocol in pediatrics cases can reduce the cumulative fluoroscopy dose by more than 50% [4–9].

Intra-Procedural Precautions

Specific intra-procedural technical precautions should always be practiced while performing interventional cerebral/spinal angiography from arteriotomy to closure to ensure the safety of the procedure and minimize complications rates. Arteriotomy Access and Closure will be discussed in a later chapter in this text.

Catheter Selection

Choosing an optimal catheter is one of the most important steps in interventional cerebral/spinal angiography, because it is one of the main factors determining stability of the catheter position, which in turn affects the operative time, course, and outcome. Choosing a suboptimal catheter can contribute to the incidence of complications such as catheter herniation, difficulty tracking of microcatheters/devices, vasospasm, dissection, or thromboembolism. Select-catheters and guide-catheters vary in tip shape, size, length, and flexibility. The decision to choose a catheter should be based on individualized patients factors such as his/her neurovascular anatomy (blood vessels' size and length), vascular health (tortuosity and atherosclerosis), and goal of intervention (catheter's final position and microcatheters/devices used). The guide-catheter's inner diameter should not only handle anticipated microcatheters/devices, but should also permit adequate injections with these microcatheters/devices in place. Generally, guide-catheters that are more rigid proximally, more flexible distally, and have a higher distal inner/outer diameter ratio (thin walled) are more favorable to achieve a stable position, track easily, and minimize complications [10].

Vessel Selection

Vessels should be selected by advancing a diagnostic catheter over a guide-wire. It is generally safer to advance the catheter over a guide-wire to keep the catheter away from the vessel wall and prevent vasospasm or dissection, especially in case of tortuous or atherosclerotic vessels. Advancing the catheter directly while puffing

contrast frequently (without a guide-wire) should be reserved for relatively straight, healthy vessels, with negligible atherosclerotic disease (typically younger patients). Larger guide-catheters should be advanced over a smaller select-catheter over a guide-wire to avoid large step-offs between the catheter tip and the guide-wire. This prevents vessel wall trauma and thromboembolism. Vessels can also be selected with a select-catheter, followed by an exchange with a guide-catheter over an exchange length guide-wire. This method should be reserved for very challenging anatomy since it carries a higher risk of thromboembolism; therefore, giving additional heparin should be considered in these cases, with the caveat that there is an increased risk of postoperative hematoma formation at the arteriotomy site. Finally, restricting vessel selection to only high yield and necessary blood vessels is a reasonable strategy to minimize complications [11–13].

Vascular Complications

Catheter-related complications are associated with the catheter position prior to or during angiography. These primarily include the catheter itself limiting the blood flow into smaller blood vessels, increasing the risk of hypoperfusion and thromboembolism. Using a smaller catheter, a faster heparinized saline flush rate, and administering a bolus of heparin intravenously can help prevent these complications. Vasospasm is a common catheter-related complication, which can also lead to hypoperfusion or thromboembolism. It can be managed by retracting the catheter tip to a more proximal position, appropriate rotation away from a vessel wall, and injecting an intra-arterial vasodilator (e.g., calcium channel blocker or nitrate). Vessel dissection is a more serious catheter-related complication, which can also lead to hypoperfusion or thromboembolism. Managing vessel dissection generally depends on whether there is limitation of distal blood flow. If the dissection is not flow limiting, aborting the procedure and starting an antiplatelet medication is a reasonable option. Many practitioners begin an antiplatelet agent or heparin while the patient is still on the table and repeat serial angiography every several minutes to ensure that there is no progression of the dissection. If the dissection is flow limiting, angioplasty with a balloon or emergent stenting with concurrent administration of an IV antiplatelet medication may be necessary. It should be noted that extra caution must be taken to avoid vessel perforation, catheterization of a false lumen, and thromboembolism when treating the dissection [14].

Thromboembolic complications, such as air embolism, can be prevented by thoroughly examining the syringes and flush lines for microbubbles, double flushing the catheter after removing the guide-wire, using a meniscus-to-meniscus technique when attaching the catheter to syringes or flush lines, and connecting the catheter to continuous heparinized saline flush lines whenever possible. Another thromboembolic complication is vessel-to-vessel atherosclerotic plaque embolism, which can be prevented by carefully reviewing previous vascular imaging studies and current angiographic runs to localize these atherosclerotic plaques and avoid scrapping against them. Also, new thrombi can form within the catheter lumen or over the

guide-wire, and this can be prevented by adequate flushing techniques—as previously discussed—and by minimizing the guide-wire time. Additional intravenous heparin boluses can be administered in longer therapeutic cases to minimize thrombus formation when multiple catheters and embolic material are required, while monitoring the activated clotting time (ACT); otherwise, the heparin in the heparinized saline flush lines is adequate for diagnostic and shorter therapeutic cases. Thromboembolic complications can be managed by either chemical or mechanical thrombectomy, based on the blood clot burden and location. Chemical thrombectomy can be achieved by intra-arterial injection of an antiplatelet agent such as abciximab or eptifibatide, considering the freshness of the thrombus, or a fibrinolytic such as tPA [15–17].

Angiographic Runs

Hand or automated power injections can be used for angiographic runs. Hand injections must be tailored to vessel size and flow rates, and they have the benefit of immediate adjustment of power and volume by the interventionalist. Under-injecting necessitates repeat angiography with additional contrast and radiation. Over-injecting can lead to vessel injury, introduction of air, and reflux into more proximal vessels. Automated power injections carry the advantages of obtaining better quality images, reducing radiation exposure to the operating team, using less contrast, and reducing the risk of air embolism with the continuous connection to the heparinized saline flush line. Power injections also carry the disadvantage of a potential risk of traumatizing the blood vessel wall due to their higher flow rates, causing vasospasm or dissection. These complications can be minimized by achieving a stable catheter position away from the blood vessel wall and increasing the injection rate gradually. Generally, a rate rise of 0.2 mL/s is adequate; with a goal rate of 10 mL/s in the common femoral, subclavian, and common carotid (cranial view) arteries; 6 mL/s in the vertebral, common carotid (cervical view), and internal carotid arteries; and 4 mL/s in the external carotid arteries. Both approaches are valid and require vigilant observation by the proceduralist.

Additional Potential Complications

In addition to the aforementioned complications, anesthesia-related complications, contrast-related complications, and postoperative neurologic complications can still occur. It is beyond the scope of this chapter to discuss the anesthesia-related complications, but as previously addressed, direct communication with the anesthesiologist prior to an intervention can help mitigate overall risks.

Contrast-related complications include allergic reactions and CIN. Allergic reactions may range from a mild reaction to anaphylaxis. As previously discussed, reviewing the patient's allergy history is crucial, and pre-medicating allergic patients with corticosteroids and antihistamines should be considered per the Radiology

department's contrast protocol, as these differ between institutions. Despite these preoperative measures, complications can still occur and it is essential to have rapid delivery of intravenous/intramuscular rescue medications, such as epinephrine, diphenhydramine, and steroids, to manage emergent anaphylaxis in the angiography suite [18, 19]. In the case of active CIN, aggressive hydration should carry into the postoperative period with avoidance of nephrotoxins and serial monitoring of renal function. In severe cases, a nephrology consultation is advised [20–24].

Neurologic complications such as transient ischemic attack, ischemic stroke, or intracranial hemorrhage also occur in less than 1% of the diagnostic cases. This risk is higher in older patients, atherosclerotic blood vessels, and more complex interventional procedures. A 2924 patients study reported a 0.34% rate of neurologic complications and no permanent deficits with diagnostic cerebral angiography. A 2899 patients study reported a 1.3% rate of neurologic complications and a 0.5% rate of permanent deficits. Also, a 1517 patients study reported a 2.6% rate of neurologic complications and 0.3% of permanent deficits. Though neurological complications are low, practicing the safety techniques listed earlier in this chapter to prevent vessel injury or thromboembolic complications can reduce the incidence of these complications. Careful review of the angiographic runs, minimizing sedation/anesthesia, and examining the patient at the end of the intervention can help identify and manage these complications earlier. Management of ischemic complications is generally based on the timing of diagnosis and location of the vessel occlusion. For this reason, serial neurological exams need to be performed both intraoperatively and postoperatively as harbingers of potential complications such as transient ischemic attack, ischemic stroke, or intracranial hemorrhage. For ischemia, treatment may include administration of intravenous/intra-arterial antiplatelet agents, fibrinolytics, mechanical thrombectomy, or angioplasty. Management of hemorrhagic complications may include reversal of heparin or antiplatelet agents or temporary/permanent embolization of the bleeding vessel or lesion. These will be discussed in more detail in later chapters [25–31].

Conclusion

Interventional cerebral/spinal angiography is the gold standard procedure to help diagnose and treat an extensive array of cerebral/spinal vascular disorders, such as acute ischemic stroke, cerebral aneurysms, arteriovenous malformations, dural arteriovenous fistulas, trauma, malignancy, and other neurovascular diseases. Meticulous preoperative preparation, comprehensive knowledge of the neurovascular anatomy and pathology, mastering the interventional technique, anticipating and managing possible complications, and careful postoperative care are all critical steps towards reaching good outcomes and minimizing complication rates. All members of the angiography suite team should be involved in a systematic approach to prepare an operative environment that would lead to a safe and successful interventional cerebral/spinal angiography procedure.

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Part II

Surgical Procedures

Carotid Endarterectomy

12

Christopher M. Loftus

Checklist: Carotid Endarterectomy (Insertion of Indwelling Shunt)

Equipment needed	Procedural steps
OR technicians • Soft-shoe Fogarty clamp (for common carotid) • Two (2) bulldog clamps (for ECA and ICA) • Indwelling shunt (centerpoint pre-marked) Nursing • Two (2) pre-selected shunts are available in the room (one opened on tray) Anesthesia/Neuromonitoring • Establish neurological baseline with EEG and SSEP • Appropriate anesthesia to ensure insure accurate readings • Availability of additional resources (neurologist) if additional interpretation is required • Pentobarbital/propofol available Neurosurgery • Confirms all equipment present and functional • Discuss with team criteria for shunting	Identify and dissect • Common, internal, and external carotid artery (gently) • Superior thyroid artery • Place sutures around each Initiate and engage • 5000 Units heparin IV • Pott's tie of the superior thyroid artery • Notify anesthesia and team of imminent cross-clamping • Cross clamp (ICA, CCA, ECA in that order!) • Identify criteria for shunting based on EEG, SSEP, and blood pressure. If necessary: • Raise BP 15% (as tolerated) • Complete arteriotomy with Pott's scissors • Place distal (ICA) part of shunt into ICA and look for back-bleeding • Clamp shunt and place proximal portion into CCA as you loosen the ligature on the CCA • Secure with Rommel • Assess EEG/SSEP • Proceed with endarterectomy Removal of shunt • Primary or patch closure of endarterectomy • Prior to final stitches, clamp shunt in two regions proximal and distal to midpoint of shunt • Cut shunt and remove common carotid side, back-bleed, and reclamp • Remove shunt from ICA side, back-bleed, and reclamp • Close remaining portion of patch or arteriotomy

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Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Stroke	Inadequate perfusion at cross-clamping	Increase BP Shunt placement	Be prepared to shunt
Stroke	Embolus at surgery	Too late	Expose ICA well above plaque Give heparin bolus early Gentle dissection of vessels Place distal shunt into normal vessel, not plaque
Nerve injury	Traction or transection	Recovery with time	No fixed retractors Preserve all nerves Strong knowledge of anatomy
Wound infection (rare)	Comorbidities Diabetes	Wound management, drainage, antimicrobial therapy	Bloodless dry surgery Use surgical drain in sheath Copious irrigation
MI	Systemic vascular disease	Medical therapy in ICU Give aspirin every day including day of surgery	Pre-op cardiac evaluation Skilled anesthesia Some consider locoregional anesthesia

Introduction

In the hands of experienced surgeons, anesthesiologists, and neurocritical care intensivists, patients undergoing CEA experience a low incidence of complications, with common complications tending to be transient [1–8]. But despite the rare incidence of devastating complications, their clinical course can evolve rapidly, and patients may deteriorate unless there is immediate recognition of untoward events and quick intervention to reverse them.

Procedural Overview

Our Technique for CEA

In planning for successful CEA, the surgeon has technique choices to make, such as use of local or general anesthesia, intraprocedural neuroprotective agents, intraoperative monitoring and the linked need for intraoperative carotid shunting, and endarterectomy type, whether linear or eversion, primary repair, microscopic repair, or carotid patch grafting.

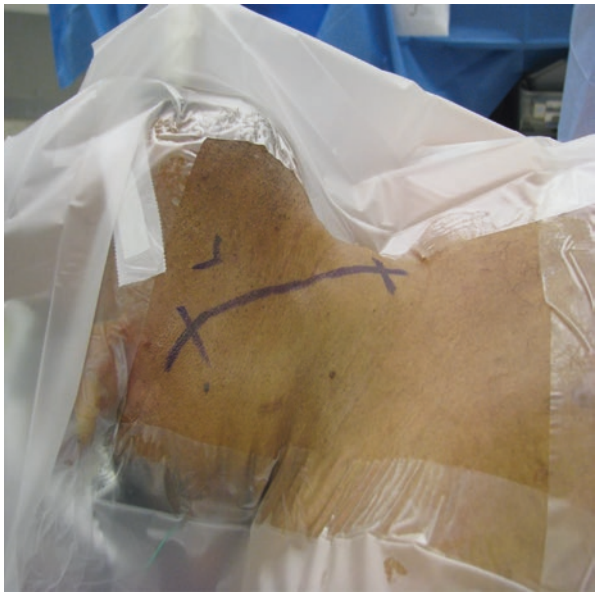

Fig. 12.1 Standard vertical incision for a right CEA. The incision is along the anterior sternocleidomastoid edge, and the angle of the mandible is marked for height orientation. The head is turned away from the side of interest to facilitate exposure of the ICA

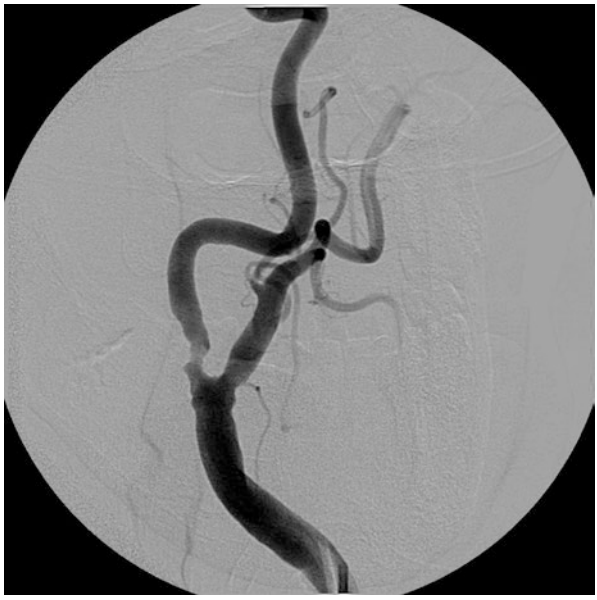

Fig. 12.2 Antero-posterior DSA image of a medially rotated internal carotid configuration, which will make surgical exposure and potential shunt insertion more difficult than in a routine case. It is important to understand this anatomy in the preoperative analysis of the case

As I perform and teach carotid surgery, the patient is positioned supine with the head turned variably to the contralateral side (Fig. 12.1), according to the ICA and ECA relationship on preprocedural imaging (Fig. 12.2), and with the neck slightly extended by placement of an interscapular roll. I utilize concomitant EEG and SSEP monitoring. A linear so assess ischemia and the need for indwelling shunt. The

skin incision is vertical, made along the anterior border of the sternocleidomastoid muscle. The platysma is then incised sharply, and blunt self-retaining retractors are placed, staying superficial on the medial side to prevent injury to the laryngeal nerves. (Once deep to the platysma layer, we use only blunt fishhook-type (Lone Star) retraction, to prevent nerve injury). The dissection is then carried along the anterior aspect of the sternocleidomastoid muscle. The carotid sheath is entered, and the internal jugular vein and ansa cervicalis nerve are identified and mobilized laterally and medially, respectively. The common facial vein is then found medially and ligated to further facilitate lateral mobilization of the internal jugular.

The surgeon should carefully dissect the common carotid artery (CCA) while avoiding injury to the vagus nerve, which typically lies along the posterior aspect of the carotid vessels. Then the dissection is carried rostrally to expose the origins of the internal carotid artery (ICA), external carotid artery (ECA), superior thyroid artery, and occasionally some anomalous ECA branches. Anesthesia should be aware at this time of possible reflex bradycardia and hypotension that may occur with stimulation of the carotid bulb, although with increasing experience we almost never see this and essentially never need to anesthetize the carotid bulb. As the dissection continues rostrally, the hypoglossal nerve should be identified and should be carefully mobilized medially. Once the ICA distal to the plaque has been exposed, 0 silk ties are passed around the CCA, ICA, and ECA, with a rubber Rummel tourniquet to the CCA, in preparation for possible shunting. The superior thyroid artery is secured with a temporary "Pott's tie" 0 silk ligature. At the first visualization of the CCA, before the real arterial dissection begins, the patient is given an intravenous dose of 5000 IU heparin, so that intravascular thrombosis does not occur during the period of temporary carotid occlusion. (We do not routinely re-dose heparin, we do not routinely check ACT levels, and we never use protamine for heparin reversal.) Atraumatic vascular clamps are then applied as follows: first, on the ICA, then on the CCA, and, finally, on the ECA. The superior thyroid artery is occluded with the encircling Pott's tie. *Note that the ICA is occluded first and never declamped until the repair is complete (unless a shunt is placed)*. This sequence affords maximal brain protection from embolized plaque or thrombus. An arteriotomy is then begun with an #11 blade in the CCA just below the bifurcation and is extended into the internal carotid artery distal to the plaque using Potts scissors (Fig. 12.2). The proximal end of the plaque is circumferentially separated from the wall of the artery with the use of a Penfield 4 dissector, which allows complete transection of the plaque proximally. The plaque is then elevated and carefully separated from the wall of the artery at the origin of the ECA through a wall inversion technique, and the stump is sharply divided. This is followed by a similar but more delicate feathering technique, for the ICA plaque to prevent flap formation.

During cross-clamping, I place a shunt when the monitoring neurologist identifies a change in the EEG or SSEP or both after cross-clamping. Our threshold is low; we shunt immediately and without hesitation for any perceived monitoring change. Additionally, in our experience, the arteriotomy is closed with a patch graft, which has reduced to 0 our rates of acute post-op occlusion and long-term restenosis. This is sutured with two limbs, first from distal to proximal on the medial side with the use of a running 6-0 Prolene suture and then two suture lines on the lateral side that meet in the middle and are tied together at their meeting point after

backbleeding and evacuation of all air and debris from the lumen. After the final knot is secured, we complete the declamping first by unclamping the ECA, then the CCA, waiting 10 s, and, finally, opening the ICA. In this way any potential residual air or debris passes harmlessly into the ECA circulation and not to the brain.

Complication Avoidance and Management

Complications associated with CEA can be *wound related*, *systemic*, or *neurological*. Wound-related complications include hoarseness, nerve injury, hematoma, arterial disintegrity, and infection. Systemic complications are primarily cardiac, including MI. Neurological complications include TIA and stroke.

Arterial leak or disruption is, fortunately, an exceedingly rare complication of CEA. (We have actually never experienced an acute arterial leak, nor have we ever had to reexplore a fresh CEA patient for hematoma or airway compromise, and we attribute this good fortune to meticulous hemostasis and assiduous attention to the details of the arterial closure.) If there is an acute arterial leak, patients will have a swollen neck and will demonstrate signs of airway compromise such as dyspnea and dysphagia; they may also demonstrate symptoms of cerebral ischemia. Prompt protection of the airway is imperative as an enlarging hematoma can cause tracheal deviation, making intubation progressively more difficult. After securing an airway, the correction can only be achieved by reoperation. In desperate cases, the incision may be opened at the bedside to alleviate pressure from the hematoma (I have actually never done this). If the wound can be explored at that time, theoretically the surgeon can locate the artery and clamp it to maintain temporary hemostasis and allow time to get the patient to the operating room. Obviously this is a salvage situation that anyone would wish to avoid if at all possible. In a delayed loss of arterial integrity, patients may present days to weeks after a CEA, though the pattern of symptoms progresses without the same rapidity. A mass below the skin may slowly form and be pulsatile. Imaging should be obtained to confirm the diagnosis, and carotid duplex or angiography can identify a pseudoaneurysm at the arteriotomy site. Fevers and cellulitis often present at this time as the etiology of pseudoaneurysms is often linked to postoperative wound infections. The Texas Heart Institute's series of 4991 CEAs found that 35% of postoperative pseudoaneurysms could be directly linked to *Staphylococcus* or *streptococci* wound infections. Other patients in their series with pseudoaneurysms, but no frank evidence of wound infections, did have prolonged operative times, postoperative hypertension, and bacteremia—all factors that commonly contribute to wound infections [9]. Given their infectious etiology, treatment for these patients should include debridement of the surgical wound and washout of any potentially infectious nidus. The arteriotomy site should be examined, and direct repair should be carried out if possible; otherwise, other vascular strategies, like bypass of the diseased segment, may be needed. Realistically, in the present era, we would look first at an endovascular strategy as the low-risk option for arterial disruption, with or without infection, when the presentation is delayed.

Cerebral ischemia that follows CEA may or may not be symptomatic, but has been reported in approximately 5% of CEA patients. Neurological symptoms in the immediate postoperative period must always be evaluated promptly with imaging of

the arterial repair. Minor episodes, like TIAs, or major stroke, like hemiparesis, may reflect embolic phenomena from a denuded arteriotomy bed or may signal a complete occlusion of the carotid. In the rare case where a patient shows neurological changes post-op, we evaluate the repair immediately with the fastest available method, usually CTA, or, if not, duplex ultrasound. Most cases prove to be widely patent repairs and will resolve spontaneously. For this reason, we do not rush back to surgery without imaging; it is almost never necessary and for the most part the problem resolves on its own. If the vessel is occluded, of course, an immediate exploration and reconstruction is the best option. In our practice acute occlusion has been essentially eliminated by the use of universal Hemashield patch grafting. This has been confirmed by others. In a series by Sundt et al., patients treated with patch grafts had a 0.8% rate of occlusion versus a 4% rate among patients treated with primary closure, an improved outcome in patients with patch closure (Figs. 12.3 and 12.4).

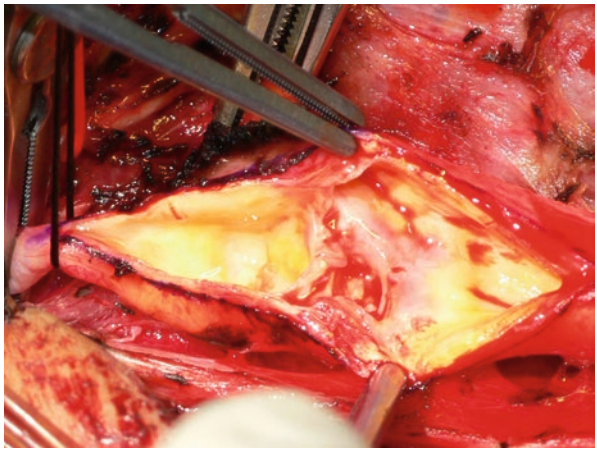

Fig. 12.3 Surgical exposure of an open carotid bifurcation showing a complex ulcerated plaque and an atherosclerotic web, both contributing o carotid stenosis. The plaque removal has not yet started

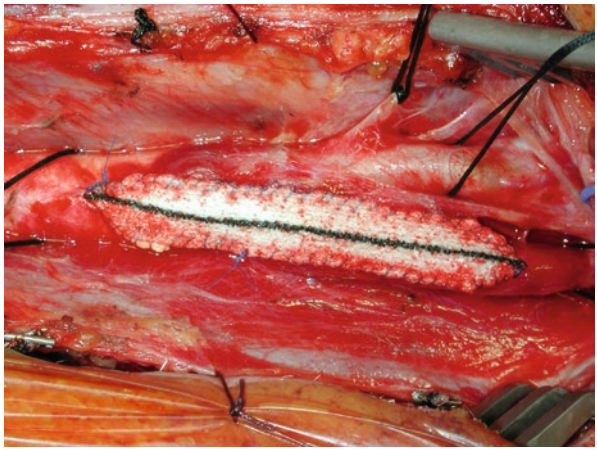

Fig. 12.4 The competed arterial repair with a Hemashield patch angioplasty, following unclamping, in a left carotid case

A severe cerebral hyperperfusion state may occur in <1–3% of CEA patients. The exact etiology is unknown, but chronic ischemia may disrupt the normal autoregulation of cerebral arteries, which may not be able to handle the correction of cerebral blood flow. Several studies have evaluated postoperative cerebral perfusion and found transient elevations in cerebral blood flow of 20–40% for several days following CEA. In a hyperperfusion state caused by flow dysregulation, however, cerebral blood flow may increase 100–200% above baseline. Typically, these pathologic elevations begin 3–4 days following a CEA, but they may even occur up to 1 month from the time of surgery. Patients suffering from hyperperfusion syndrome may show signs of headache, ipsilateral eye pain, face pain, vomiting, confusion, visual disturbances, focal motor seizures, or focal neurologic deficits. If hyperperfusion syndrome is suspected, immediate steps should be taken to lower blood pressure to a normal range, usually with labetalol or clonidine. Antihypertensive therapy with strict normotensive goals is necessary for at least 6 months, while cerebral autoregulation is reestablished. A CT scan has been recommended as the first-line imaging study of choice and may demonstrate ipsilateral hemispheric petechial hemorrhages, ipsilateral basal ganglia hemorrhage, and parieto-occipital white mater edema, all of which may be indicative of hyperperfusion syndrome.

While acute hemorrhagic and ischemic complications are worrisome, the more common issue seen is transient cranial nerve injury, which occurs with low but predictable regularity following CEA [10]. In the NASCET trial, cranial nerve injury was found to occur in 8.6% of patients. Studies carried out more recently have demonstrated lower (~5%) rates. Most nerve deficits will result from traction injury of the hypoglossal nerve or the marginal mandibular branch of the facial nerve. Also at risk in the standard exposure, however, are the recurrent laryngeal, vagus, and (occasionally) the accessory nerves, as well as the cervical ganglia of the sympathetic trunk.

Preoperative nerve evaluation is important, particularly in the case of hypoglossal or recurrent laryngeal nerve palsies contralateral to the proposed CEA. We have seen residual nerve injuries from contralateral carotid surgeries, as well as tracheostomy and other neck procedures. When there are contralateral nerve palsies, we prefer an endovascular strategy to avoid the devastating possibility of a bilateral laryngeal or hypoglossal injury.

Postoperative cranial nerve palsy incidence is best predicted by the length and anatomical difficulty of the CEA [10]. Surgeries lasting greater than 2 h have a 50% greater chance of causing a cranial nerve injury for each additional 30 min of operative time. In our practice, as mentioned earlier, we have moved away from fixed retractors to a fishhook Lone Star retraction system, and this change has markedly reduced our incidence of nerve injury to almost 0.

Durability and Rate of Recurrence

Recurrent carotid stenosis after carotid endarterectomy can occur as a result of neointimal hyperplasia (for stenosis recurring within 24 months of surgery) and from recurrent atherosclerosis (after 24 months). In the carotid artery, the bifurcation

creates shear stress related to turbulent, high pressure arterial blood flow leading to endothelial damage and a focal, recurrent inflammatory cascade that leads to progressive deposition of atheromatous plaque which gradually compromises the integrity of the carotid arterial lumen. These forces remain present after CEA, making the patient susceptible to recurrent atherosclerosis over the course of several years.

A small but finite incidence of recurrent carotid stenosis occurs after CEA. Most studies quote a symptomatic recurrence rate of approximately 4–5%. In one study of noninvasive follow-up after CEA, a 4.8% recurrence rate of symptomatic carotid restenosis was found, with an additional 6.6% asymptomatic restenosis. As mentioned earlier, authors who use universal patch graft techniques have reported lower restenosis numbers (1% symptomatic, 4–5% total at 2 years follow-up).

Aside from technical shortfalls at the time of surgery, it is difficult to establish risk factors associated with recurrent carotid stenosis. Continuation of tobacco smoking postoperatively has been accepted as a significant risk factor, although hypertension, diabetes mellitus, family history, aspirin use, coronary artery disease, and lipid studies were not found to be significant risk factors.

Redo CEA can be performed for restenosis, although, in general, it should be regarded as a high-risk procedure, as reoperation can lead to more cranial nerve injuries and local complications. There has also been an increased incidence of stroke reported in patients undergoing redo CEA. Accordingly, and contrary to our previous teachings, we now recommend CAS for recurrent *symptomatic* carotid disease and a course of watchful waiting with annual imaging for *asymptomatic* recurrence [11, 12]. In truth, with the adoption of universal patch grafting in our practice for a number of years, we see almost no recurrent disease in our surgical patients, and most of the patients whom we either follow or refer for CAS have been referred for complex management after surgery was done elsewhere.

Clinical and Radiographic Follow-Up

How should routine post-CEA patients be followed long term? Given the quick availability and noninvasive nature of Doppler ultrasonography, we elect to perform an ultrasound on the patient the day after CEA to verify wide patency and establish a baseline. We follow our CEA patients for life and typically obtain a repeat Doppler ultrasound at 3 months and then annually. Once stability has been established over an extended period, surveillance at longer intervals may be appropriate. Termination of surveillance is reasonable when the patient is no longer a candidate for intervention.

Summary of Complications

Potential Complications that are of concern:

1. Stroke
2. Nerve injury
3. Arterial problems, leaks, aneurysms, wound infections
4. Medical issues, primarily MI

1. Stroke: Why would someone have a stroke? (A) There isn't enough blood flow to the brain. The remedy for this involves neurological monitoring, in our case EEG/SSEP, and placement of an indwelling shunt if the monitoring changes indicating cerebral ischemia. CEA complications can be *acute* or *delayed*. (B) An embolus of plaque, clot, or air passes up the ICA to the brain. The remedy for this is meticulous technique, giving adequate heparin, dissecting with a low-touch technique, and never clamping across a plaque or passing a shunt through an area of plaque. The ICA must be protected at all times and never declamped until the repair is complete, declamping at other times could expose the ICA and the brain to emboli. Finally, the sequence of declamping must be studied and memorized so that any debris is flushed into the ECA, never the ICA. (C) The vessel occludes post-op. The remedy for this is meticulous technique and, in our practice, universal patch grating.
2. Nerve injury: The surgeon must be familiar with the location and function of the hypoglossal, vagus, accessory, recurrent and superior laryngeal nerves, and the ansa hypoglossi. Injuries can occur from traction, transection, or cautery. The remedy is, first, the use of fishhook retractors rather than fixed retractors and, second, adopting a policy as we have of never cutting any nerves (like the ansa) instead choosing to work in and around them.
3. Arterial problems, hematomas, leaks, aneurysms, wound infections: Fortunately these are almost never events. Wound infections are almost nonexistent, I have seen only one in 30 years, which resolved with exploration and antibiotic treatment. I have seen one delayed (4 years) asymptomatic false aneurysm, which we treated with a stent. We take every precaution to prevent leaks, and we do not close unless the wound is arid dry. We place a medium hemovac in the carotid sheath in every case. Regarding the suture line, we use reinforcing sutures routinely to prevent unraveling (which I have never seen happen), and we never grasp the Prolene suture with forceps, which would weaken it. If someone mistakenly grasps it, I oversew that entire wall again for certainty with a new suture. If there is a hematoma post-op, as can happen in prosthetic cardiac valve patients who need heparin maintained post-op, one must assure the integrity of the suture line immediately. We used to do angiography, but now we do CTA or MRA to acquire this data. *I have never in my career reoperated a carotid surgery for a wound hematoma*. I attribute this to careful and meticulous technique at the primary operation.
4. Medical issues, primarily MI: The remedy for these issues is a proper preoperative medical clearance, a skilled anesthetist, patients housed in the NSICU post-op, and continuation of daily aspirin before, during, and after the operation. The phenomenon of dysautoregulation hemorrhage in patients with tight stenosis is avoided by ICU management with tight BP control.

Conclusion

Carotid endarterectomy must have a very low complication rate in order to benefit patients, especially in the asymptomatic population. Thus, it is imperative that in addition to proper patient selection and an appropriate medical work-up,

meticulous care be taken at each step of the procedure to ensure success. Anticipating and understanding the critical elements that can cause a complication will help to ensure success.

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Aneurysms of the Anterior Circulation

13

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Checklist: Anterior Circulation Aneurysms (One of Two—Management of Intraoperative Rupture)

Equipment needed	Procedural steps
OR Technicians • Temporary clips • Permanent clips • Microdissectors • Microscope, with ICG angiography • EVD catheters available • Micro-Doppler flow probe • Cotton Nursing • Mannitol • Hypertonic saline • Anticonvulsant • Direct vasodilators • Staff pager/cell phone numbers for endovascular neurosurgery and neurointerventionalist Anesthesia/Neuromonitoring • ICP monitoring • Burst suppression • Adenosine • Cardiac defibrillator in place Neurointerventionalist • Groin prepped for intraoperative angiography • Radiolucent Mayfield clamp Neurosurgery • EVD • Bypass plan • Staff pager/cell phone numbers for endovascular neurosurgery and angiography	Identify and dissect • Proximal, distal, neck, then dome Initiate and engage • Alert *entire* team • Suction to area with large suction tips to identify source • Apply fixed retractor to free both hands • Place temporary clips • Reexamine rupture site • Anesthesia: burst suppression • Anesthesia: evaluate cardiovascular adjuncts (i.e., adenosine) Repair and reconstruct • Gently dissect free surrounding arachnoid if traction on structures is noted • Clip reconstruct or place pilot clip at rupture site • Release temporary clips • Identify additional bleeding • Rupture at neck of aneurysm may require clip-wrap or cotton-clipping • If unsuccessful, consider trapping • Assess patency of parent and daughter vessels • Perform ICG • Adjust clips as needed • Assess acute vessel spasm • Assess need for direct vasodilators (i.e., papaverine) Perform, as needed • Additional imaging • EVD

Checklist: Anterior Circulation Aneurysm (Two of Two—Management of Cerebral Edema)

Equipment needed	Procedural steps
OR Technicians • Temporary clips • Permanent clips • Microdissectors • Microscope, with ICG angiography • EVD catheters available • Micro-Doppler flow probe • Bypass instruments • High speed drill Nursing • Mannitol • Hypertonic saline • Anticonvulsant • Direct vasodilators • Staff pager/cell phone numbers for endovascular neurosurgery and neurointerventionalist Anesthesia/Neuromonitoring • ICP monitoring • Burst suppression • Hyperventilation • Mannitol • Hypertonic saline • Elevate head of bed Neurointerventionalist • Groin prepped for intraoperative angiography • Radiolucent Mayfield clamp Neurosurgery • EVD • Bypass plan • Staff pager/cell phone numbers for endovascular neurosurgery and angiography	Identify and inspect • Elevate head of bed or reverse Trendelenburg • Modest hyperventilation (end-tidal CO2 of 25 mmHg) • Avoid hypertension • EVD drainage of CSF • Cisternal drainage of CSF • Evaluate for additional bone removal Initiate and engage • Alert *entire* team • Place or remove temporary clips • Anesthesia: burst suppression • Anesthesia: evaluate hypertonic adjuncts • Consider mild hypothermia Repair • Open lamina terminalis if possible • Consider Paine's point ventricular puncture and drain • Identify any bleeding • Assess patency of parent and daughter vessels (as possible cause of edema) • Adjust clips as needed • Assess acute vessel spasm Perform, as needed • EVD • Additional bone removal • CSF diversion

Complication Avoidance Flowchart

Complication	Cause	Avoidance
Retraction injury	• Use of fixed brain retractors	• Plan appropriately sized craniotomy and obtain adequate skull base exposure (i.e., drilling of sphenoid wing) • Perform wide splitting of the Sylvian fissure • Release CSF from basal cisterns
Venous infarction	• Sacrifice of Sylvian veins	• Avoid coagulation/division of large Sylvian veins
Arterial infarction	• Perforator clipping • Prolonged temporary clipping • Clip-associated parent artery stenosis	• Perform circumferential dissection and inspection of aneurysm • Avoid more than 3 min of proximal artery temporary clipping prior to reperfusion • Confirm adequate parent vessel caliber and blood flow using intraoperative angiography
Intraoperative aneurysm rupture	• Disruption of thrombus on aneurysm rupture site • Aneurysm neck tear	• Obtain proximal parent vessel control prior to dissecting the aneurysm • Generously release adjacent arachnoid to avoid traction on the aneurysm rupture site or neck

Introduction

Cerebral aneurysms of the anterior circulation include those that arise from the internal carotid artery (ICA) or any of its terminal branches. Although the indications for an endovascular approach to aneurysm treatment continue to expand, microsurgical treatment remains the preferred option for many patients with select anterior circulation aneurysms. The established durability, versatility, and effectiveness of microsurgical clip ligation for treating anterior circulation aneurysms set the standard by which all newer technologies must be judged. In this chapter, we provide a comprehensive review of the considerations necessary to effectively treat anterior circulation aneurysms microsurgically while avoiding common pitfalls..In addition to reviewing the salient general preoperative and intraoperative matters of relevance to anterior circulation aneurysm surgery, we also discuss the specific considerations for aneurysms in each location.

Historical Background

The surgical treatment of aneurysms has continued to evolve since Norman Dott performed the first direct treatment of a ruptured anterior circulation aneurysm in 1931 [1, 2]. Dott reportedly fashioned a left frontal osteoplastic bone flap, approached the ipsilateral ICA from a lateral subfrontal trajectory, dissected distally to the ICA bifurcation, and finally moved toward the proximal middle cerebral artery (MCA) where brisk arterial bleeding was encountered from the aneurysm's dome. At this point a muscle wrap was used to tamponade the rupture site. Dott's patient made a remarkable recovery and returned to full functionality prior to dying from heart disease 11

years later. Such a feat was certainly remarkable in itself but more so considering that Dott accomplished this without the benefit of preoperative imaging, a surgical microscope, fine microinstruments, or modern monitoring and anesthesia.

The next major advancement in aneurysm surgery came when Walter Dandy performed the first clip ligation of another anterior circulation aneurysm in 1937 [3]. Dandy's patient presented with a complete third cranial nerve palsy due to compression from a posterior communicating artery aneurysm. In his seminal case report on the matter, Dandy explains that "An ordinary flat silver clip was placed over the neck of the sac and tightly compressed, obliterating it completely. The clip was flush with the wall of the carotid artery." The patient did exceptionally well after suffering a 3-day bout of delirium tremens postoperatively. The preoperative oculomotor palsy fully resolved 7 months after surgery.

Although Dandy is often credited with ushering in the modern era of cerebral aneurysm surgery, Yasargil's moniker as the "father of microneurosurgery" is a testament to his manifold contributions not only to cerebrovascular surgery but to neurosurgery as a whole. Yasargil's advocacy for routine use of the operating microscope during aneurysm surgery, development of modern aneurysm clips, elaboration of subarachnoid basal cistern anatomy, popularization of cerebral bypass techniques, and refinement of the "workhorse" frontotemporal/pterional craniotomy are just a small sampling of his contributions to cerebrovascular surgery [4].

Procedural Overview

Equipment

In addition to the standard tools necessary to turn a craniotomy flap and provide adequate skull base exposure (adjustable electric operating table, high-speed drill, various rongeurs, etc.), there are a number of specific instruments recommended to facilitate efficient and safe microsurgical clip ligation of anterior circulation aneurysms.

Skull Clamp and Retractors

A radiolucent three-point skull fixation clamp is utilized for positioning prior to cerebral aneurysm surgery. Rigid head stabilization is essential to ensure safety and accuracy during delicate microsurgical maneuvers including deep drilling, arachnoid and aneurysm dissection, microvessel suturing, and aneurysm clipping. The radiolucent property of the skull clamp enables intraoperative catheter cerebral angiography to be performed without obstruction from radiopaque metal (Fig. 13.1).

We routinely utilize fishhooks attached to a Leyla bar by rubber bands to provide scalp and temporalis muscle retraction during the surgery. Such retraction not only facilitates low-profile exclusion of tissue from the operative field of view but also assists with muscle and scalp hemostasis (Fig. 13.2). A retractor system such as

Greenberg or Budde Halo apparatus should be rigidly secured to the skull clamp in case brain retraction becomes necessary, especially in the setting of subarachnoid hemorrhage when diffuse cerebral edema is present and intraoperative aneurysm rupture is more prevalent (Table 13.1).

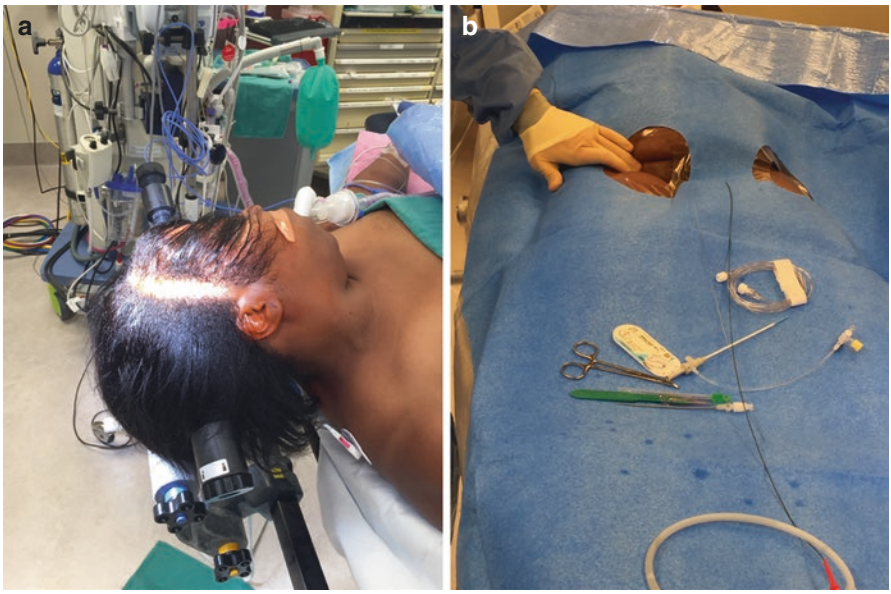

Fig. 13.1 Cranial fixation and intraoperative angiography. The head is secured in a three-point radiolucent skull clamp and rotated about 30° contralateral to the operative side. The planned curvilinear incision from the widow's peak to the anterior tragus is outlined by the strip shave (**a**). The groin is prepped and draped allowing an introducer sheath to be placed either pre- or intraoperatively in preparation for catheter angiography (**b**)

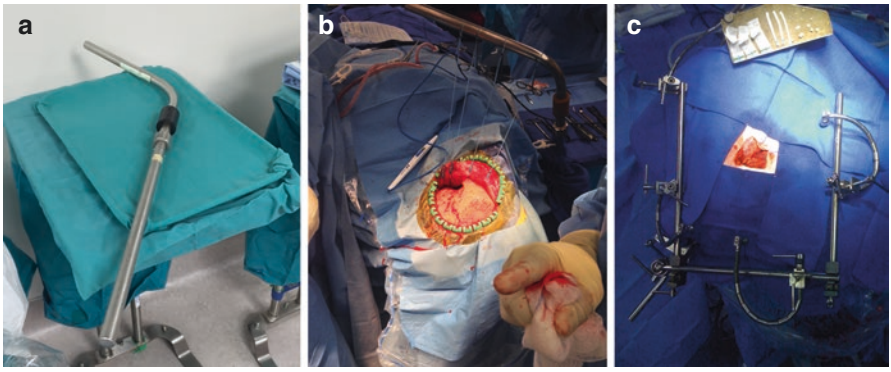

Fig. 13.2 Retractor setup for a pterional approach. The Leyla bar is used routinely in the operative setup for anterior circulation aneurysm surgery (**a**). It facilitates low-profile scalp and temporalis muscle retraction giving access to the keyhole and entire frontotemporal region (**b**). A brain retractor system such as the Greenberg should be assembled in case its use becomes necessary (**c**)

Table 13.1 Checklist for managing intraoperative aneurysm rupture

• Attempt to clear the operative field of blood using one or more suctions as needed
• Placement of a fixed brain retractor may be needed to free both hands for additional microsurgical manipulation
• Suction on wet cotton within the field to improve the surface area cleared
• Consider temporary cardiac pause with adenosine if blood is not easily cleared
• Initiate burst suppression and place a temporary clip on the proximal feeder artery if possible
• Determine the rupture site on the aneurysm and place a suction tip over this point to halt extravasation
• Free remaining arachnoid and perforators from the aneurysm neck and dome
• Clip the aneurysm neck if the rupture site is on the fundus; alternatively a temporary "pilot clip" that occludes the rupture site can be helpful prior to definitive direct neck clipping
• A tear at the neck of the aneurysm may require a clip-wrap or cotton-clipping strategy as outlined by Barrow and Spetzler (Neurosurgery. 2011 Jun; 68: 294–9)
• In the event that cotton clipping is ineffective, aneurysm trapping from the parent vessel may be necessary
• Consider a bypass strategy if trapping is performed

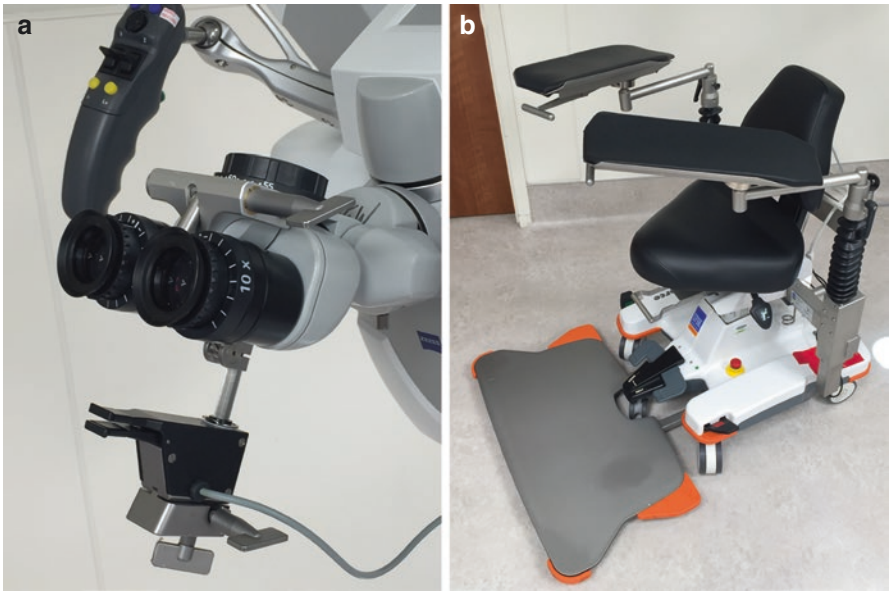

Fig. 13.3 The operating microscope and chair. A microscope equipped with a mouthpiece is helpful for allowing uninterrupted bimanual work within the operative field (**a**). Alternatively, foot pedal control may be preferred. A comfortable chair with an armrest can also facilitate the performance of fine microsurgical maneuvers (**b**)

Microscope

An operating microscope equipped with either foot pedal controls or a mouthpiece is essential for allowing fine adjustments to the focus, zoom, and field of view without removing either hand from the operative field (Fig. 13.3). It is also

recommended that the microscope be equipped with an indocyanine green (ICG) fluorescence filter such that intraoperative videoangiography can be performed. Alternative or additional filters for fluorophores such as fluorescein have also been utilized in aneurysm surgery [5].

Microinstruments

Fine tip bipolar cautery, arachnoid knives, microscissors, a variety of angled microdissectors, and variable strength suctions with teardrop finger controls (Fig. 13.4) are important tools that facilitate microsurgical exploration during aneurysm surgery. A microvessel anastomosis set including—at a minimum—fine jeweler forceps, tying forceps, and a microneedle driver is an essential component of the vascular neurosurgeon's toolbox. While vessel suturing is typically not needed during most anterior circulation aneurysm surgeries, one should always be prepared to perform a bypass or repair an injured vessel—typically with a 9-0 monofilament suture. In addition, we routinely utilize micro-Doppler ultrasound to confirm vessel patency after clip placement prior to obtaining an angiogram.

Pharmacological Adjuncts

Several medications are routinely given to the patients in the operating room prior to the commencement of aneurysm surgery. Prophylactic antibiotics with skin flora coverage such as cefazolin should be given prior to making an incision. Seizure

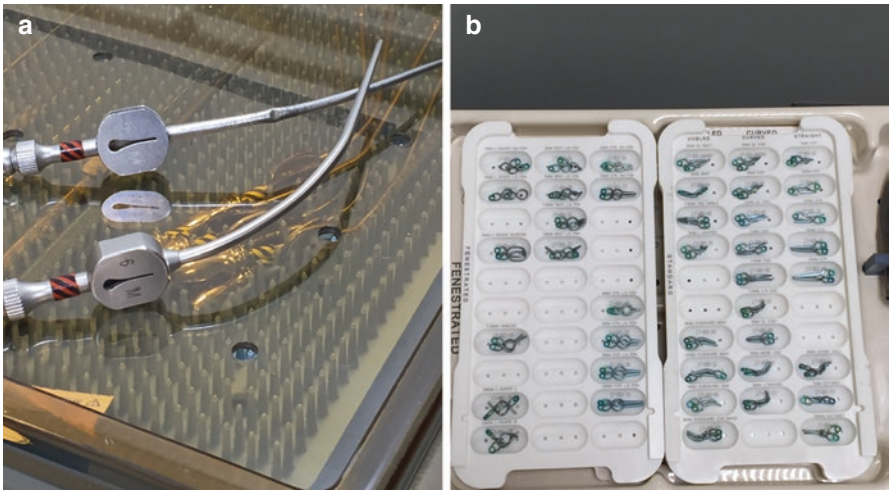

Fig. 13.4 Microsurgical suctions and aneurysm clips. Suction injury to surrounding vessels and brain structures can be avoided with the use of teardrop finger-controlled suctions during microsurgery (**a**). An aneurysm clip set including a variety of straight, angled, curved, and fenestrated clips is an essential part of the cerebrovascular surgeon's toolbox (**b**)

prophylaxis with levetiracetam or phenytoin is also prudent. Mannitol at a dose of 0.5–1 g/kg reduces cerebral water content thus relaxing the brain and may have additional microcirculatory rheological effects thought to be neuroprotective. Similarly, dexamethasone at a dose of 10 mg may have beneficial effects in terms of reducing brain edema as well as reducing postoperative nausea and vomiting. Blood glucose should be kept in the normal range using an insulin infusion if necessary. Additional agents such as adenosine to effect temporary flow arrest and local vasodilators including nicardipine and papaverine should be available if needed. Intra-arterial cerebral vasodilator agents such as verapamil may also be of utility in the treatment of severe intraoperative vasospasm.

Brain Relaxation

The benefits of mannitol and steroids have already been mentioned for the purposes of effecting brain relaxation. It goes without saying that basic principles of proper patient positioning should be followed including having the head above the level of the heart and minimizing venous outflow obstruction with aggressive head turning. Additional strategies for achieving further brain relaxation include instituting moderate hyperventilation, placement of a preoperative external ventricular or spinal drain, placement of an intraoperative ventriculostomy, and performing in situ cisternal cerebrospinal fluid evacuation (Table 13.2).

Hyperventilation

Moderate short-term hyperventilation with a goal end-tidal CO_2 of 25–30 mmHg causes cerebral vasoconstriction which results in reduction of both cerebral blood flow and blood volume. This cascade in turn reduces intracranial pressure which clinically manifests as a more relaxed brain. While effective, moderate hyperventilation should be instituted with caution to prevent ischemic sequelae especially in the setting of vasospasm. Thus, maintenance of normotension or even moderate hypertension is prudent when hyperventilation is instituted.

Table 13.2 Checklist for managing intraoperative cerebral edema

• Elevate the head of bed or put the patient in reverse Trendelenburg position
• Initiate modest hyperventilation to an end-tidal CO_2 of 25 mmHg
• Avoid hypertension
• Ensure that mannitol has been given, may consider giving an additional bolus of hypertonic saline
• Evacuate CSF from the basal cisterns and/or open the lamina terminalis if possible
• Open the spinal drain if one was placed preoperatively
• Initiate burst suppression and ensure that the patient is modestly hypothermic
• Place a Paine's point external ventricular drain if necessary

CSF Drainage

As a matter of protocol at our institution, all patients presenting with poor clinical grade subarachnoid hemorrhage or symptomatic hydrocephalus will have a preoperative external ventricular drain (EVD) in place. A temporary spinal drain placed in the operating room after anesthesia induction is most commonly utilized for good clinical grade subarachnoid hemorrhage patients who do not have symptomatic hydrocephalus. This is also a consideration when an interhemispheric approach is utilized since access to the subarachnoid cisterns is limited. Should immediate intraoperative CSF drainage become necessary in a patient without an EVD or spinal drain, a Paine's point ventriculostomy can be easily placed after the dura is opened. Brain relaxation can be further facilitated by wide opening of the Sylvian fissure and the basal cisterns including the chiasmatic, lamina terminalis, and carotid cisterns.

Sylvian Fissure Dissection

Sylvian fissure dissection is generally the first microsurgical step for gaining access to most anterior circulation aneurysms. A wide, generous splitting allows the frontal and temporal lobes to become untethered and provides unimpeded access to the basal cisterns (Fig. 13.5). When the Sylvian fissure is split in this fashion, minimal or no fixed brain retraction is necessary. The depth, length, and direction of Sylvian fissure dissection are partially dictated by the location of the aneurysm and partially the result of surgeon preference. In general, middle cerebral artery aneurysms require relatively deep and lateral dissection into the Sylvian fissure. In contrast, proximal ICA and anterior communicating artery aneurysms require less deep and more medial Sylvian fissure dissection.

Developmentally, middle cerebral artery branches exclusively irrigate either the frontal lobe or the temporal lobe and do not cross the Sylvian fissure, whereas veins

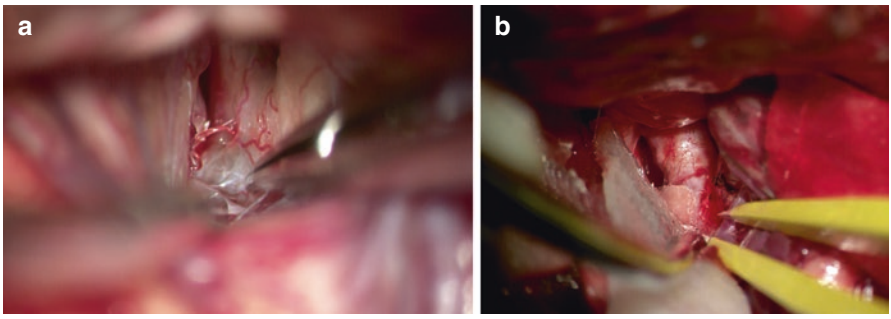

Fig. 13.5 Opening the basal cisterns. After Sylvian fissure dissection, arachnoid may be generously freed posteriorly toward the optic chiasm and lamina terminalis (**a**). The optico-carotid cistern is opened, freeing the internal carotid artery to provide proximal blood flow control (**b**)

do not strictly follow this rule. Thus, arteries should never have to be divided during Sylvian fissure dissection, while this is sometimes necessary for crossing veins. Nonetheless, large draining veins to the sphenoparietal sinus should be spared when feasible to avoid complications resulting from venous congestion. Veins tend to run more closely in association with the temporal lobe, so it is often more favorable to begin the Sylvian fissure arachnoid dissection biased toward the frontal side. Use of meticulous microsurgical technique with strict avoidance of subpial dissection is emphasized to ensure the best possible result.

Cerebral Protection

Cerebral protection strategies during aneurysm surgery aim to reduce ischemic neuronal injury that may result from reduced local or global oxygen delivery. Such a state may occur secondary to either intentional or unintentional reductions in cerebral blood flow. Intentional local blood flow reduction occurs most commonly during temporary clipping. Intentional global blood flow reduction may be due to induced hypotension or temporary cardiac pause after adenosine injection. Unintentional local blood flow reduction may be secondary to fixed brain retraction or vasospasm. Similarly, unintended global blood flow reduction can also result from diffuse cerebral vasospasm or hypotension. Specific strategies including institution of mild hypothermia, induction of burst suppression, and maintenance of mild hypertension may be helpful in mitigating the downstream effects of reduced neuronal oxygen delivery.

Hypothermia

While deep hypothermia is incontrovertibly known to be neuroprotective, the benefits of mild hypothermia are less definitive. The systemic complications associated with induction of deep hypothermia have rendered this technique of historical interest for aneurysm surgery [6]. In contrast, mild hypothermia is readily tolerated by most patients and seems to at least not be harmful. Given the theoretical benefits of even mild reductions in the cerebral metabolic rate from temperature reduction, we routinely aim for a core temperature of approximately 34–35 °C until the aneurysm has been secured.

Burst Suppression

Similar to the effect of hypothermia on cellular energy consumption, neuronal burst suppression can significantly reduce the cerebral metabolic rate of oxygen consumption. While barbiturates are no longer routinely utilized for this purpose, propofol-induced burst suppression is advocated by some practitioners during temporary clipping [7]. This is frequently done in combination with mild induced hypertension to facilitate perfusion via collateral pathways.

Neuromonitoring

Electrophysiological monitoring with electroencephalography and, more recently, bispectral index monitoring is necessary if true burst suppression is desired intraoperatively. Additional monitoring of motor and somatosensory evoked potentials has utility in terms of predicting postoperative ischemic injury. Nonetheless, these modalities are not absolutely sensitive or specific and thus may give a false sense of security. This is especially the case during long periods of temporary clipping. Alternatively, we favor limiting the duration of temporary clipping to cycles of 3 min occlusion followed by 5 min of reperfusion without the routine use of eletrophysiological monitoring.

Craniotomy

The vast majority of anterior circulation aneurysms can be approached from either a frontotemporal/pterional craniotomy or from a frontal parasagittal craniotomy. In rare circumstances, an alternative craniotomy may be used in cases such as a distal middle cerebral artery aneurysm (usually a mycotic M4 aneurysm) or if a decompressive craniectomy must also be performed. Specific modifications to the pterional craniotomy including orbital extension or an orbitozygomatic approach are rarely necessary. Additional variations such as the "mini-pterional" or a lateral supraorbital craniotomy can also be utilized, particularly in the unruptured setting. Similarly, the parasagittal craniotomy as utilized for interhemispheric approaches to distal anterior cerebral artery aneurysms (DACA) may be altered to accommodate the anatomy of each unique case.

Pterional Craniotomy

The basics of this "workhorse" cranial approach are familiar to most neurosurgeons; however, some points are worth reviewing [8]. First, there are several options for how to dissect the temporalis muscle for exposure to the region. This includes (1) anterior reflection as part of a curvilinear myocutaneous flap extending from the widows peak to the anterior tragus, (2) posterior reflection after making a muscle incision just posterior to the fat pad, (3) interfascial or subfascial dissection allowing posterior reflection from the lateral orbital rim, or (4) posterior inferior reflection over the zygoma after both dissections from the lateral orbital rim and making a posterior muscle belly incision extending from the superior temporal line to the root of the zygoma. While all the aforementioned treatments of the temporalis muscle inevitably result in some atrophy, we favor the anteriorly reflected myocutaneous flap for its simplicity as well as the favorable cosmetic results.

Another important point regarding the pterional craniotomy for anterior circulation aneurysm surgery is that the lesser sphenoid wing and lateral orbital roof should

be generously drilled flat to the depth of the superior orbital fissure. Indeed routine unroofing of the posterior orbit as advocated by Yasargil is ideal but not necessary for most cases. Similarly, extensive anterior temporal and high anterior frontal bone removal is frequently not necessary. Deepening the bone removal along the lesser sphenoid wing leads to the anterior clinoid process and optic canal roof. The indications for anterior clinoidectomy are further discussed in the section on specific aneurysms. Although either extradural or intradural anterior clinoid removal is generally acceptable, we favor the intradural approach for aneurysm surgery. The anterior clinoid process has three attachments to the skull base including the optic canal roof, the lesser wing of the sphenoid bone, and the body of the sphenoid bone via the optic strut. A 2 mm diamond burr or ultrasonic aspirator with bone attachment may be used to remove these connections allowing the clinoid to be freed.

Parasagittal Craniotomy

The parasagittal craniotomy can be modified in terms of size and rostro-caudal placement. This is based both on the specific anatomy of the aneurysm to be treated as well as on the location of bridging veins to the superior sagittal sinus. While certainly not necessary, frameless stereotaxy has some utility in aneurysm surgery for the precise placement of this particular bone flap. Proximal A2 aneurysms require a more rostral bone flap placement than is needed for distally located anterior cerebral artery aneurysms. In general, a non-dominant interhemispheric approach is favored. The bone flap is planned such that it spans the superior sagittal sinus and is eccentric to the right side. The degree of patient neck flexion warranted is determined by the aneurysm's location. A supine or lateral patient position may be utilized. Although we favor the supine position, it is recognized that in the lateral position with the approach side facing down, gravity assists with opening up the interhemispheric corridor.

Considerations for Specific Aneurysms

Cavernous and Clinoidal Segment Aneurysms

Cavernous and clinoidal ICA segment aneurysms are generally not treated microsurgically. Indeed most such aneurysms do not require any treatment at all, even when they become quite large. This is due to the fact that they rupture at an exceedingly low rate and furthermore are extradural in location [9]. Large symptomatic cavernous aneurysms can be effectively treated with flow diversion in most instances. Some large clinoidal segment aneurysms may extend intradurally past the distal dural ring which would elevate the level of concern for its capacity to result in subarachnoid hemorrhage. When such an aneurysm is unruptured, it is often favorable for some form of endovascular treatment including simple or balloon-assisted

coiling, stent-assisted coiling, or flow diversion. In the rare setting of subarachnoid hemorrhage from a clinoidal segment aneurysm not amenable to either simple or balloon-assisted coiling, clip ligation is prudent. Microsurgical clip ligation is also favored if there is optic nerve compression resulting in visual disturbance since direct aneurysm dome decompression can be simultaneously accomplished.

An anterior clinoidectomy with complete opening of the distal dural ring to expose the distal and proximal aneurysm neck is mandatory to treat clinoidal segment aneurysms. Ipsilateral cervical ICA dissection to gain proximal control is recommended to safely approach these aneurysms.

Ophthalmic Segment Aneurysms

Ophthalmic segment aneurysms include three separate anatomic types including ophthalmic artery aneurysms, superior hypophyseal artery aneurysms, and dorsal carotid aneurysms. The specific considerations for each aneurysm type are unique and reviewed separately.

Ophthalmic artery aneurysms arise at or just distal to the takeoff of the ophthalmic artery. The aneurysm projection is typically superiorly, approximately perpendicular to the parent ICA. Intradural inspection is necessary to determine whether an anterior clinoidectomy is necessary to expose the proximal neck of this aneurysm. In many cases, a clinoidectomy is unnecessary, and adequate neck exposure is either already present or necessitates only release of the falciform ligament around the optic nerve. Much like for clinoidal segment aneurysms, ophthalmic artery aneurysms generally present with little proximal intradural ICA available to allow for temporary clipping. Proximal control is best gained by exposing the cervical ICA in this situation. Alternatively, temporary flow arrest with adenosine can be utilized to facilitate aneurysm softening and neck clipping.

Superior hypophyseal artery aneurysms project from the medial surface of the ICA distal to the dural ring. Like clinoidal segment aneurysms, superior hypophyseal aneurysms tend to have a low rupture risk and are often followed conservatively. If microsurgical clipping is elected, the anatomy generally requires use of a right-angled fenestrated clip with the ICA within the fenestration. Interestingly, exposure of superior hypophyseal aneurysms from a contralateral approach may actually give the most direct view and facilitate more straightforward clipping.

Dorsal carotid wall aneurysms arise without relation to a specific arterial branch. The saccular variety can often be directly clipped in a very straightforward fashion. Frequently, however, dorsal carotid aneurysms are of the blood blister type and do not have a discreet neck. These aneurysms are most favorable for clip-wrapping with Gore-Tex. A mild degree of non-flow limiting ICA stenosis is generally acceptable at the site of wrapping, indicating that the clip has adequately cinched the Gore-Tex around the bleed site.

Communicating Segment Aneurysms

Communicating segment aneurysms include those of the posterior communicating and the anterior choroidal arteries. Notable points regarding the clipping of aneurysms in this segment include ensuring that anterior thalamoperforating arteries are excluded from the clip blades, preoperative recognition of fetal posterior cerebral arteries with attention to intraoperative preservation during clipping, and, finally, uncompromising regard for maintaining the patency of the anterior choroidal artery.

A subfrontal approach with minimal or no Sylvian fissure splitting is one way to access simple aneurysms in this region especially when there is no subarachnoid hemorrhage (Fig. 13.6). Alternatively, it is more generally recommended to open the medial aspect of the fissure to provide wider access and limit the need for fixed brain retraction. Intradural proximal ICA control is usually easily accessible without the need for anterior clinoidectomy.

While communicating segment aneurysms have historically been considered among the simplest aneurysms to clip, this also tends to be true regarding the feasibility for coiling them. Thus, in the current "endovascular era," communicating segment aneurysms that are best treated microsurgically are generally of higher complexity than was seen in prior generations.

Carotid Terminus Aneurysms

The important principles to keep in mind when approaching aneurysms at the ICA bifurcation are similar to those in other locations: establish early proximal control, completely dissect the aneurysm dome from surrounding arachnoid adhesions, and avoid perforator injury or occlusion. Thus, with regard to obtaining early proximal control, it is sometimes feasible to commence dissection by

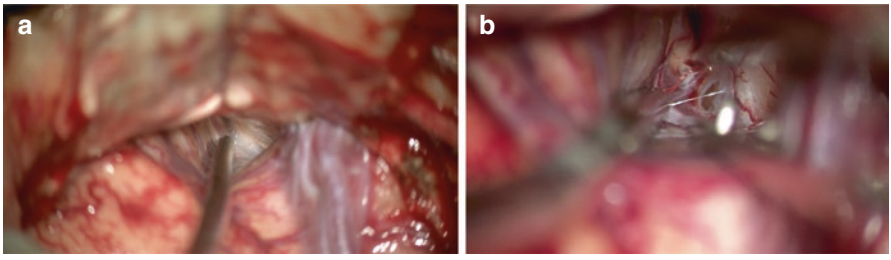

Fig. 13.6 Lateral supraorbital corridor. The ipsilateral optic nerve is readily visible on initial subfrontal dissection with no Sylvian fissure opening (**a**). Such an approach to the anterior communicating region is facilitated by opening the lamina terminalis to release CSF from the ventricular system (**b**)

opening the carotid cisterns and progressing distally toward the horizontal aspect of the Sylvian fissure until the aneurysm is encountered. Alternatively, lateral to medial opening of the Sylvian fissure can be elected much in the way that middle cerebral artery bifurcation aneurysms are exposed. Important perforators to be aware of include the recurrent artery of Heubner and the anterior choroidal artery which course medial to the aneurysm on the operator's blind side. M1 lenticulostriate vessels that are adherent to the aneurysm should be dissected free prior to clipping.

Anterior Communicating Artery Aneurysms

Anterior communicating artery aneurysms are often more complex than is initially appreciated. During the microsurgical treatment of these aneurysms, it is important to strive for identification of all incoming and outgoing arteries affiliated with the anterior communicating complex. These vessels include bilateral A1, bilateral A2, bilateral recurrent artery of Heubner, perforators from the posterior-superior aspect of the communicating artery, and the anterior communicating artery itself. The surgeon should have preoperative awareness of all anatomic variations in the region such as non-coronal orientation of the communicator, the presence of fenestrated or accessory communicators, or the persistence of a median artery of the corpus callosum resulting in three A2 vessels.

Distal Anterior Cerebral Artery Aneurysms

Distal anterior cerebral artery aneurysms (DACA) include those occurring distal to the anterior communicating artery. Often referred to as pericallosal aneurysms, the prototypical type occurs in relation to the origin of the callosomarginal artery. Anatomically, these aneurysms commonly occur at or just distal to the genu of the corpus callosum. These aneurysms are best approached from a frontal interhemispheric corridor. On occasion, a more proximal A2 aneurysm can be accessed from a lateral subfrontal corridor in a similar manner to the approach for anterior communicating artery aneurysms. Again, it is wise to be aware of any anatomic variations to the arteries in the region such as the presence of an azygous or accessory A2s.

Middle Cerebral Artery Aneurysms

Middle cerebral artery aneurysms (MCA) may include those occurring on the M1, those arising at the MCA bifurcation, or less commonly aneurysms that are found on branches more distally along the arterial tree. M1 aneurysms are commonly found either in association with lenticulostriate perforators or at the

origin of an anterior temporal branch artery. Lenticulostriate aneurysms often project perpendicular to the parent M1 vessel with the dome buried in brain parenchyma making them difficult to locate. MCA bifurcation aneurysms are the most commonly observed type of MCA aneurysm. They are often wide-necked, large, and have a complex anatomy, making them less favorable for endovascular treatments. Classically, wide and deep splitting of the Sylvian fissure is advocated to approach these aneurysms although more minimalistic strategies have been reported [10]. Distal MCA aneurysms are infrequently seen but are more commonly mycotic in nature as compared to aneurysm found in other anterior circulation locations. An initial trial of antibiotic therapy is reasonable for many such mycotic aneurysms. If this conservative management fails to result in aneurysm regression, consideration should be given for direct clipping or resection.

Conclusion

Cerebral aneurysms of the anterior circulation have been safely and effectively treated surgically for nearly a century. Anterior circulation aneurysms are varied and a unique surgical solution must be devised for each case. It is important however to adhere to general principles including ensuring adequate skull base exposure, performing wide Sylvian fissure splitting, progressively opening the subarachnoid cisterns, securing proximal parent artery control, and completely dissecting the aneurysm from surrounding structures prior to clipping. Microsurgical refinements along with their utilization by dedicated practitioners continue to advance the field cerebrovascular surgery allowing more complex aneurysms to be durably and definitively treated.

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Aneurysms of the Posterior Circulation

14

Vernard S. Fennell and Peter Nakaji

Abbreviations

BRAT	Barrow Ruptured Aneurysm Trial
CN	Cranial nerve
CSF	Cerebrospinal fluid
OZ	Orbitozygomatic
PCA	Posterior cerebral artery
PCoA	Posterior communicating artery
PICA	Posterior inferior cerebellar artery
SCA	Superior cerebellar artery
VA	Vertebral artery

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Checklist: Microsurgical Treatment of Intraoperative Rupture of Posterior Fossa Aneurysm

Equipment needed	Procedural steps
OR Technicians • Temporary clips • Permanent clips • Microdissectors • Microscope, with ICG angiography • EVD catheters • Micro-Doppler flow probe • Bypass instruments Nursing • Mannitol • Hypertonic saline • Anticonvulsant • Direct vasodilators • Staff pager/cell phone numbers for endovascular neurosurgery and neurointerventionalist Anesthesia/neuromonitoring • ICP monitoring • Burst suppression • Adenosine • Cardiac defibrillator in place Neurointerventionalist • Groin prepped for intraoperative angiography • Radiolucent Mayfield clamp Neurosurgery • EVD • Bypass plan • Staff pager/cell phone numbers for endovascular neurosurgery and angiography	Identify and dissect • Proximal, distal, neck, and then dome Initiate and engage • Alert *entire* team • Place temporary clips • Reexamine rupture site • Anesthesia: burst suppression • Anesthesia: evaluate cardiovascular adjuncts (i.e., adenosine) Repair and reconstruct • Clip reconstruct • Release temporary clips • Identify additional bleeding • Assess patency of parent and daughter vessels • Perform ICG • Adjust clips as needed • Assess acute vessel spasm • Assess need for direct vasodilators (i.e., papaverine) Perform, as needed • Additional imaging • EVD

EVD external ventricular drain, *ICG* indocyanine green, *ICP* intracranial pressure, *OR* operating room

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Rupture	Fragility of aneurysm dome, adherence to associated structures	Visualization, temporary clipping, dissection, permanent clipping	Reduce traction of cortex during dissection, particularly in cases with subarachnoid hemorrhage
Parent, daughter, or perforator vessel occlusion	Inadequate visualization	Further dissection and reclipping	Circumferential visualization Intraoperative microscopic ICG angiography
Cranial nerve palsy	Excessive manipulation		Reduce CN manipulation CN electromyography
Edema	Inadequate venous drainage	CSF release, hypertonic medication, elevate head of bed	Careful positioning
	Cytotoxic injury	CSF release, hypertonic medication, elevate head of bed	

CN cranial nerve, *CSF* cerebrospinal fluid, *ICG* indocyanine green

Introduction

Patients with posterior fossa aneurysms can be quite complex to treat and manage. Complications in posterior fossa surgery have been described infrequently in the surgical literature [1]. About 10–15% of intracranial aneurysms arise from the posterior circulation. They are most often found at the basilar bifurcation, the superior cerebellar artery (SCA) origin, and the posterior inferior cerebellar artery (PICA) origin. The potential complications of this type of aneurysm differ, depending on the specific pathology. Many of the principles for avoiding complications during microsurgical treatment of posterior fossa aneurysms are associated not only with the angioarchitecture of the aneurysm but also with the particular surgical approach selected. The various approaches to posterior fossa aneurysms are the workhorses of skull base surgery: orbitozygomatic (OZ), subtemporal transpetrosal, suboccipital, retrosigmoid, far-lateral, and combined approaches that incorporate aspects of various preceding approaches. Nonvascular complications related to these approaches are well documented (e.g., cerebrospinal fluid [CSF] leak, meningitis, wound infection, cranial nerve (CN) palsy, hydrocephalus, hematoma, cerebellar mutism, and mortality). Posterior fossa surgery is generally associated with greater morbidity and mortality compared to supratentorial approaches; thus, care must be taken when approaching lesions in the posterior circulation.

Complications of Microsurgery

The complications that are associated with microsurgical treatment of posterior circulation aneurysms have been reported anecdotally as well as in the surgical literature. They are consistent with many of the complications associated with aneurysm surgery and with complex skull base approaches (Figs. 14.2, 14.3, 14.4, and 14.5). Complications related to the surgery include, but are certainly not limited to, CSF leak and infection. With regard to treating the aneurysm itself, complications include aneurysm rupture, parent or daughter vessel occlusion, perforator occlusion, CN palsy, stroke, and edema.

In a study of intraoperative and postoperative complications in 221 patients with vertebral artery (VA) or PICA aneurysms, 66 patients experienced complications; of those 66 patients, 13 had a poor outcome and 10 died [2]. The intraoperative and postoperative complications reported were intraoperative aneurysm rupture ($n = 16$), perforating vessel injury ($n = 2$), inadvertent arterial occlusion ($n = 10$), deep arterial hypotension during surgery ($n = 1$), postoperative hematoma ($n = 10$), postoperative significant spasm ($n = 8$), rebleeding from the treated aneurysm ($n = 4$), septicemia ($n = 13$), meningitis ($n = 8$), respiratory complications ($n = 8$), bleeding diathesis ($n = 1$), pulmonary embolus ($n = 2$), and multiple medical complications ($n = 13$).

Complications of posterior fossa microsurgery have been reported in multiple series [3–8]. In a large series of vertebrobasilar aneurysms, including VA and PICA aneurysms (vertebrobasilar, $n = 1767$; VA + PICA, $n = 221$) [3], CN complications were observed in 28% of the patients preoperatively, 47% immediately

postoperatively, and 22% at follow-up. Abducens nerve (CN VI) palsy was most common in the setting of rupture ($n = 26$, 11%), with 75% of these patients experiencing a complete recovery [3].

A major cause of morbidity as it relates to VA, PICA, and vertebrobasilar junction aneurysms is injury to lower CNs, most commonly the glossopharyngeal, vagus, spinal accessory, and hypoglossal nerves (CN IX–XII). These injuries can result in dysphagia, dysarthria, dysphonia, and inadequate airway protection. The risk may be due in part to variable VA and PICA anatomy. Most injuries are caused by retraction when working through and around the CNs. In a series by Drake et al. [3], more than 20% of the 1767 patients with VA or PICA aneurysms had CN IX or CN X deficits in the immediate postoperative period; 65% of the deficits were transient, but four patients had severe dysphagia that required tracheostomy. Thus, large VA and PICA aneurysms are often predictive of potential CN deficits, with patients subsequently requiring longer recovery after treatment.

In many instances, specific aneurysm morphology and angioarchitecture influence surgical decision-making. Large and giant aneurysms, especially VA aneurysms, often have a higher propensity toward parent vessel occlusion at the clip site than other types of aneurysms [2]. However, depending on the relative location on the parent vessel, vessel sacrifice with a clip can be fairly well tolerated. Blood flow to medullary perforating vessels can be compromised during surgical treatment, which can be fatal or which can lead to a poor outcome.

Although intraoperative rupture is not common, with reported rates of 5–10% [2], it is the most dangerous operative complication. Drake et al. [3] reported an intraoperative rupture rate of 7% in a vertebrobasilar aneurysm series of 1767 patients (221 VA + PICA); of 16 patients with intraoperative rupture, 4 died and 1 was severely disabled. Because of this risk, trapping and revascularization techniques should be used cautiously, and potential adverse events should be taken into consideration during operative planning.

The use of transclival approaches to reach posterior fossa aneurysms has been described, and although this approach may provide enhanced visualization, it can also lead to CSF leak with or without meningitis. With the transclival approach, many series have had a 50% rate of CSF leak, meningitis, or both [2, 4–7]. This can happen despite adjunctive measures, such as the use of a lumboperitoneal shunt, external ventricular drain, or fibrin glue.

Outcomes

Overall Outcomes

Current data suggest that for posterior fossa aneurysms, at least for ruptured aneurysms, outcomes with endovascular coil therapy may be better than with surgical clipping [5, 8–11]. Six-year outcome data from the Barrow Ruptured Aneurysm Trial (BRAT) [12] appear to somewhat favor coiling of select posterior circulation aneurysms.

In the BRAT, patients with ruptured PICA aneurysms versus those with ruptured non-PICA aneurysms had poorer outcomes, defined by modified Rankin scale scores >2, at discharge and at 1-, 3-, and 6-year follow-up. In the analysis of 471 patients with ruptured aneurysms, 238 were randomized to surgical clipping and 233 to endovascular coiling treatment; most surgically treated PICA aneurysms had an unfavorable outcome (70.6% of 19 patients). However, surgically treated aneurysms in the upper basilar artery tended to have more favorable outcomes in the BRAT [12].

In other large series reported in the literature [3, 4], up to two-thirds of VA aneurysms were well treated with neck clipping. It can be deduced from the results of those series that only a few select large saccular aneurysms might be unsuitable for clipping and should be treated with an approach similar to dissecting fusiform aneurysms, such as proximal ligation or stent or coil placement.

Samson et al. [8] reviewed the factors associated with poor surgical outcomes in 300 basilar apex aneurysms. These factors were poor clinical grade (Hunt-Hess grades of IV or V), age >65 years, thick basal clot, aneurysm size >20 mm, and symptoms of brainstem compression.

Spetzler et al. [7] and Drake et al. [3] have also reported excellent patient outcomes of 82–87% with microsurgical management of vertebrobasilar aneurysms in their series. The same reported series also revealed low operative morbidity and mortality of 2.4–5.1%. Thus, patient selection appears to weigh heavily in decision-making for treatment approaches for these lesions.

Complete Obliteration

Microsurgical clipping has a higher rate of complete obliteration than endovascular approaches. Large series of posterior circulation aneurysms, both unruptured and those associated with subarachnoid hemorrhage, show superior obliteration rates with microsurgery compared to endovascular treatment [1–3, 12].

Retreatment

Studies of microsurgical clipping have also shown lower rates of recurrence as well as lower retreatment rates compared to endovascular coil embolization. In two series, the retreatment rate after microsurgical clipping was as low as 6% compared to upward of 16% after endovascular treatment [12, 13].

A review of 6-year outcome data on ruptured aneurysms in the randomized BRAT cohort showed that aneurysms in the posterior circulation that were treated endovascularly had higher retreatment rates than aneurysms treated with microsurgical clip ligation [12]. However, this finding did not change overall outcomes at the 1-, 3-, or 6-year mark. In the BRAT, microsurgical clip ligation of aneurysms was shown to be exceedingly durable. It resulted in excellent obliteration rates with low rates of recurrence and little need for retreatment and comparable rates in anterior and posterior circulations.

Procedural Overview

Posterior circulation aneurysms have a higher likelihood of being treated by open microsurgical clipping than by endovascular coiling. Aneurysms in these locations are often not amenable to endovascular coiling because they have broad necks, aberrant or not easily identified branches, or fusiform morphology. Overall, patients with these lesions are more likely to be younger than those who present with aneurysms in other locations, to have fewer comorbidities, and to have better Hunt-Hess grades in cases of subarachnoid hemorrhage.

Determining the most efficacious approach for PICA aneurysms and the most suitable craniotomy should take into consideration the distance from the aneurysm base to the foramen magnum, as well as the distance of the aneurysm from the midline. For PICA aneurysms high above the foramen magnum, a condylectomy would likely not be needed. The approach to basilar apex aneurysms is predicated in part on the relative position of the complex, whether the aneurysm is high or low riding with respect to the posterior clinoid, and the subsequent need for drilling or an upward trajectory. The most effective approach for SCA and posterior cerebral artery (PCA) aneurysms is related to the proximal or distal location of the aneurysm in the interpeduncular, ambient, and crural cisterns along the P1, P2, and S1 segments. Nevertheless, we believe that most posterior circulation aneurysms can be effectively treated with a few skull base approaches (Table 14.1, Fig. 14.1). However, we would be remiss in ascribing outcomes to approach alone. The exceptional and dedicated work of the microsurgical masters has revealed to us time and time again that approach selection matters but is by no means the sole arbiter in complication avoidance.

Table 14.1 Cranial approaches to posterior circulation aneurysms

Territory	Trajectory	Aneurysm location	Cranial exposure
Basilar apex	Anterior superior	Basilar tip	OZ, subtemporal
		PCA	OZ, pterional
		SCA	OZ
		Upper basilar artery	OZ
Basilar trunk	Lateral	AICA	Retrosigmoid, transpetrosal
		Mid-basilar	Combined supratentorial/infratentorial, extended middle fossa, transoral, endonasal transclival
Vertebral trunk	Posterior inferior	Vertebral artery	Midline suboccipital
		PICA	Far lateral
		Vertebrobasilar junction	Extended far lateral, combined

AICA anterior inferior cerebellar artery, *OZ* orbitozygomatic, *PCA* posterior cerebral artery, *PICA* posterior inferior cerebellar artery, *SCA* superior cerebellar artery

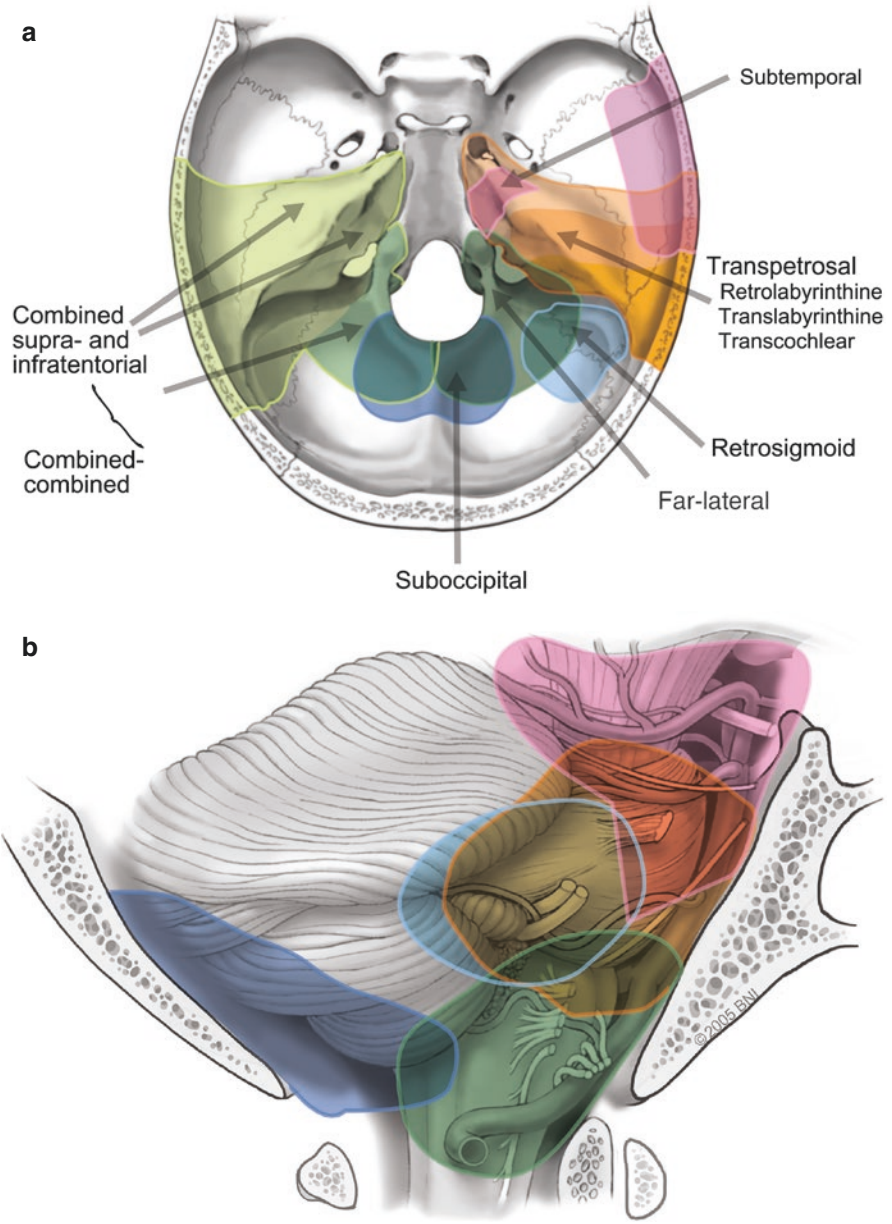

Fig. 14.1 Artist's illustrations show angles of approach to the posterior fossa in the axial (**a**) and sagittal (**b**) planes; approaches can be classified broadly as posterior or lateral and as supratentorial or infratentorial. Used with permission from Barrow Neurological Institute, Phoenix, Arizona

Craniotomy

The procedural steps for microsurgical clipping are consistent with the type of craniotomy needed for approach. A vast array of cranial exposures is possible, and detailed and exhaustive descriptions of each approach are well reported in the literature. Herein, we briefly describe the four most common approaches for surgical treatment of posterior circulation aneurysms (Figs. 14.1, 14.2, 14.3, 14.4, and 14.5).

Modified Orbitozygomatic Craniotomy

The patient should be positioned supine, with a gel roll often placed under the ipsilateral shoulder. We position the patient's head in a radiolucent Mayfield head holder with the head turned 20°–30° to the contralateral shoulder. The head is then tilted posteriorly to the floor and secured in the Mayfield clamp. We then make a curvilinear incision 1 cm anterior to the tragus, proceeding to the midline or as far as the contralateral mid-pupillary line, if necessary. The incision is made from medial to lateral, stopping at the superior temporal line. At this point, we continue the incision in a superficial fashion to preserve the superficial temporal artery for use in any potential revascularization. The scalp flap is reflected anteriorly and held in place with fishhooks. Next, we make an incision in the temporalis fascia just posterior to the orbital rim, being careful not to incise the temporalis muscle. The

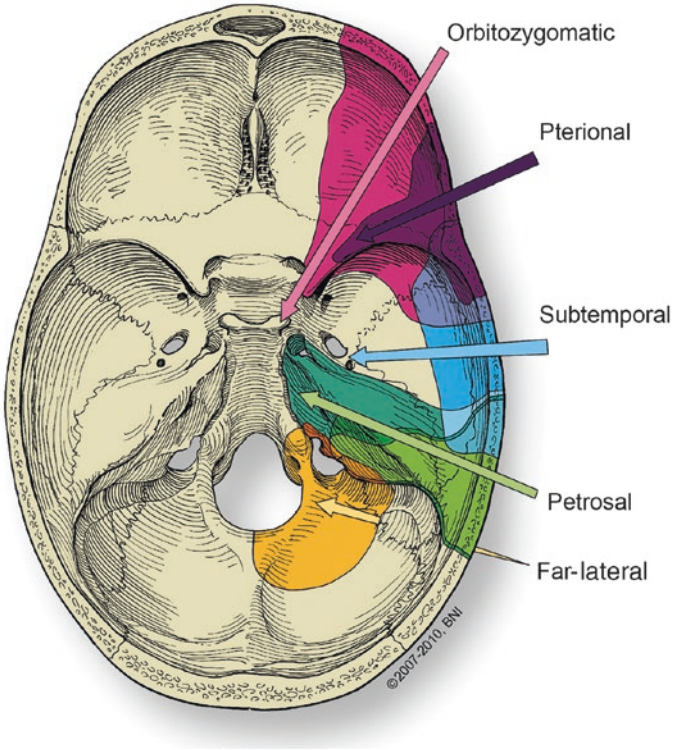

Fig. 14.2 Artist's illustration showing the multiple angles of approach to the posterior fossa in the axial planes. Used with permission from Barrow Neurological Institute, Phoenix, Arizona

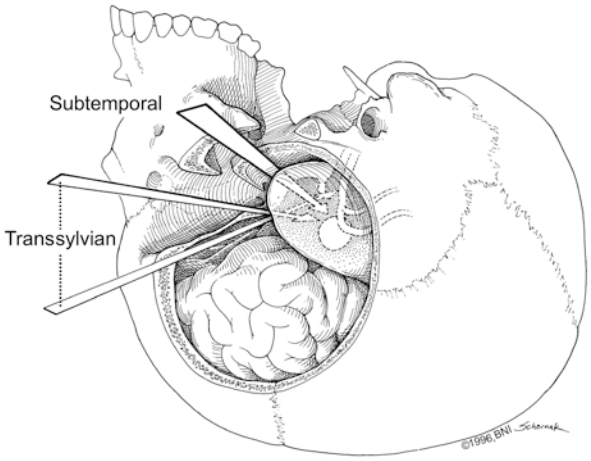

Fig. 14.3 Artist's illustration showing the main difference between the approach angles when an upper basilar artery aneurysm is accessed from an orbitozygomatic approach rather than from a subtemporal one. The wide craniotomy and flush drilling of the floor of the middle fossa combined with an orbitozygomatic osteotomy provide the advantages associated with each approach. Used with permission from Barrow Neurological Institute, Phoenix, Arizona

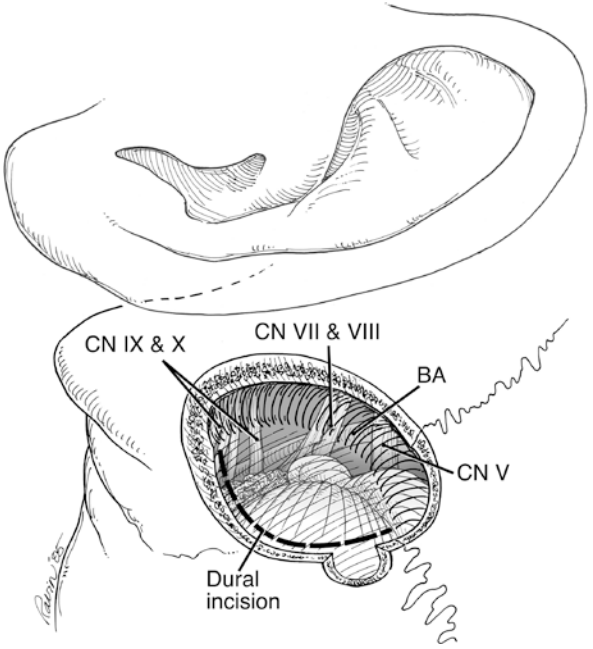

Fig. 14.4 Artist's illustration showing a retrosigmoid craniotomy with complete exposure of the sigmoid sinus. Opening the dura mater as close as possible to the sinus allows it to be pulled and the sinus to be retracted to maximize use of this approach. The basilar artery (*BA*) is located deep at the bottom of the approach. *CN V* trigeminal nerve, *CN VII* facial nerve, *CN VIII* vestibulocochlear nerve, *CN IX* glossopharyngeal nerve, *CN X* vagus nerve. Used with permission from Barrow Neurological Institute, Phoenix, Arizona

temporalis fascia is reflected anteriorly in a subperiosteal fashion along the lateral orbital rim. The temporalis muscle is bluntly dissected inferiorly to superiorly and then reflected inferiorly, leaving a 5- to 7-mm cuff of muscle and temporalis fascia at the superior temporal line. Care is taken to avoid excessive monopolar cautery. A bur hole is placed at the keyhole, at the frontal sphenoidal junction. Ideally, the upper half of the bur hole exposes the frontal dura, while the lower half exposes the periorbita. A second bur hole is placed in the temporal bone as close to the zygoma as possible. The bur holes are connected with a craniotome, and a frontal temporal craniotomy is rendered. To free the periorbital, we then carefully dissect the periosteum with a Penfield 1 dissector or a small Tessier dissector. The orbitotomy is performed with a sagittal saw, a C1 drill bit, or a bone scalpel. Careful attention is paid to protect the frontal lobe and orbit during the cuts. The orbitotomy is removed

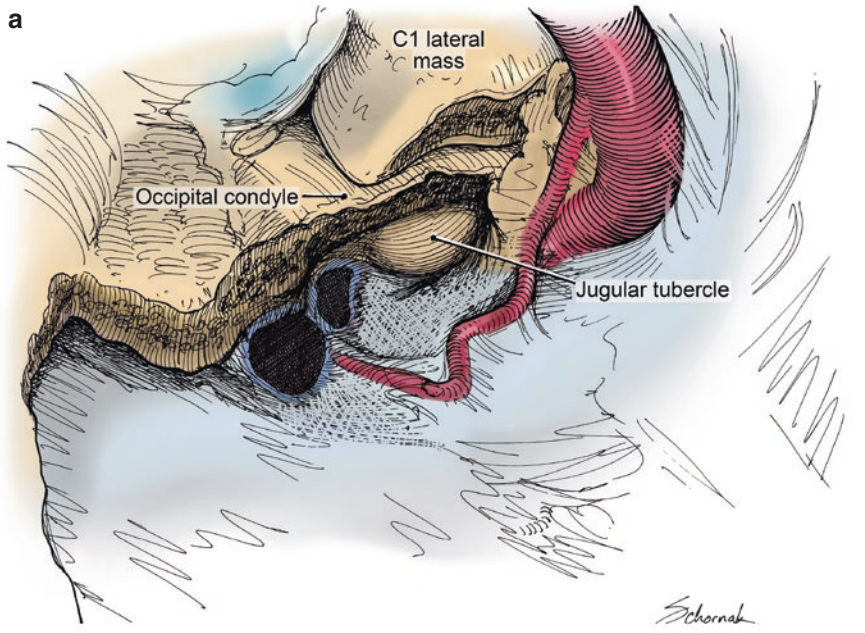

Fig. 14.5 (**a**) Artist's illustration showing the extensive drilling of the occipital condyle that leads to extradural exposure of the jugular tubercle. Sometimes the jugular tubercle shadows the visualization of the vertebrobasilar junction or interferes with the attempt to obtain distal vascular control during dissection of the aneurysm. (**b**) Artist's illustration showing the surgical exposure once the dura mater has been opened. The intradural vertebral artery is visible, and the dura is retracted with stitches in the soft tissues. *CN XI* spinal accessory nerve, *PICA* posterior inferior cerebellar artery. (**c**) Magnification of panel B showing that the posterior inferior cerebellar artery (*PICA*) can be followed from its emergence from the vertebral artery to its lateral and tonsillar segments. Note the exposure obtained from the anterior and lateral aspects of the cervicomedullary junction and the proximity of the spinal accessory nerve (*CN XI*) to the dura mater. The hypoglossal nerve (*CN XII*) is shown in multiple fascicles. *CN IX* glossopharyngeal nerve, *CN X* vagus nerve. Reprinted with permission from Baldwin HZ, Miller CG, van Loveren HR, Keller JT, Daspit CP, Spetzler RF: The far-lateral/combined supra- and infratentorial approach. A human cadaveric prosection model for routes of access to the petroclival region and ventral brain stem. J Neurosurg 81(1):60–68, 1994

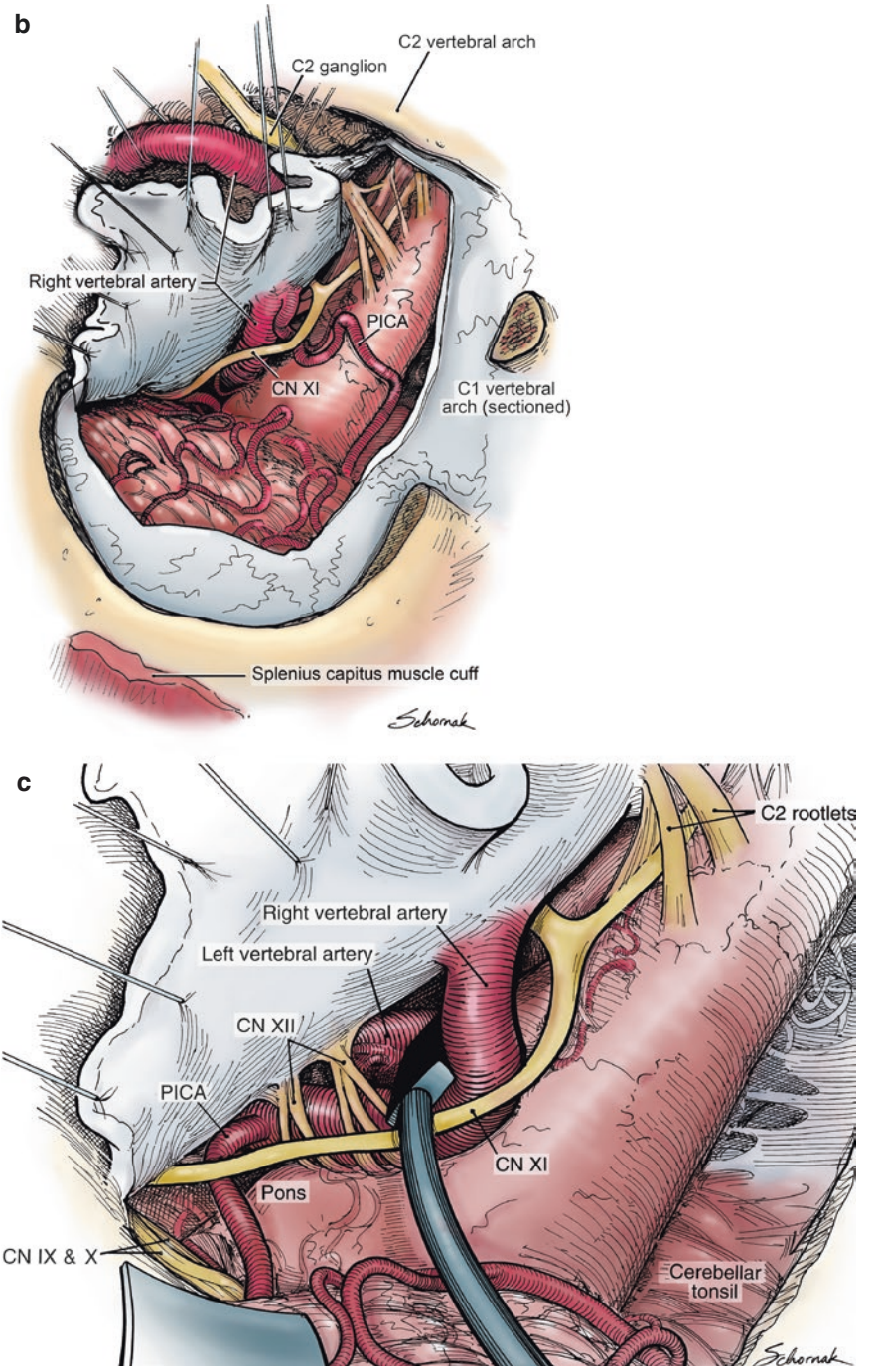

Fig. 14.5 (continued)

in one piece. The orbital osteotomies are medial to the supraorbital foramen/notch and lateral to the frontal-zygomatic suture. The orbital osteotomies are completed with a small mallet and osteotome. The bone is further removed with a rongeur down to the superior orbital fissure to achieve a flat trajectory. If an anterior clinoidectomy is needed, it can be done in an extradural fashion at this point. A C1 drill bit is used to drill pilot holes, and 4.0 nylon suture is used to tack up the dura. The dural opening is created in a C-shaped semicircular fashion from frontal to temporal. The dura is tacked up with sutures so that the trajectory is flat. Epidural hemostasis is crucial and the surgical field must be meticulously maintained before proceeding with the dural opening.

Far-Lateral Craniotomy

The patient is positioned in a three-fourths prone or modified park bench position with the side of the aneurysm upward. The dependent arm is placed in a padded sling and a roll is placed under the dependent axilla. The head is placed in a radiolucent Mayfield head holder. The head is then flexed anteriorly, rotated away from the aneurysm, and then laterally flexed such that the nose is oriented toward the floor and the ipsilateral mastoid process is highest in the field. It is crucial for the ipsilateral shoulder to be rotated anteriorly so that it is out of the surgical field. We place neurophysiological monitoring leads before positioning and obtain baseline somatosensory evoked potentials and motor evoked potentials. We also monitor CN electromyography. Navigation is used to localize the extracranial VA trajectory. We plan a parasagittal incision localizing on the VA. After incision, the muscular layers are traversed, layer by layer, with blunt dissection under each layer; this is followed by mobilization. Liberal use of navigation is used to identify the VA and the posterior arch of C1. Blunt dissection is performed medial to lateral along the posterior arch of C1, being careful not to use excessive monopolar cautery. The VA is identified in the sulcus arteriosus, and the course is followed to the dural entrance. A C1 laminectomy is rendered medial to the sulcus arteriosus. Additional C1 lamina is removed with a rongeur. A lateral suboccipital craniotomy is then rendered. An extradural occipital condylectomy is performed with a 4-mm diamond bur, with copious irrigation and protection of the extradural component of the VA. Bleeding from the condylar emissary vein can be managed with bone wax. The medial one-third of the condyle should be drilled for a flat trajectory when the condyle begins to slope anteriorly. The dura is opened in a curved fashion from the lateral edge of the craniotomy, extending inferiorly below the level of C1 such that no bony prominence is visible through the dura. The dura is then tacked up laterally for a flat trajectory.

Retrosigmoid Craniotomy

The patient is positioned in a radiolucent Mayfield head holder, supine with the head turned away from the aneurysm. We place shoulder bolsters under the ipsilateral shoulder if limitations in the patient's range of motion preclude other positioning. We keep the sagittal midline parallel to the floor and then extend the neck laterally to lower the vertex and flex it to open the occipital cervical angle. We often use navigation to accurately plan a linear incision just medial to the transverse-sigmoid junction. The transverse-sigmoid sinus is skeletonized, and the required

craniotomy is rendered with a craniotome. At times, it may be necessary to extend the craniotomy inferiorly. The dura is opened under the microscope. We position the microscope such that the dural opening is right at the transverse-sigmoid junction. The cerebellopontine cisterns or the foramen magnum are opened quickly to allow CSF release and cerebellar relaxation.

Suboccipital Craniotomy

The patient is positioned prone on gel rolls with the head placed in a radiolucent Mayfield head holder. The head is flexed anteriorly, and the shoulders are taped as deemed appropriate. We plan a suboccipital midline incision, depending on the level of the aneurysm. The paraspinous muscles are dissected laterally, and the craniotomy is rendered as the incision will allow. We take the superior edge of the craniotomy just below the torcula and transverse sinuses. The cisterna magna is opened before starting microsurgical dissection.

Dissection

The dissection steps for surgically treating posterior circulation aneurysms vary slightly, depending on the approach selected. As a general guideline, we like to proceed with dissection as follows: (1) proximal vessels, (2) distal vessels, (3) aneurysm neck, and (4) aneurysm dome. As a result of the varied approaches to posterior circulation aneurysms, it is prudent to base the microsurgical dissection strategies on the particular approach being used.

Modified Orbitozygomatic Approach

Sylvian dissection is performed in the usual fashion. The frontal parietal sinus is carefully observed to assess the need for sectioning. When possible, we endeavor to keep this structure intact. We use dynamic retraction in lieu of rigid retractors. The arachnoid membrane along the skull base is divided and cut. The opticocarotid and oculomotor-carotid triangles are then opened sharply. The membrane of Liliequist is opened, and the dissection is deepened down to the basilar artery. If an intradural anterior or posterior clinoidectomy is needed, it can be done at this time. The dura is cut sharply and then bluntly dissected off the bone with microcurettes. A 2-mm diamond-tipped, covered bur is used for anterior or posterior clinoidectomy, if needed. Copious irrigation is mandatory to prevent heat transfer from the drill. This will likely require intermittent cessation of drilling to maintain adequate visualization. Invasion into a pneumatized anterior clinoid can be packed with muscle autograft, fat, or fibrin glue. After the bone work is completed, the basilar trunk is further evaluated. Dissection of the basilar trunk just inferior to the circumference of the SCA is rendered to identify a perforator-free area for proximal control. Depending on the location of the aneurysm (basilar apex, S1, proximal S2, P1, or P2) in relation to the perforators, the remainder of the dissection is conducted along the ipsilateral SCA and PCA and then to the contralateral branches. Next, the neck of the aneurysm and then the dome are

dissected. Careful attention is paid to perforators, especially contralateral perforators that may be obscured; doing so is especially important when dissecting basilar apex aneurysms. If revascularization is required, appropriate sites for donor vessel anastomosis should be identified and prepared (Table 14.2). In cases where additional exposure is needed, the posterior communicating artery (PCoA) can be sectioned. This can be done at the junction of the PCoA with the PCA in a perforator-free zone; it can be particularly effective in patients with a short PCoA. This type of sectioning should not be done in the case of a fetal PCoA or when the PCoA caliber is significantly larger than the ipsilateral P1 segment.

Far-Lateral/Retrosigmoid Approach

Dissection of PICA aneurysms can proceed by following the VA as it enters the dura up to the aneurysm. The approach to the aneurysm is determined by whether the aneurysm is located superior or inferior to the hypoglossal nerve. We first locate and section the dentate ligament. Patients may require chemical paralysis intraoperatively if movement of CN XI causes the muscle to contract, with the caveat, of course, that further neurophysiological monitoring will be impaired. After proximal control of the VA is achieved, the caudal loop of the PICA is identified and traced to the PICA-VA convergence. Dissection is conducted along the distal VA for distal control toward the vertebrobasilar junction. The aneurysm neck is then dissected, followed by dissection of the dome. We dissect the medullary side first and then the clival side.

Clip Placement

Upper One-Third of the Basilar Artery

Before applying temporary clips, we place the patient in a state of pharmacologic burst suppression. A temporary clip may be applied in a perforator-free zone inferior to the SCAs. The microscope should be mobilized to visualize the aneurysm neck and any associated perforators. The circumference of the neck is carefully inspected for perforators. Temporary clips may be removed upon achieving the appropriate trajectory that allows for visualization of the aneurysm neck and the distal clip tines. After clip placement, we carefully explore to assess for perforators in the clip construct before removing temporary clips. We then obtain microscopic indocyanine green angiography to evaluate parent and daughter vessels, aneurysm obliteration, and, particularly, adequate flow through the perforating vessels.

Basilar Trunk, Lower Basilar, and Vertebral Artery Branches

We prefer to use simple clipping techniques whenever possible. Multilobulated aneurysms are clipped as though each lobe is a separate aneurysm until the aneurysm is obliterated. For PICA and VA aneurysms, we often use a tandem clip construct with a fenestrated clip. We are prepared, if necessary, to trap the aneurysm with an array of revascularization techniques (Table 14.2).

Table 14.2 Options for bypass in the posterior circulation

Vascular territory	EC-IC low flow	EC-IC high flow	IC-IC low flow	IC-IC high flow
Basilar apex	STA → SCA	ICA/ECA → SCA	PCA → SCA	VA → SCA (w/RAG) MCA → SCA (w/RAG)
	STA → PCA	ICA/ECA → PCA		VA → PCA (w/RAG) MCA → PCA (w/RAG)
Basilar trunk	OA → PICA	ICA/ECA → AICA	AICA → PICA	VA → AICA (w/RAG)
Vertebral trunk	OA → PICA		PICA → PICA	VA → VA (w/RAG)
				VA → PICA (w/RAG)

AICA anterior inferior cerebellar artery, *EC* extracranial, *ECA* external carotid artery, *IC* intracranial, *ICA* internal carotid artery, *MCA* middle cerebral artery, *OA* occipital artery, *PCA* posterior cerebral artery, *PICA* posterior inferior cerebellar artery, *RAG* radial artery graft, *SCA* superior cerebellar artery, *STA* superficial temporal artery, *VA* vertebral artery

Complication Avoidance and Management

The most frequent complications encountered during microsurgical management of posterior fossa aneurysms are aneurysm rupture, vessel occlusion, edema, and CN injury. With careful planning, most of these complications can be avoided or managed (see Complication Avoidance Flowchart).

Intraoperative Aneurysm Rupture

Management of intraoperative rupture of posterior fossa aneurysms is similar in approach to managing supratentorial aneurysm ruptures (see Checklist). A calm and measured approach is crucial. It is useful to understand that intraoperative rupture occurs in 5–10% of cases and that the rate does not diminish with operative experience, only the time of the rupture progresses with experience. When an aneurysm ruptures, it is crucial to obtain proximal and distal control before dissection of the aneurysm neck or dome. We use the Rhoton 6 dissector to ensure we are able to place a clip. With suction in hand, we identify a location of proximal control, place the distal clip, and then reestablish visualization. We then inspect the neck of the aneurysm and the dome. If it is safe to do so, we then place clips to ligate the aneurysm. If appropriate visualization is not possible, we place a suboptimal clip to control the hemorrhage and allow for further dome dissection, if necessary. We then reestablish visualization and reexamine the neck of the aneurysm for perforators. After perforators have been identified, we then optimally place the clip. Depending on the site of rupture, it may be necessary to augment the clip with a small portion of cotton pledget. When bleeding is brisk, it may be necessary to place an additional or larger suction device for assistance. We do keep blood pressure normal at these times to facilitate appropriate irrigation of the cortex via collateral circulation.

Parent or Daughter Vessel Occlusion

If we observe parent or daughter vessel occlusion after clip application, we will perform intraoperative indocyanine green angiography. If occlusion is confirmed, we replace temporary clips, as needed. We then remove the permanent clip and, if it is deemed necessary, conduct further dissection to improve visualization. If occlusion occurs as the result of an excessive inflow jet, and if it is not alleviated well with temporary clipping, we institute the periodic use of adenosine for additional control. We often apply vasodilators to vessels that have been significantly manipulated. We then liberalize blood pressure after permanent clipping is complete.

Intraoperative Edema

Cerebellar swelling can be a significant issue during surgical treatment of posterior fossa aneurysms. To reduce swelling, we use adjunctive measures such as hypertonic saline, mannitol, and hyperventilation. Mechanistically, we elevate the head of the bed to improve venous return. The most direct approach is CSF diversion. In the setting of subarachnoid hemorrhage, we routinely place an external ventricular drain to release CSF. For treating unruptured aneurysms, we rely heavily on CSF release from the cerebellopontine angle cisterns and the foramen magnum.

Cranial Nerve Injury

Injury to CNs during aneurysm surgery is most pronounced in the lower CNs (CN IX–XII). Most injuries are related to stretch injury as a result of manipulation and dissection. We use neurophysiological monitoring of the CNs to assess function throughout the operation. Working in optimal angles, especially with respect to PICA aneurysms, is also helpful in avoiding nerve injury. The hypoglossal nerve is a useful anatomical marker, and the optimal dissection can be performed either above or below the nerve.

Conclusion

Microsurgical approaches to posterior circulation pathology continue to be a challenging and important area of neurosurgery and aneurysm management. The complexity of aneurysms in the posterior circulation certainly warrants a multidisciplinary approach for sustained and successful treatment. Effectively avoiding and managing potential pitfalls continues to be of paramount importance in a comprehensive approach to these complex lesions.

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Arteriovenous Malformations of the Anterior Fossa

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Checklist: Hemorrhagic Complication Management in AVM Microsurgery

Equipment needed	Procedural steps
Surgical • Emergency suction • Bipolar electrocautery • Vessel microclips, aneurysm clips • Irrigation • Thrombin-soaked cotton pads • Hemostatic product (Gelfoam, Floseal, etc.) • Microscope • Retractors • Rhoton dissectors • EVD, if needed • Drill, to expand craniotomy if needed for decompression Anesthesia • Blood pressure and ICP monitoring • End-tidal CO_2 monitoring and manipulation via respiratory rate • Blood transfusion • Crash cart Pharmacologic • Mannitol/Hypertonic Saline (23.4%) • Anticonvulsant • Antihypertensive/vasopressors • Paralytic Neurointerventionalist • Femoral artery access • Guide or diagnostic catheter • Guide wire • Microcatheter, microwire • Balloon microcatheter • NBCA glue	Identification • Visible hemorrhage • Hemodynamic changes, ICP changes • Identify source: arterial, nidus, venous occlusion Initiate and Engage • Alert entire team, communicate clearly • Backup OR tech, nursing, anesthesia availability • Maintain systolic blood pressure <100 mmHg with antihypertensives • End-tidal CO_2 <30 mmHg with hyperventilation • Open EVD if available • Osmotic agents if ICP >20 mmHg • Maintain cerebral perfusion in sustained bleeding with transfusion, vasopressors • Inform neurointerventionalist • Prepare crash cart Repair • Maximize visibility with suction, irrigation, retraction, head position • Cauterization of visible bleeder with irrigating bipolar • Application of microclips for small perforating arteries or aneurysm clips for large feeding arteries • Obtain proximal exposure of thin, friable perforators that tend to retract with cauterization • Nidus or small vessel bleeding: thrombin-soaked cotton products or hemostatic agents • Avoid packing of arterial bleeding which can result in hematoma formation out of visible field • Venous occlusion: rapid resection of remainder of nidus and coagulation of remaining arterial feeders If Needed: • EVD placement • Expand craniotomy for further boney decompression • Endovascular intervention (balloon tamponade, parent vessel sacrifice, glue embolization)

Complication Avoidance Flowchart

Complication	Cause	Management	Prevention
Intraoperative hemorrhage	1. Nidus penetration 2. Venous injury 3. Residual AVM 4. Retraction injury	1. Hemostasis with bipolar cautery, clip placement, gentle tamponade, or Gelfoam 2. Reevaluation of the true plane between the malformation and brain and widening the diameter of the dissection 3. Use cell saver and blood transfusion when severe blood loss is anticipated 4. Identify the residual AVM and further microsurgical resection	1. Judicious use of preoperative embolization 2. DSA and CTA localization of residual nidus, deep perforators, and venous drainage 3. Meticulous dissection technique 4. Control of deep feeding arteries near the end of dissection 5. Preserve venous drainage until major sources of arterial flow can be isolated and occluded 6. Gradual increase of blood pressure 10–15 mmHg above preoperative BP and inspection for 15 min before dural closure to identify residual AVM 7. Confirm complete resection on intraoperative angiogram or Doppler ultrasound
Normal perfusion pressure breakthrough/ occlusive hyperemia	1. Failed autoregulation of AVM feeders due to prolonged ischemia-related steal phenomenon adjacent to AVM nidus	1. Increase cerebral perfusion pressure (CPP) by EEG-burst suppressive anesthesia with phenobarbital 2. Systemic arterial BP reduction (systolic 80–90 mmHg) with sodium nitroprusside or nicardipine 3. Hemorrhagic brain tissue should be resected along with the AVM with absolute hemostasis 4. Pharmacological reduction of ICP 24-h post-resection	1. Staged preoperative embolization 2. Complete resection should be confirmed with intraoperative angiography

(continued)

Complication	Cause	Management	Prevention
Postoperative hemorrhage	1. Residual AVM 2. Normal perfusion pressure breakthrough	Early detection and surgical decompression ± microsurgical resection	1. Gradual increase of blood pressure 10–15 mmHg above preoperative BP & inspection for 15 min before dural closure to identify residual AVM 2. Confirm complete resection on intraoperative angiogram or Doppler ultrasound 3. Pharmacological reduction of ICP 24-h post-resection

Introduction

Cerebral arteriovenous malformations (AVMs) comprise 1.5–4% of all intracranial lesions, approximately one-tenth as often as intracranial aneurysms [1]. AVMs are the second most identifiable cause of subarachnoid hemorrhage after cerebral aneurysms, accounting for 10% of all cases of subarachnoid hemorrhage [1]. The majority (80%) of the AVMs are supratentorial distribution with 65% in the lobar and 15% in the deep location [2]. They usually occur as single lesions, but as many as 9% are multiple [2]. According to the American Stroke Association, 1 in 200–500 people have an AVM, while 50% of patients suffer intracranial hemorrhage and 25% of AVM patients experience seizures at some point in their lives. Also, 5–15% of AVM patients report severe headaches because of the increased intracranial pressure and a similar percentage of patients exhibit neurological deficits.

Modern management of cerebral AVMs is centered around a multidisciplinary approach involving endovascular embolization, microsurgical resection, and stereotactic radiosurgery, which can be used as an isolated modality or more commonly as part of a multimodality treatment plan. Typically, embolization is used as an adjunct to radiosurgery or microsurgery to eliminate the risk factors for hemorrhage or to eliminate specific compartments of the AVM, facilitating subsequent treatment. The role of embolization in Spetzler-Martin grade I–II AVMs is debatable [3]. Typically, these lesions are resected with microsurgery.

Procedural Overview

The concept of complication avoidance should be applied at pre-, intra-, and post-treatment stages in the cerebral AVM management. Detailed understanding of the angiographic and functional anatomy, familiarity with the natural history, multidisciplinary evaluation, multimodality approach, realizing patient current functional status and outcome expectations, clear risk stratification, and effective communication are vital successful management of the cerebral arteriovenous malformations.

Pretreatment Evaluation

Digital subtraction angiography (DSA) is the investigation of choice in the evaluation of cerebral arteriovenous malformations (AVMs) due to its unparalleled spatial and temporal resolution in the evaluation of angioarchitectural features, nature of the nidus (compact or diffuse), high-flow fistulous communication within the nidus, and predictive risk factors for hemorrhage such as intranidal, flow-related aneurysms, venous stenosis, single draining vein, deep venous drainage, and deep cerebral location. Multiplanar magnetic resonance imaging (MRI) is helpful in precise localization, evaluating adjacent eloquent regions and surrounding parenchymal changes such as edema, gliosis, and encephalomalacia. Thorough understanding of these findings is vital in choosing the appropriate single/multimodality treatment. Functional MRI is increasingly used in patients with AVMs centered in the eloquent locations for better delineation of the speech, motor, and cognition areas, which helps in better surgical planning and risk stratification. Be aware of the differential diagnosis such as "proliferative angiopathy" mimicking large AVM with diffuse nidus.

A multidisciplinary team of cerebrovascular microsurgeons, endovascular neurosurgeons, interventional neuroradiologists, and radiosurgeons should evaluate each brain AVM patient on a case-by-case basis and determine the optimal treatment modality or combination of modalities for the goal of complete AVM obliteration while minimizing risk. When endovascular embolization is agreed upon as a treatment modality, the role of the embolization should be clearly outlined, i.e., curative, adjuvant, or palliative.

Patient Selection Based on Natural History of Cerebral AVMs

The first step in the complication avoidance is "justification of treatment risk." If the cumulative lifetime estimate of an AVM rupture based on the natural history far exceeds the immediate risks of treatment for a patient, the treatment is justified. To make this decision, a thorough knowledge of AVM natural history is mandatory. The attempts to clearly delineate the natural history of the cerebral AVMs began decades ago and continue to pose a considerable challenge owing to a remarkable degree of heterogeneity not only in study design but also in the results.

Natural History of Ruptured AVMs

Hemorrhage is the most common presentation in up to 53% of the cerebral AVMs. Estimated risk of rebleeding after hemorrhage from cerebral AVMs is approximately 6% during the first year and 2% per year up to 20 years after the initial hemorrhage [4, 5]. The average interval between the bleeding events was reported to be 7.7 years [6]. Although the ubiquitous maxim of "previously ruptured vascular malformations have a higher risk of rerupture" among cerebrovascular neurosurgery was not favored by the original AVM studies by the Ondra et al. [6] and the Toronto group [7], these were overturned by the recent studies in the same cohort and longer follow-up [8, 9]. More recent meta-analysis by Gross et al. based on the nine natural history studies from 1986 to 2009 confirmed prior AVM hemorrhage is a significant risk factor for subsequent bleeding with a hemorrhagic risk of 4.5% (3.7–5.5%), and risk of recurrent hemorrhage in the first year after initial hemorrhage ranges from 6 to 15% [10].

Natural History of Unruptured AVMs

Average risk of hemorrhage in unruptured AVMs was estimated at 2–4% [5, 6] per year based on individual series, while a 2.2% (1.7–2.7%) risk was quoted by the meta-analysis [10]. The annual incidence of de novo epilepsy in patients with cerebral AVMs is 1–4%. Population-based study with longest follow-up of 23.7 years reported AVM-related risk of mortality and morbidity per annum at 1 and 1.7%, respectively [6]. Deferring the treatment until AVM becomes symptomatic carries a significant risk because of the mortality and morbidity rates from initial hemorrhage of approximately 17 and 40%, respectively, to a significant long-term neurological morbidity and mortality of as high as 35 and 29%, respectively [11–13].

The ARUBA trial [14] is the first study comparing medical management to surgical care on patients with unruptured cerebral AVMs and a Rankin score <2. The trial states that 30.7% of patients in the interventional arm reached the primary endpoint of death or stroke, a threefold higher rate than the medical management arm, and concluded that the medical management alone is superior over the intervention in the management of the unruptured cerebral AVMs. While the trial provides important data, it has received plenty of criticism concerning its study design and the credibility of its findings. Our institutional experience involving retrospective review of all the unruptured intracranial AVMs (n = 64) with completed treatment over a 12-year period (2003–2015) with same endpoints as ARUBA showed that risk of symptomatic stroke or death in our cohort (7.8%) was significantly lower (p = 0.004) than the "interventional arm" in the ARUBA trial. Moreover, the one-time upfront risk of 7.8% with intervention in our group was not only comparable to the 10% incidence of death or stroke reported over a short time interval of <3 years among the medically managed ARUBA population but also provides a permanent curative treatment with a 97% of angiocure.

Risk of Hemorrhage

Based on the evidence available from the natural history studies, the angioarchitectural features and their association with hemorrhagic presentation were categorized in Table 15.1.

To minimize the variability in the prediction of long-term risk of hemorrhage based on available statistics among the neurosurgical community, Kondziolka et al. [15] suggested the below formula to estimate the lifetime risk of hemorrhage in patient not treated for an AVM based on multiplicative law of probability.

Table 15.1 Angioarchitectural characteristics of cerebral AVMs related to risk of hemorrhage

Consistent risk factors	Inconsistent risk factors	Potential risk factors	Potential protective factors
• Exclusive deep venous drainage (2.4%) • Single draining vein • Venous stenosis • High mean arterial pressure in the feeding artery	• Prior hemorrhage (3.2%) • Intranidal aneurysm (1.8%) • Small nidus; <3 cm (1%) • Deep location (2.4%) • Venous stasis	• Systemic hypertension • Vertebrobasilar supply • Perforator supply • Increasing age • Smoking • Pregnancy	• Arterial stenosis • Neoangiogenesis • Venous recruitment

$$\text{Risk of hemorrhage} = 1 - (\text{Annual risk of no hemorrhage})^{\text{Expected years of remaining life}}$$

This formula assumes some degree of population homogeneity and uniformity of the AVM natural history and provides a quick means of estimating lifetime risk of hemorrhage in a clinical setting.

The formula was further simplified estimating the cumulative risk of hemorrhage based on patient's age at the time of discovery of a brain AVM, which can be predicted by using a formula [15, 16]:

$$\text{Lifetime risk (\%)} = 105 - \text{Patient age in years}$$

Younger patients have longer life expectancy and therefore higher cumulative lifetime risk of rupture. As AVM in older patients are significantly associated with several high-risk angioarchitectural features of rupture, it is important to stratify older patients based on the high-risk factors in the treatment decision analysis.

Timing of AVM Treatment

Ruptured AVMs

The timing of the AVM treatment after intracranial hemorrhage requires careful consideration. A hematoma secondary to AVM rupture of significant size or precarious location may result in mortality or permanent morbidity due to primary or secondary (edema) mass effect. Although small hematomas and occasionally large (usually lobar) hematomas can be managed nonsurgically, those that produce significant obtundation or herniation syndromes should be evacuated on emergency basis. Simultaneous removal of AVM with hematoma should be considered only when the lesion is small and located immediately adjacent to the clot cavity. Complete resection of the AVM should be confirmed with intra- or postoperative angiogram (Fig. 15.1). With an aggressive approach to AVM resection after acute hemorrhage, reversible neurological deficit can be permanent, as the surrounding parenchyma is more vulnerable to injury in this setting. Jafar et al. [17] reported only 50% of the patients without significant neurological deficit following acute AVM surgery. Heros and Samson [18] reported that control of intracranial pressure (ICP) with careful hematoma evacuation and delayed AVM treatment continue to be the preferred management for ruptured cerebral AVMs. In case of small hemorrhages or neurological deficit, a delay of several weeks may be indicated prior to AVM treatment. The interval delay in the ruptured AVM treatment allows resolution of cerebral edema, peri-hematoma inflammation, plateau of recovery from neurological deficit, liquefaction, and contraction of the hematoma with reduced mass effect on the AVM nidus leading to both improved radiological evaluation and ease of surgery (Figs. 15.2 and 15.3). Once the intracranial dynamics are normalized, proper preoperative radiographic evaluation, surgical planning, and treatment can proceed in an organized fashion. Delaying treatment for 4 weeks after initial hemorrhage subjects the patient to a low (<1%) risk of rehemorrhage [19] and may result in spontaneous thrombosis of the AVM in rare instances [20].

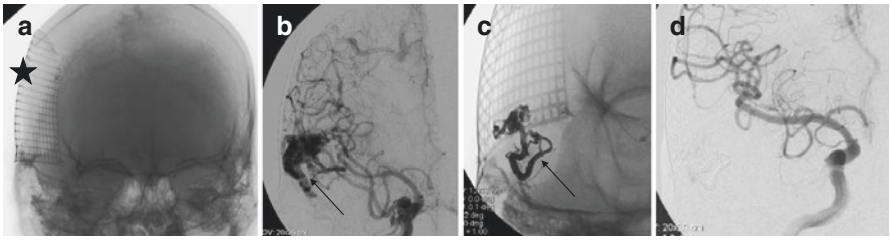

Fig. 15.1 Residual AVM following decompressive craniotomy and hematoma evacuation. Forty-eight-year-old patients with decompressive craniotomy and hematoma evacuation for spontaneous right-sided hemorrhage (**a**) in China, presented 13 years later with headaches. Based on CTA findings, catheter angiogram was performed which demonstrated right temporal AVM (**b**) just beneath the surgical site. This was successfully treated with onyx embolization (**c**) and no residual filling on the post-embolization angiogram (**d**). This highlights the importance of catheter angiogram in patients with spontaneous intracranial hemorrhage for initial or follow-up evaluation of underlying vascular abnormalities

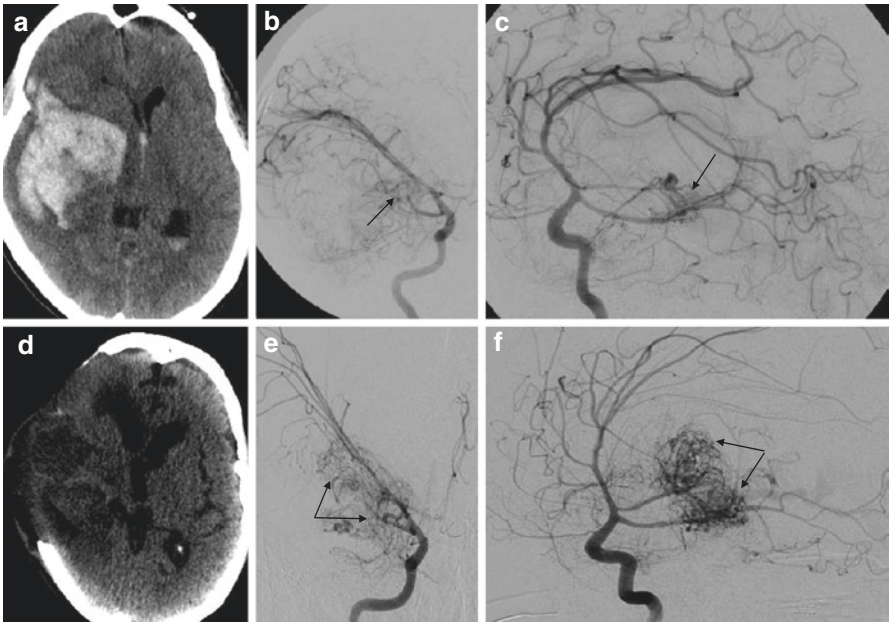

Fig. 15.2 Improved visualization of AVM following hematoma resolution. Ruptured basal ganglia AVM (**a**) with initial catheter angiogram (**b** and **c**) demonstrated significant mass effect with vascular distortion and faint visualization of small AVM nidus. Follow-up CT at 6 weeks (**d**) after decompressive craniotomy showed hematoma resolution and encephalomalacia. DSA at 6 weeks (**e** and **f**) shows marked improvement in the visualization of nidus due to reduced mass effect, which argues against embolization of ruptured AVMs in acute phase

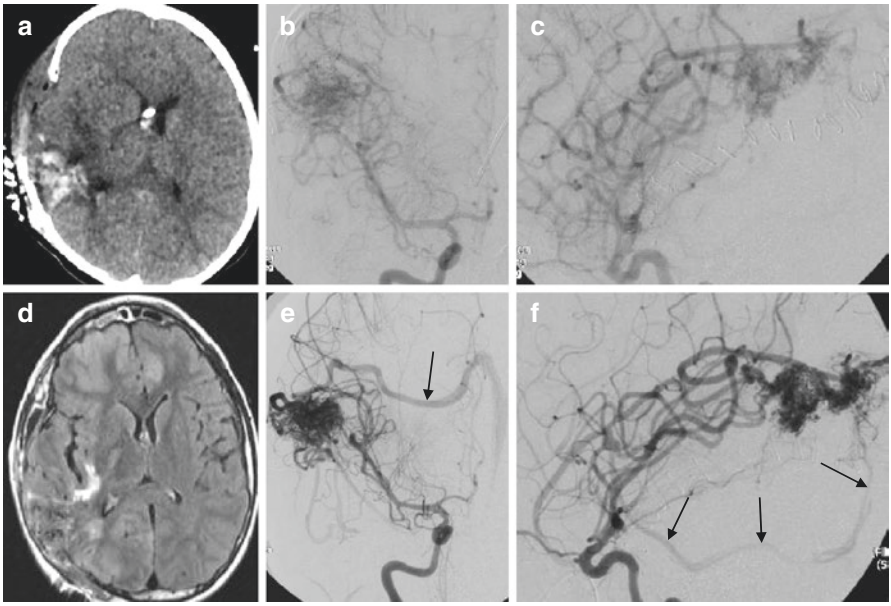

Fig. 15.3 Poor visualization of angioarchitectural features in acute phase angiogram. Ruptured right parietal AVM following decompressive craniotomy and hematoma evacuation (**a**). DSA in acute phase (**b** and **c**) shows poor opacification of nidus and nonvisualization of the draining vein. Follow-up MRI at 4 weeks (**d**) showed partial resolution of cerebral edema and mass effect. DSA at this point (**e** and **f**) shows better visualization of the AVM nidus and angioarchitectural features. Better understanding of the draining vein location minimizes the embolization risk, which again favors conservative approach in the acute phase

Unruptured AVMs

Treatment of unruptured AVMs needs careful evaluation of the complications and outcome related to the treatment against the natural history of these lesions. The angioarchitecture of the AVM should be thoroughly evaluated prior to embolization (Figs. 15.4 and 15.5) is mandatory to recognize high-risk factors flow-related or intranidal aneurysms (Fig. 15.6), venous ectasia, venous stenosis, venous hypertension and high-flow shunt with steal phenomenon.

Steal phenomenon is a known cause for progressive neurological deficit in the absence of intracranial hemorrhage or increased size of AVM. These patients benefit from more aggressive approach, especially with partial embolization. Failure to respond quickly may result in an irreversible deficit that could have been prevented. These deficits have been attributed to a steal phenomenon, as AVM theoretically recruits arterial flow away from the normal brain. Partial embolization is the preferred initial step in the management of this situation resulting in temporary amelioration of the steal symptoms and potential reduction of the post-resection perfusion problems.

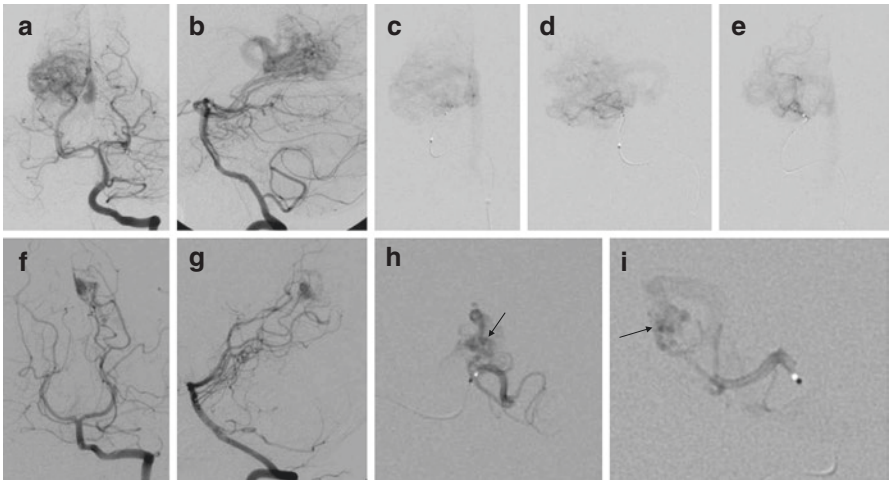

Fig. 15.4 Favorable and unfavorable angioarchitectural features of AVMs. Two different patients with unruptured occipital AVMs showing favorable and unfavorable anatomy for AVM treatment. Patient-1 (**a–e**) shows right occipital AVM with diffuse nidus (**a** and **b**). Super selective microcatheter exploration again shows diffuse nidus with intervening normal parenchymal vasculature (**c–e**), which is a high-risk factor for post-procedure neurologic deficit. In contrary, patient-2 (**f–i**) with left occipital AVM shows compact nidus, with two definite arterial feeders and draining vein, an excellent scenario for treatment. Patient-1 is currently managed conservatively while patient had stereotactic radiosurgery

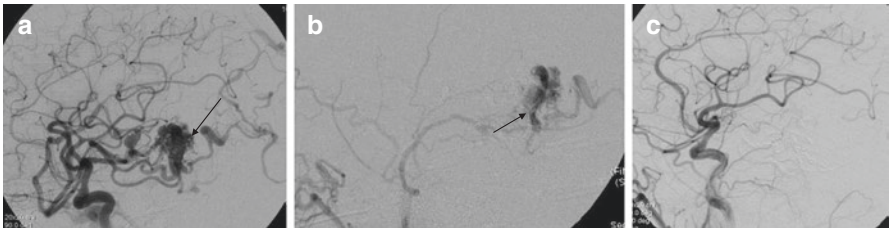

Fig. 15.5 Dural and pial contribution for temporal AVM. The angioarchitecture features of the AVM should be thoroughly evaluated prior to proceeding with embolization. In contrary to the conventional notion of pial feeders for brain AVMs, this patient with temporal AVM has both dural and pial feeders (**a**). The dural contribution from posterior division of middle meningeal artery (MMA) is better appreciated on the dedicated external carotid (ECA) angiogram (**b**). Good preoperative onyx embolization required both pial and dural approach. Good preoperative onyx embolization required both pial and dural approach (**c**)

Venous hypertension, mass effect, and ischemia caused by the high arterial flow with limited venous drainage, venous arterialization, stenosis, or occlusion are the other potential causes for progressive neurological symptoms and irreversible cerebral damage in patients with unruptured cerebral AVMs. Partial staged embolization is a preferred choice to ameliorate the risk factors associated with progressive neurological deficit or hemorrhage and convert a high-risk AVM to a more suitable microsurgical target for complete resection.

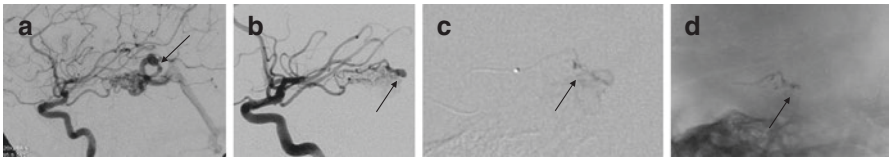

Fig. 15.6 Intranidal aneurysm—High-risk factor for hemorrhage in AVM. Ruptured thalamic AVM with intranidal aneurysm (*black arrow*) and deep venous drainage in to vein of Galen (**a** and **b**). The intranidal aneurysm being a known high-risk factor for hemorrhage was obliterated with super selective microcatheterization (**c**) and onyx embolization (**d**). Further management of this deep AVM in the eloquent region was performed with stereotactic radiosurgery

Pretreatment Functional Evaluation

As a part of complication avoidance, accurate risk analysis for treatment of individual AVMs is crucial which includes functional evaluation of the surrounding brain parenchyma. In patients with congenital AVMs, the locations of the cerebral functions may be altered through developmental plasticity. Pretreatment functional evaluation can be used to identify functionally active cortex even in unexpected locations, which helps to choose an appropriate therapeutic modality for AVM treatment. Delineation of the active tissue from the malformation allows safer placement of boundaries for radiosurgery or selection of resection planes. Information about physiologic significance can be gathered from various diagnostic tests developed to evaluate local cerebral parenchymal function and blood flow such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI), magnetoencephalography, relative perfusion measurement, and invasive provocation.

Recognize the Differential Diagnosis: AVM Mimics

Cerebral Proliferative Angiopathy

Cerebral proliferative angiopathy (CPA) , previously known as “diffuse nidus type AVM” or “holohemispheric giant AVM,” is present in an estimated 2–4% of all brain AVMs [21]. Proliferative angiopathy may be confused with true cerebral AVMs and thought to represent a diffuse nidus. Seizures and disabling headaches are the most common clinical symptoms at presentation in cerebral proliferative angiopathy, occurring significantly more often than in the AVM population. Progressive neurologic deficits and transient ischemic attacks are also possible, whereas hemorrhage is exceptional [22]. The risk of hemorrhage is extremely rare at presentation; however, if a hemorrhagic episode has occurred, the risk of recurrence seems to be high compared to classic brain AVMs [22].

The most striking feature is the presence of normal-appearing neural tissue intermingled between these vascular channels, whereas perivascular gliosis is only mild, with additional capillarogenesis within the subcortical region. This implies that the

brain tissue within the "nidus" of the CPA is functional, like brain tissue found in between the abnormal vascular channels present in capillary telangiectasias. The lack of clear early venous drainage on dynamic images is the key to differentiating this disease from classic brain AVM. A multifactorial analysis by a French group evaluating angioarchitectural features in relation to hemorrhagic risk showed that the association of arterial stenoses with angiogenesis was the only factor associated with a reduced risk of hemorrhage. This typical association of proximal arterial stenoses with angioneogenesis in cerebral proliferative angiopathy explains the extremely low risk of hemorrhagic presentation in the natural history of CPA compared to classic brain AVMs. Because the pathomechanism of proliferative angiopathy is mainly due to cortical ischemia (as proved with perfusion-weighted studies), there have been reports of successful treatment with pial synangiosis (EDAS) or burr-hole therapy to enhance supply to healthy brain tissue from the external carotid artery.

Complication Avoidance and Management

Complications during the microsurgical management of cerebral AVMs are undeniable. Despite wide variability in the morbidity and mortality rates of the published microsurgical series, the microsurgical series report superior occlusion rates than the embolization. The major microsurgical series of AVM treatment were summarized in Table 15.2.

Table 15.2 Summary of complications and outcomes of the published surgical series

Series, year	Patients	Age (mean)	Morbidity and mortality (%)	Occlusion (%)	S-M grade
Abad JM, 1983	70		11.0	81.4	
Jomin M, 1985	128		21.0	92.9	
Spetzler RF, 1986	100		4.0	100.0	I–V
Andrews BT, 1987	28	34	10.7	67.9	
Heros RC, 1990	153		8.4	100.0	I–V
Deruty R, 1993	64		18.8	93.7	I–V
Sisti MB, 1993	67		1.5	94.0	I–III
Hamilton MG, 1994	120	36	8.3	100.0	I–V
O'Laorie SA, 1995	56	36	5.3	92.9	I–V
Tew JM, 1995	39	30	15.4	97.4	III–V
Malik GM, 1996	156	33	14.7	95.8	
Schaller C, 1998	150	35	13.3		I–V
Pikus HJ, 1998	72		8.3	98.6	I–III
Hassler W, 1998	191		11.0		I–V
Pik JHT, 2000	110	38	2.7	98.8	I–III
Hartmann A, 2000	124	33	6.0		I, II
Solomon RA, 2000	86		1.2	90.7	
Stapf C, 2002	240	34	1.7	93.8	
Morgan MK, 2004	220		1.4	98.6	I, II
Lawton MT, 2005	224	38	7.1	98.0	I–V
Spears J, 2006	175	40	13.5		I–IV
Bradac O, 2013	74	40	1.4	97.3	I–IV
Theofanis T, 2014	264	38	7.8	100.0	I–V

Intraoperative Hemorrhage: Venous Injury/Retraction Injury

While most AVM microsurgical resections are challenging with some form of bleeding due to nature of lesions, some of the problems are avoided with careful planning and technique. Endovascular embolization should be judiciously used in selected AVMs to reduce the risk of hemorrhagic complications and to assist in surgical removal. Injury to major venous drainage pathway of the AVM may require an attempt to repair the vein, particularly in those lesions lacking major alternate venous drainage. Hemostasis techniques like bipolar cautery, clip placement, gentle tamponade, or Gelfoam itself or in combination may be required to preserve venous drainage until major sources of arterial flow can be isolated and occluded. In cases where substantial blood loss is anticipated, use of cell saver may be helpful.

Arterialized veins are differentiated from the feeding arteries by high-magnification inspection for the thickness of the vessel wall and degree of pulsations, often higher in the arteries. The vessels can be temporarily occluded with bipolar or temporary clips to assess for distal collapse or color change (vein) versus continued pulsations (artery).

Significant retraction of the brain parenchyma in the parasagittal approaches must be avoided to minimize the injury to the draining veins. Venous infarction, hemiplegia, and parietal lobe syndromes will likely result from sacrifice of posterior draining veins. Excessive retraction of the temporal lobe near the vein of Labbe could result in venous-related parenchymal damage and serious neurological sequelae. To minimize excessive venous retraction, brain resection is recommended to access AVMs in two specific locations: (i) corpus callosum for deep parasagittal malformations and (ii) inferior temporal gyrus for deep temporal AVMs [23]. Routine-induced hypotension to control bleeding during AVM resection should be viewed with caution as the normal parenchymal vessels are already dilated to counteract the arteriovenous (AV) shunting from AVM, and hypotension would result in ischemia [24]. In extreme circumstances of high-flow, poorly controlled bleeding, hypotension may be used as a strategy.

Bleeding During AVM Resection

Arterial bleeding from the AVM is usually controllable with judicious bipolar use and gentle tamponade, either manually or with self-retaining retractor. As dissection of the AVM proceeds into deeper portions of the lesion, persistent bleeding may indicate that the nidus has been violated. Reevaluation of the true plane between the malformation and brain and widening the diameter of the dissection will permit control of this type of bleeding. Control of deep perforating vessels near the end of dissection is the most challenging task in AVM surgery [24]. Maximally dilated with very thin walls, these arteries are fragile and resistant to bipolar cautery. Tamponade is generally ineffective and may obscure deep bleeding into the parenchyma or ventricular system. Patience and clear identification of the margins of the vessels are key to hemostasis in this area, as premature vessel rupture leads to retraction into the white matter with continued bleeding. Following these vessels for some distance may reveal a portion of the vessel that is more amenable for cautery.

An array of maneuvers may be necessary for achieving control of these vessels such as the use of routine microaneurysm clips, specially designed microclips, and clip occlusion followed by cautery, bipolar cautery of an exposed length of the vessel, and tangential cautery of the exposed length of the vessel. Morgan et al. reported 24 complications in their series of 112 patients with AVM resection. Hemorrhagic complications accounted for 25% of total complications (5/24) including fatal intraoperative hemorrhage in three patients, fatal normal perfusion pressure breakthrough (NPPB) in one patient, and a nonfatal intraoperative hemorrhage in one patient. Overall 80% of the hemorrhagic complications (4/5) were fatal [25].

Yasargil et al. reported requirement of blood transfusion in 30% (124/414) of their AVM resection. Of these 124 patients, 51% required up to 500 mL transfusion, 31% required 500–1500 mL transfusion, and 19% required more than 1500 mL transfusion. Six patients were reported to have out of control bleeding requiring >5 L of transfusion; two patients died and four patients had good outcome [3].

Residual AVM

Occasionally, a daughter nidus may be disconnected from the major nidus during AVM resection. The retained malformation may be the cause of persistent intraoperative bleeding. Although intraoperative angiography is the best way to detect residual nidus, this study is not always available or feasible. Doppler sonography is helpful for identifying retained AVM [26]. Usually daughter nidus is hidden in a sulcus closely related to the main nidus and is connected by one or two vessels. Through inspection of the resection cavity after the surgeon feels the AVM has been completely resected occasionally reveals a swollen, tense or deformed margin that usually represents residual malformation. Routine elevation of the patient's blood pressure 10–15 mm Hg above preoperative levels and inspection for 15 min before dural closure may also identify retained AVM and prevent complications or need for additional AVM therapy. At our center, we routinely perform intraoperative angiography to confirm complete resection, and re-exploration will be pursued if angiogram reveals evidence of persistent arterial to venous shunting.

Brain Swelling

Brain swelling during neurosurgical procedures by no means is unique to the surgery performed for AVMs, and the specific pathophysiology of the lesions presents additional challenges. General causes such as hypercapnia from obstruction of the endotracheal tube or ventilator disconnection should be ruled out first. Venous drainage compromise must be ruled out by checking patients positioning. The head should be elevated above the heart and care should be taken not to flex, extend, or rotate the head excessively to avoid the risk of jugular venous compression resulting in excessive bleeding, brain swelling, and damage to the normal brain parenchyma.

Once these are ruled out, specific complications for AVM surgery must be explored including occult bleeding, obstructive hydrocephalous from intraventricular bleeding, and cerebral edema from dysautoregulation.

Occult Bleeding

In patients with ruptured AVM with intraparenchymal hematoma, a portion of the AVM may become isolated from the surgical exposure and bleed when its venous drainage is disconnected. This may result in significant brain swelling with no immediately apparent cause. Often, this rapidly expanding hematoma will rupture into previous plane of resection. This requires expanding the pane of resection to include the hematoma cavity, and circumferential dissection must continue after the hematoma has been evacuated. The potential consequences from such hemorrhage include parenchymal damage from compression and vascular injury during evacuation and control of bleeding. There is also potential for rupture into the ventricular system which can result in obstructive hydrocephalous.

Obstructive Hydrocephalous

The ventricular system is entered during many AVM resections; hence precautions to prevent complications of expected bleeding into the ventricular system are important. The precautions include placement of cotton sponges to block exposed entry points during resection and removal of all identifiable intraventricular clot with extensive irrigation of the exposed ventricular system before closure. Occasionally bleeding into the ventricle may be occult and present only as global or focal brain swelling, accompanied by bradycardia, sudden hypertension, or change in the vital signs. Premature entry into the ventricle secondary to deep dissection with inadequate circumferential exposure of the AVM is the likely source of such bleeding. When suspected the ventricle must be immediately exposed through the ependymal wall and the clot evacuated. The site of bleeding must be methodically identified and secured.

Normal Perfusion Pressure Breakthrough/Occlusive Hyperemia

Normal perfusion pressure breakthrough (NPPB) is a one of the known causes for intraoperative cerebral edema. This is originally described by Spetzler and Wilson [27], subsequently reported, and challenged by other experienced neurosurgeons [28, 29]. This is characterized by acute massive brain swelling with a firm, distended herniating margin of the brain around the malformation with multiple bleeding points that are resistant to coagulation. The theory states that the brain around the AVM was subjected to prolonged ischemic steal, resulting in chronic dilatation and loss of autoregulation of the brains' arteries to divert the blood from AVM. These vessels are putatively unable of autoregulation when normal perfusion is established

by resecting the AVM nidus. The adjacent brain capillary breakthrough results in edema and hemorrhage.

When NPPB occurs intraoperatively, it usually appears toward the end of the resection when the high-flow shunt has been removed. Treatment consists of immediate brain protection, elevated cerebral perfusion pressure (CPP) by EEG-burst suppressive anesthesia with phenobarbital, and systemic arterial blood pressure reduction (systolic 80–90 mm Hg) with sodium nitroprusside or nicardipine [28]. This approach usually arrests spread of cerebral edema, allowing for craniotomy closure. Hemorrhagic brain tissue should be resected along with the AVM with absolute hemostasis, and complete resection should be confirmed with intraoperative angiography. The occurrence of NPPB was reported between 1 and 2% with 0–100% mortality in various AVM series [30, 31].

The ICP should be lowered by pharmacological means over the next 24 h under barbiturate coma. Non-contrast CT head should be performed for any unexplained alteration. If the surveillance CT demonstrates no progression, the patient should be weaned from antihypertensive agent over the next 12–24 h provided the ICP remains controlled and systemic blood pressure does not rise inappropriately. Subsequently, the patient can be weaned from the barbiturate over the next 24 h.

Prevention of NPPB) is the best form of treatment. High fistula flow with a paucity of flow entering the immediately adjacent brain is the angiographic hallmark predicting this condition. Staging AVM treatment with repeat operative approaches and/or endovascular embolization technique can be effective prophylaxis. This approach theoretically allows restoration of autoregulation at a gradual pace, as high-flow shunt is gradually and methodically reduced.

Postoperative Hemorrhage/Cerebral Edema

"Residual AVM" is the most common cause of the postoperative hemorrhage, and a daughter nidus is one of the most frequent causes of the retained lesion usually left on the wall or in the adjacent sulcus to the main area of nidus resection. The residual compartments are usually resected from the bulk of the nidus during the attempt to follow the resection plane along the embolic material of the lesion. Residual AVMs were reported up to 17% on postoperative angiography after AVM resection and are responsible for immediate and delayed rebleed accounting for 40–50% of spontaneous intracranial hemorrhage following AVM resection requiring re-exploration [31].

Normal perfusion pressure breakthrough (NPPB) is a rare but potential cause of postsurgical bleeding. Mayo Clinic group reported "occlusive hyperemia" in 6.4% of their 295 AVM resections, a phenomenon of otherwise unexplained brain hemorrhage or edema occasionally seen after the resection of high-flow AVMs [32]. Post-resection angiography in these patients consistently demonstrated slow flow in formal AVM feeders, their parenchymal branches, and impaired venous drainage in the region of resection. Authors postulated that stagnant flow in the arterial feeders produces hypoperfusion significant enough to cause ischemia with resultant hemorrhage and/or edema further complicated by venous outflow obstruction. This results in a vicious cycle of hyperemia, swelling, and worsened arterial stagnation.

Early diagnosis followed by aggressive medical and surgical management of these hemorrhagic complications of AVM surgery is essential to preserve the lowest rates of morbidity and mortality that are possible with the treatment of cerebral AVMS.

Vascular Thrombosis

Retrograde thrombosis back to the point of a proximal major branch has been reported as cause for delayed postoperative neurological deficit. Old age, larger AVM size, marked dilatation, and elongation of the feeders were identified as potential risk factors for this complication.

Epilepsy

Literature review shows that 27–38% of the patients with AVMs gave epilepsy before treatment and 4–30% develop new seizures after treatment [24, 33]. Most seizure disorders associated with AVMs are effectively controlled with antiepileptic medications, and patient with malformations in epileptogenic regions should routinely be treated prophylactically with these agents. Seizures were eliminated in roughly 18% of patients in whom arterial feeders were eliminated by ligation or embolization [34]. Complete resection AVM increases seizure-free outcome to approximately 56% of patients. Directed seizure surgery with AVM resection can result in up to 75% chance of seizure-free outcome [35, 36].

Residual AVM/Regrowth

Regrowth of the AVMs after angiographic evidence of complete resection is a reported entity. Yasargil et al. [3] reported five patients of complete AVM resection and documented regrowth of the AVM requiring additional surgery 1–7 years after the initial surgery. Four of these patients had rehemorrhage before regrowth was discovered. Patterson et al. [37] and Forster et al. [38] reported one case each of delayed rebleeding after complete AVM resection in their series. Lavine et al. reported recurrent hemorrhage following complete resection of the malformation and good recovery in two patients with cocaine and methamphetamines abuse, which were presumed to have precipitated the presentation.

Conclusion

Patient selection, evaluation of comorbidities, risk stratification, treatment justification against natural history, and decision analysis for treatment are vital in avoiding the complications. Patients must be evaluated on individual basis and discussed in multidisciplinary team meeting (MDT) involving professions from neurosurgery, endovascular neurosurgery, radiosurgery, and critical care. Complications are to be expected even in the hands of most skilled cerebrovascular neurosurgeons who deal with large number of AVMs.

Familiarity with these complications, high index of suspicion, early detection, and appropriate management are essential to achieve good outcomes that are possible with microsurgical treatment of these lesions.

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Arteriovenous Malformations of the Posterior Fossa

16

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Checklist: Surgical Treatment of Posterior Fossa AVMs

Equipment needed	Procedural steps
Anesthesia • Arterial line • Mannitol • ICG if used • Blood transfusion if needed Radiology • C-Arm • Intraoperative angiography Neurosurgery • Microscope • Neuro-navigation setup • Microdissection tray • Irrigating bipolar cautery • Aneurysm clips, temporary and permanent	Preparation • Recognize angle of approach from preoperative MRI and DSA Localizing and positioning • Head position according to lesion location: prone if vermian or hemispheric location, park bench if approaching via cerebellopontine angle • Intraoperative navigation as needed AVM resection • Wide bone removal to foramen magnum to open cisterna magna and allow cerebellar relaxation • Begin with arachnoid dissection to identify any feeding artery and draining veins on the cortical surface • Circumferential dissection of AVM by separation of plane between AVM nidus and surrounding normal tissue • Cauterize feeding arteries while preserving major draining vein as last pedicle • Occlude draining vein after occlusion of all feeding arteries • Intraoperative angiography to confirm obliteration of AVM • Hemostasis

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Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Post-operative hemorrhage	Residual AVM	Reoperation and/or salvage radiosurgery	Intraoperative DSA to confirm obliteration
	Inadequate Intraoperative Hemostasis	Consider reoperation	Meticulous Intraoperative Hemostasis
	Normal Perfusion Pressure Breakthrough	Consider reoperation	Assessment of hemodynamics before treatment Consider pre-operative staged embolization if high risk
Infarction	Intraoperative occlusion of en passage arteries	None	Ensure knowledge of angioarchitecture to identify non-feeding arteries

Introduction

Posterior fossa arteriovenous malformations (pAVMs) or infratentorial AVMs are a relatively rare subset comprising approximately 7–15% of all AVMs [1–3]. These AVMs draw particular attention as they are presumed to be more aggressive with respect to the natural history of hemorrhage and may sustain increased risk of treatment complications due to their proximity to critical functional structures such as the brainstem and cranial nerves [1].

The pAVMs consist mainly of cerebellar AVMs and brainstem AVMs, although there have been reports describing cerebellopontine angle (CPA) AVMs as another distinct location [4]. Despite being classified together in the posterior fossa location, the pretreatment assessment, treatment strategy, approach, postoperative care, and associated complications for AVMs vary between the cerebellar location and brainstem location and therefore need to be separately discussed. In general, AVMs in the superficial cerebellar location have a favorable risk profile and may be safely treated with surgical resection; conversely, deep cerebellar AVMs or brainstem AVMs have a significantly higher risk of postoperative complications and are preferred to be managed with radiosurgery or embolization [2].

Within the context of the two major locations (brainstem and cerebellum), pAVMs can be further categorized in detail based on the specific locations of the nidus. In a review article by Almeida et al., the authors classified pAVMs into eight distinct groups, which elucidate the anatomical relationships between each subgroup and affected cranial nerves. The classification scheme is demonstrated in Table 16.1 [2].

Table 16.1 Classification of posterior fossa arteriovenous malformations

Name	Location	Arterial supply	Cranial nerves
Midbrain	Midbrain	SCA	IV and V
Pontine	Pons	SCA/AICA/PICA	VI, VII, VIII
Medullary	Medulla	PICA	IX, X, XI, XII
Suboccipital	Suboccipital surface of the cerebellum	PICA	IX, X, XI, XII
Petrosal	Petrosal surface of the cerebellum	AICA	VII and VIII
Tentorial	Tentorial surface of the cerebellum	SCA	IV and V
Vermian	Vermis	SCA/PICA	–
Tonsillar	Cerebellar tonsils	PICA	–

Abbreviations: *SCA* superior cerebellar artery, *AICA* anterior inferior cerebellar artery, *PICA* posterior inferior cerebellar artery
Source: Almeida JP et al., Management of posterior fossa arteriovenous malformations, 2015, Surgical Neurology International

Clinical Presentation

Hemorrhage is the most common presentation in patients with pAVMs. Compared to an overall hemorrhage risk of 20–50% in all AVMs [5], numerous reports have documented an increased risk in pAVMs, with 63.9–92% of all pAVMs patients presenting with hemorrhage [1, 6, 7]. Some studies attributed the higher risk of hemorrhagic presentation to sampling bias, as pAVM patients generally present with hemorrhage because fewer other acute symptoms such as seizures occur [2, 6, 7]. Regardless of etiology, the high proportion of hemorrhagic presentation in pAVM is particularly concerning as the limited capacity for hematoma expansion due to close proximity to critical anatomical structures and associated obstructive hydrocephalus may result in rapid neurological compromise that requires immediate neurosurgical interventions. Herniation and brainstem compression due to mass effect from acute posterior fossa ICH are more frequent than supratentorial ICH and can be catastrophic (Fig. 16.1). Additionally, obstructive hydrocephalus frequently occurs in conjunction with infratentorial hematoma as a result of direct compression on the fourth ventricle or casting within the aqueduct or fourth ventricle due to concurrent intraventricular hemorrhage (IVH). Infarction may also develop from compression of posterior circulation vessels due to significantly increased intracranial pressure in the infratentorial space.

In contrast to supratentorial AVMs where seizure is generally the most frequent manifestation followed by hemorrhage, patients with pAVMs rarely present with seizure; instead, approximately 28% of all unruptured pAVMs patients present with progressive neurological deficits [7]. Cranial nerve palsies can be present due to mass effect of the nidus or from ischemic attacks due to blood steal phenomenon of high-flow AVMs. The affected cranial nerve is closely related to the location of the AVM, as shown in Table 16.1. Other non-specific symptoms such as headache, imbalance, or weakness may be present, but these are relatively rare compared to the aforementioned clinical presentations.

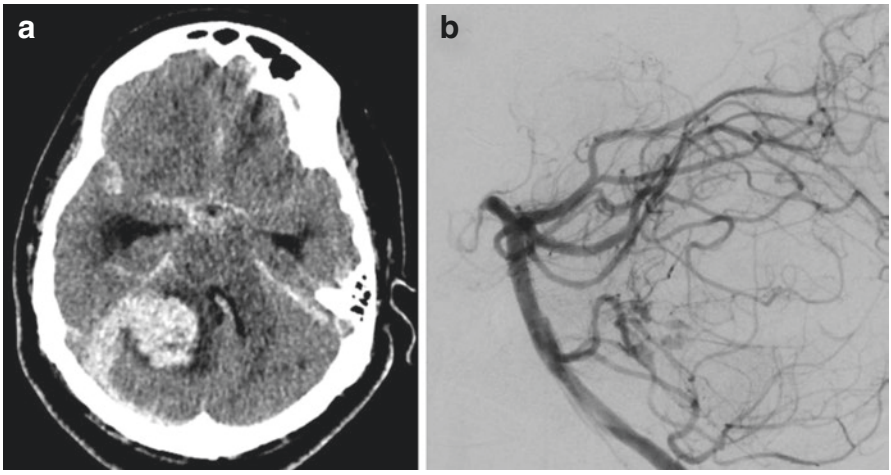

Fig. 16.1 (**a**) Axial CT of a 56-year-old woman presenting with large hemispheric ICH combined with IVH and SAH and surrounding edema causing leftward displacement of fourth ventricle and supratentorial hydrocephalus with dilated temporal horns. (**b**) Subsequent DSA demonstrated a small (1.5 cm) AVM nidus fed by AICA

Natural History of Hemorrhage and Risk Factors

Several studies examining the natural history of hemorrhage have revealed an annual hemorrhage rate of 4.7–11.6% [2, 6–8], which is significantly higher than the reported risk of hemorrhage of AVMs in the general population (2–4% per year), suggesting that pAVMs are indeed more prone to rupture than their supratentorial counterparts. Although the mechanism is unclear, some have proposed that increased frequency of deep venous drainage and venous outflow tortuosity in posterior fossa AVMs may contribute to their increased risk of rupture. Similar to AVMs in other locations, the risk of hemorrhage may be significantly altered by clinical and angioarchitectural characteristics. These factors include previous history of rupture, presence of intranidal/prenidal aneurysms, venous stenosis or ectasia, and deep location [6]. Understanding the impact of these factors is critical in the assessment of overall hemorrhagic risk of pAVMs and may play a critical role in the decision-making process for treatment selection.

Overview of Management Strategy and Outcomes

The major goal of treatment is to eliminate the risk of hemorrhage while preserving the functional status of the patient. Provided with the heterogeneity of AVMs, selection of treatment strategy should involve multidisciplinary teams, and an individualized approach is encouraged for each patient. For patients with ruptured presentation or those who are deemed to have high risk of hemorrhage, definitive treatment is

warranted. Such treatment may include a multimodality approach with single or combined therapy of surgery or radiosurgery with or without endovascular embolization. Unfavorable treatment outcomes are associated with AVMs involving critical brain structures, high Spetzler-Martin grades, or poor functional status at presentation. In these patients, if hemorrhagic risk is presumed to be low, conservative management may be considered in order to avoid harm to the patient. On the contrary, for high risk patients, if the treatment benefit outweighs the risk, definitive treatment with radiosurgery as the preferred modality may be warranted. Several studies have noted satisfactory treatment outcomes in pAVM patients with good functional outcomes at presentation, as well as in elderly patients with favorable surgical risk profile [1, 9]. It should be emphasized that in patients without absolute contraindications, the threshold to initiate treatment should be reasonably lowered in pAVMs since the consequence of hemorrhage is more likely to be catastrophic in these patients.

The presence of prenidal aneurysms complicates the treatment course, and the relative rupture risk of the aneurysm weighed against the AVM should be cautiously evaluated to determine the sequence of staged treatment. It is evident in the literature that prenidal aneurysms both portend a risk of hemorrhage on their own and increase the risk of AVM hemorrhage. Therefore, for patients presenting with subarachnoid hemorrhage (SAH) with angiographic evidence of both AVM and prenidal aneurysm, bleeding from the aneurysm should be suspected; additionally, even with isolated intracerebral hemorrhage (ICH) presentation, hemorrhage from the prenidal aneurysm should be considered before concluding that the primary source of hemorrhage is the AVM.

Accurate identification of hemorrhage source is important for optimal treatment selection. If the AVM has a higher risk of hemorrhage compared to the prenidal aneurysm, an AVM-first strategy should be adopted, and flow-related aneurysms have been frequently reported to occlude spontaneously after AVM obliteration. On the contrary, if the aneurysm heralds a higher risk, it is more likely to be treated first, and an endovascular approach is frequently utilized as it provides preoperative embolization and aneurysm obliteration in a single treatment session. Notably, some literature specifically noted a higher incidence of aneurysmal hemorrhage in posterior inferior cerebellar artery (PICA) supplied AVMs [10]. In these cases, it is necessary to secure the aneurysm before considering treatment of the AVM.

Treatment outcome is affected by a variety of factors, such as the treatment modality, location of the pAVM, and Spetzler-Martin grade of the lesion. For cerebellar AVMs, surgical treatment may achieve a 92–100% obliteration rate with 75–80% favorable outcomes. For brainstem AVMs, surgical series report a 70–80% obliteration rate with 22–25% morbidity, while radiosurgery series achieve 3-year obliteration rate of 43.8–73% with 73.3–95% of patients with improved or unchanged clinical status [11, 12]. For Spetzler-Ponce Class B or C (Spetzler-Martin grade 3–5) pAVMs, the obliteration rate is as low as 52%. Overall reported posttreatment mortality is approximately 7.7%, whereas morbidity is 16.3% [7, 13].

Procedural Overview

Microsurgical Resection for pAVMs

Preoperative Evaluation

Microsurgical resection is the most commonly adopted treatment modality in definitive treatment of pAVMs. Preoperative evaluation includes magnetic resonance imaging (MRI) and digital subtraction angiography (DSA). Among these, DSA is considered the gold standard for diagnosis and assessment of the angioarchitecture of the AVM. Superselective DSA is usually performed during evaluation to provide arterial view of the nidus, locate and characterize feeding arteries and draining veins, and identify intranidal aneurysms. This information is essential for developing a strategic operative approach to the AVM and to determine whether preoperative embolization is warranted. External carotid injection should also be considered as on rare occasions the pAVMs may be concomitantly supplied by external carotid vessels. Both computed tomography angiography (CTA) and MRA are regarded as secondary options in addition to the DSA study and are likely to have been obtained prior to the DSA. Three-dimensional cone-beam CT (3D-CBCT) provides enhanced-contrasted thin-slice images with simultaneous imaging of both arterial and venous phases, which renders it an excellent adjunct to DSA and is helpful for radiosurgery planning. Brain MRI is essential for localization, defining nidus relationships to ventricles and pial surfaces, and is highly sensitive and specific for detection of concomitant silent brain hemorrhage, which factors into decision-making regarding risk of treatment. The advantage of supplementing DSA with MRI is the capability to assess anatomical relationships between the nidus and critical functional structures.

Intraoperative Adjuncts

Adjuncts include intraoperative monitoring of brainstem somatosensory-evoked potentials (SSEP) and brainstem auditory-evoked potentials (BAEP). Electromyography (EMG) and direct stimulation may be used to determine safe territories of intraoperative manipulation. The use of neuronavigation may be useful during the early phases of the approach, such as for the craniotomy to determine venous sinus location, and is less helpful in pAVMs given sufficient anatomical landmarks and brain shift from CSF drainage, but may be used to determine the borders of deep niduses in the cerebellum. Intraoperative or postoperative DSA is strongly recommended to confirm obliteration of the AVM after microsurgical resection.

Microsurgical Techniques

A wide craniotomy in treatment of pAVMs facilitates sufficient exposure of the nidus and increases working distances for navigating through surgical corridors. The choice of approach is dependent on the location of the nidus. For lesions involving midline and paramedian structures including vermian or tonsillar cerebellum, a posterior midline approach from the occiput to C1 is commonly adopted. For posterolateral lesions such as cerebellar hemispheric or lateral pontine AVMs, access

can be achieved through an extended retrosigmoid approach. Retrosigmoid craniectomy with or without far-lateral extension can be used for CPA AVMs or medullary AVMs, and a supracerebellar approach can be used for superficial cerebellar AVMs abutting the tentorium and for posterior midbrain AVMs. All posterior approaches should be particularly aware of the location of transverse and sigmoid sinuses to avoid incidental injury. In all cases, opening of the foramen magnum to allow easy access to opening the arachnoid of the cisterna magna for cerebellar relaxation is recommended.

The resection of the nidus follows general principles for AVM resection in other locations. Adequate exposure, meticulous microdissection, rigorous hemostasis, circumferential approach, and protection of major venous drainage before nidus extirpation are critical for complete obliteration while minimizing intraoperative complications. Fixed retraction should be avoided if possible to prevent extensive stretching of cranial nerves. Preemptive packing of the large subdural spaces with Gelfoam sponges to contain the dissemination of blood into the posterior fossa and cervical subdural spaces as the resection proceeds decreases the risk of subsequent hydrocephalus. Intraoperative identification of feeding arteries and draining veins through careful dissection is the first step and key to avoiding premature interruption of venous drainage. Superficial, arterialized, dilated veins overlying the plane of approach may be commonly seen and should be cautiously dissociated from the arachnoid and gently mobilized away from the focus of resection. Small, temporary clips may be applied on suspicious arteries that are potentially feeding the nidus, which are useful for recognizing and preventing injury to *en passage* vessels. Once identified, feeding arteries should be skeletonized with sharp dissection and occluded definitively with coagulation. Of note, the response to coagulation on perforators arising from perforating feeding arteries may be suboptimal given the lack of smooth muscle cell layer, and application of permanent aneurysm clip is warranted for definitive occlusion; nevertheless, hemostasis during pAVM resection should be compulsively pursued given limited tolerance for hematoma extension in the infratentorial space. A combination of bipolar coagulation, pressure, and aneurysm clips may be used to achieve satisfactory hemostasis. Separation of the nidus from the parenchyma should follow a circumferential pattern with spiral progression, creating perinidal corridors to allow mobilization of the nidus while occluding the feeders. The margin of nidus can be established through distinction between normal parenchyma and gliotic tissues or hemosiderin stains from previous hemorrhages. The nidus can be safely removed after confirmation of occlusion of all feeding arteries followed by the last step of disconnecting all major draining veins.

Radiosurgery for pAVM

Radiosurgery is the preferred definitive treatment for nonsurgical pAVMs. Overall obliteration for pAVMs in radiosurgery series reaches 75–80% at the 5-year mark. However, given the persistent risk of hemorrhage of 1–3.6% during the latency interval between treatment and obliteration [8, 14], it is generally considered as the

secondary option for patients with acceptable surgical risks. Before radiation delivery, high-resolution axial MRI images of the AVM and Dyna-CT are first registered to the treatment planning system to allow contouring of the target. Treatment margins should be cautiously determined and conformal for avoidance of irradiating critical structures. The development of an optimal treatment plan involves multidisciplinary efforts from both neurosurgery and radiation oncology. Treatment of pAVMs is usually achieved by stereotactic radiation using Gamma Knife or CyberKnife in a single session with a median dose at approximately 18–21 Gy. The utility for pre-radiosurgery embolization for AVMs is controversial since multiple studies have suggested decreased obliteration rate after radiosurgery for embolized patients.

Endovascular Embolization for pAVM

Endovascular embolization is conventionally regarded as a non-definitive adjunct therapy to surgery and radiosurgery. It is particularly useful in obliterating high-flow or deep-seated parts of the AVM to avoid devastating intraoperative hemorrhage from these compartments. Additionally, for AVMs with associated prenidal aneurysms, both aneurysm and AVM can be managed in a single embolization session before surgical management. Embolization agent includes *N*-butyl cyanoacrylate (NBCA) and ethylene-vinyl alcohol copolymer (Onyx). Under rare circumstances, coils may be used to slow intra-arterial flow. Curative embolization of pAVMs remains controversial to date due to low obliteration rate and high risk of recurrent hemorrhage and AVM recanalization. Therefore, application of embolization should be concordant with primary treatment goals of preventing future hemorrhage and preserving functional status, so that aggressive pursuit of eliminating all pedicles in patients with favorable surgical or radiosurgical risk is currently not recommended.

Complication Avoidance

Hemorrhage is the most feared postoperative complication. Progressive hemorrhage within the infratentorial space quickly exceeds the capacity for hematoma expansion and may result in poor clinical course from rapid brainstem compression and catastrophic herniation. Hydrocephalus may also occur in conjunction with IVH as a consequence of obstructive intraventricular casting at the fourth ventricle or aqueduct. In surgical patients, the source of hemorrhage is most likely from residual lesion but can also originate from inadequate intraoperative hemostasis or bleeding from “normal perfusion pressure breakthrough” (NPPB) after large AVM resection. Prevention of postoperative hemorrhage therefore requires addressing all potential bleeding mechanisms. Residual AVM may result from incomplete resection of the AVM or simply from intraoperative judgment that part of the AVM cannot be safely resected. In both cases, thorough preoperative DSA evaluation of the AVM

angioarchitecture and proximity to surrounding critical structures prepares the operator and in turn significantly lowers the likelihood of incomplete resection. Intraoperative DSA provides a mechanism for confirming complete resection and remains the optimal modality for intraoperative detection of residual AVMs. However, if intraoperative angiography is not possible due to patient position, an immediate postoperative angiogram remains essential, with return to the OR for resection of residual if feasible. For hemorrhage of other causes, rigorous hemostasis should be pursued, and staged resection or presurgical embolization should be considered for large AVMs to prevent breakthrough bleeding. A brief post-resection moderate hypertensive challenge may be considered to test hemostasis. Strict blood pressure control is recommended postoperatively to prevent bleeding from the resection bed.

Postoperative ischemic events may also occur from intraoperative injury of *en passage* arteries; it is therefore critical to identify these arteries intraoperatively and avoid incidental occlusion. Prevention of vasospasm-induced ischemia can be achieved through aggressive medical intervention under vasospasm protocol in ruptured AVM patients. Prolonged fixed retraction should be avoided to lower the chances of cranial nerve injury.

Complication Management

Postoperative hemorrhage causing neurological deterioration or at risk for doing so requires rapid hematoma evacuation, and decompressive suboccipital craniectomy may also be warranted. If the source of bleeding is suspected as residual AVM, revised resection can be attempted during hematoma evacuation. Cautious scrutiny of the resection bed for bleeding source and aggressive hemostasis are crucial for avoidance of recurrent bleeding. If combined with IVH and suspected concurrent hydrocephalus, the threshold for insertion of an intraventricular catheter should be low. For residual AVM that is determined to be high risk for further resection, postsurgical radiosurgery should be considered for complete obliteration.

Conclusion

Posterior fossa AVMs represent a small cohort of the AVM population and are challenging to manage due to their proximity to critical brain structures, deep locations, and potentially aggressive clinical courses. Additionally, due to limited space to accommodate hemorrhage in the infratentorial compartment, hemorrhagic complications for pAVMs are generally less well tolerated compared to their supratentorial counterparts. Successful management of pAVMs therefore requires appreciation of the natural history of the disease, thorough evaluation of the angioarchitecture of the pAVM and relationship to critical posterior fossa anatomical structures, and optimal balancing of the risks and benefits associated with each treatment modality. A multidisciplinary team including neurosurgeons, neuroendovascular surgeons, and radiation oncologists should participate in

shared treatment decision-making. Longitudinal patient management may require physiatrists and neurologists. Surgical resection is considered the optimal treatment modality for patients with acceptable surgical risk profile, and postoperative hemorrhage may be avoided with meticulous surgical techniques, compulsive hemostasis, and intraoperative DSA for confirmation of AVM obliteration. Presurgical embolization is useful in selected cases for reducing the number of arterial feeding vessels and lesion size to optimize surgical outcome. Stereotactic radiosurgery may also achieve satisfactory occlusion rates in patients deemed to be non-operative. Finally, a subset of pAVM patients may ultimately fare better without intervention. The potential complications associated with each possible treatment should be anticipated before initiation of the management plan so that every effort is made to avoid such complications.

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Cavernous Malformations

17

Cameron M. McDougall, Babu G. Welch, and H. Hunt Batjer

Checklist for Cavernous Malformation Surgery

Equipment needed	Procedural steps
Surgical • Surgical microscope, ideally with neuronavigational capability • Neuroendoscope: straight and angled views • Lighted bipolar forceps ± lighted retractor • Long instruments (suction, micro-bipolar, microscissor) • Ultrasound (spine lesions) • Bipolar and unipolar stimulators **Anesthesia** • Mannitol • Arterial line • Coordination with neurophysiology • ETT • $EtCO_2$ monitor • Perioperative antibiotics • Warming prophylaxis • Appropriate padding for pressure points • Central line/precordial Doppler (sitting position) **Neurophysiology** • SSEP • MEP • BAER • CN monitors • ECoG if necessary **Neurosurgeon** • Frameless stereotactic navigation	**Craniotomy** • Adequate exposure based on selected approach • Meticulous hemostasis • Appropriate durotomy—recheck with stereotaxy prior to opening • CSF drainage and cerebral relaxation **Subarachnoid Dissection** • Careful arachnoid dissection focused on maximizing exposure of pial/ependymal surface target entry zone • Mobilize neurovascular structures as necessary; attention to venous angioma • Stimulation to identify eloquent structures • Careful search for any pial discoloration/abnormality • Confirm entry point with neuronavigation **Lesion Resection** • Sharp pial/pseudocapsule entry • Widen exposure of CM with gentle stretching of fibers • *do not* resect gliotic pseudocapsule in brainstem and deep-seated lesions • Judicious use of bipolar for deep/brainstem lesions • Lesion removal with sharp dissection/suction • Gentle tamponade and irrigation to control bleeding • Endoscopic cavity inspection

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Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
New neurologic deficit	Selection of surgical corridor	–	– Study images closely – fMRI/tractography – Use surgical adjuncts (navigation, neuromonitoring, stimulation mapping)
	Surgical technique	–	– Stretch fibers – Minimize bipolar use – Gentle tamponade for bleeding
Incomplete resection	Surgical technique	Consider reoperation if symptomatic	– Endoscope – Lighted instruments
Persistent epilepsy	Inappropriate lesion selection	Consider reoperation	– Consider preoperative invasive monitoring in select cases
	Inadequate resection	Consider reoperation if possible	– Utilize ECoG – Consider cortical/subcortical or awake mapping
Venous infarction	Loss of associated DVA	–	– Select appropriate approach – Respect-associated DVA
Postoperative aspiration	New or worsened postoperative dysphagia	Intubation/trach as needed – Antibiotics – PEG if necessary	– Routine postoperative swallowing interrogation
			– Consider preop PEG/trach
Postoperative hematoma	Violation of DVA poor cavity hemostasis	Consider benefit of reoperation	– Meticulous hemostasis – Consider benefit of lining the cavity with cellulose

Introduction

Cavernous malformations (CM) represent a relatively common vascular lesion occurring in an estimated 1 in 200 people [1]. Although CMs have long been recognized as a pathological entity [2], their occult angiographic nature made them difficult to diagnose preoperatively. More than anything else, it was the introduction of MRI that contributed most to our current understanding of theses peculiar lesions and led to their routine radiographic diagnosis [1, 3].

Complication Statistics

Complications associated with CM management are dependent on only two factors that are predictable: lesion location and method of presentation. Naturally, the approaches to less accessible, or deeper, lesions will be associated with a higher

complication rate while a complete resection with minimal morbidity should be the expectation for a superficial lesion. Similar to other lesions in the family of vascular malformations, a hemorrhagic presentation may frequently increase the accessibility of CMs to surgical resection. In other words the presentation may positively influence the decision for surgical resection. In general, surgery for supratentorial CMs in the post-MRI era can be associated with risks in the range of 3–4% [4, 5].

It is this low morbidity related to the resection of superficial lesions that has resulted in a large proportion of recent neurosurgical literature being focused on brainstem location and the complications that can arise from operating in what we generally refer to as "high-priced real estate." In their series of brainstem cavernous malformations, Abla et al. reported a 36% incidence of new or worsened permanent postoperative neurological deficit and a 28.5% complication rate including three deaths [6]. Garcia et al. reported a 9.6% rate of new permanent neurologic deficit, a 28% complication rate, and one death [7].

Outcomes

For deep-seated and brainstem CMs, operative complications and, in particular, new permanent neurologic deficits tend to be closely related to clinical outcome. This pertains to the relationship between the lesion and eloquent adjacent tissue as well as the unforgiving nature of brainstem injury. In their series of brainstem cavernous malformations treated surgically, Hauck et al. found that the surgical outcome was closely related to the patient's preoperative functional status [8]. Additionally, most authors have found a significant association between improved outcomes and younger patient age [7, 9]. This may relate to superior neuroplasticity in younger patients or the medical comorbidities which accompany advancing age.

The rate of neurologic worsening following surgery for complex CMs is relatively high. However, when patients are carefully selected, surgical treatment remains a much better alternative than the often dismal natural history. Thus, although a new neurologic deficit may be an undesirable outcome, it may not actually represent an "unfavorable" outcome.

Procedural Overview

The surgical resection of challenging CMs is a highly variable endeavor. Here we present four cases which were treated at our institution.

Case 1 (Fig. 17.1)

A 25-year-old female with a history of two hemorrhagic events. Preoperatively, she had left ptosis and a left CN VI and VII palsy which were both slowly improving. She also had decreased sensation over her left face and right hemibody. Her strength

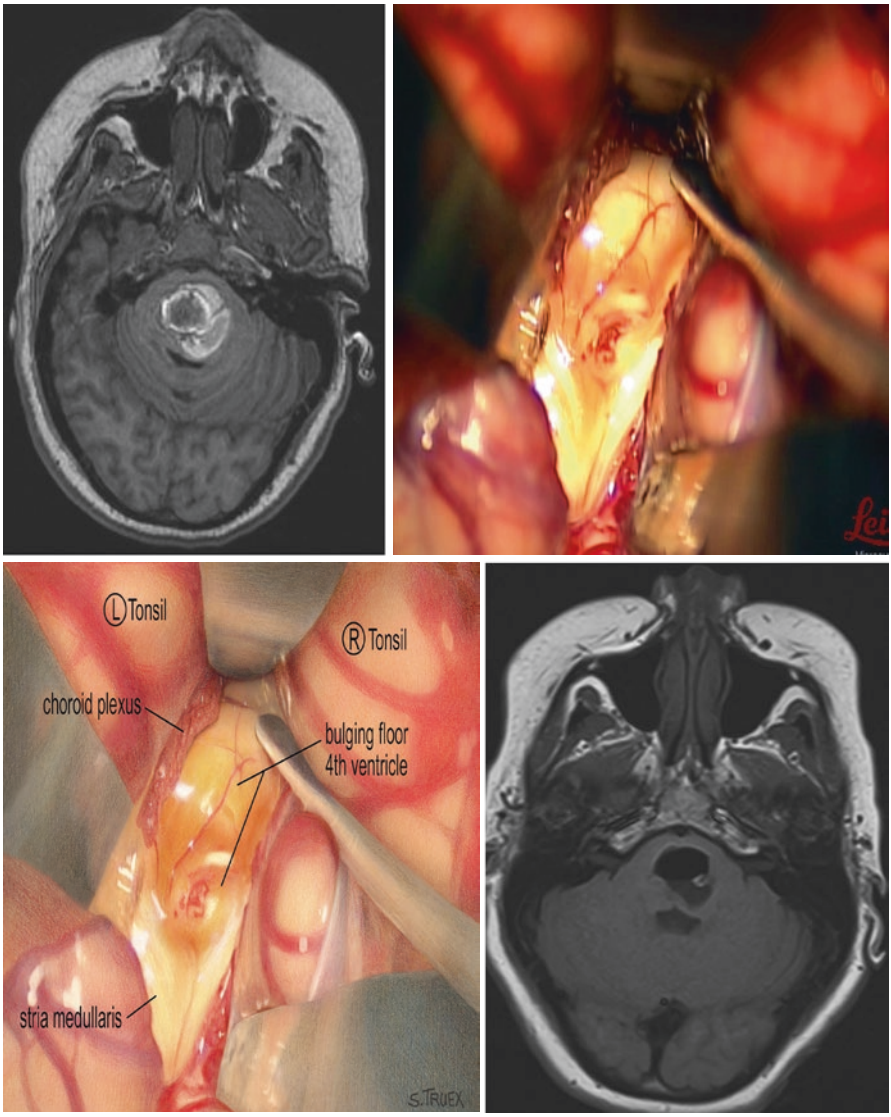

Fig. 17.1 (Case 1) Images clockwise from *top left*: (1) preoperative MRI, (2) intraoperative microscopic view, (3) postoperative MRI, and (4) cartoon of operative view 4

was normal in all four limbs. Her examination was otherwise pertinent for right-sided upper extremity dysmetria. This examination correlated with the radiological diagnosis of a CM effacing the fourth ventricular floor from the posterior pons.

A midline suboccipital craniectomy using frameless stereotactic localization with the patient in the prone position was planned. Subarachnoid dissection was performed through a telovelar approach. Neuromonitoring included SSEPs, MEPs, and bilateral CNVII monitoring.

The cerebellar tonsils were separated and the floor of the fourth ventricle identified.

A facial nerve stimulator was used to find the facial colliculi. Using a stereotactically registered probe placed through a shortened ventricular catheter, the most superficial point of entry of the CM was identified on the ventricular floor. The catheter was then gently inserted into the center of the lesion. The probe was removed, and fluid indicative of chronic hemorrhage spontaneously flowed out of the catheter. The catheter was then removed, and the entry point was gently dilated open with the tips of the bipolar. A combination of sharp dissection and suction was then used to evacuate the cavity through this opening.

Postoperatively her neurological deficits were unchanged. She did benefit from postoperative rehabilitation.

Three months following surgery, she was fully independent and had returned to work. Her left CN VI palsy had completely resolved, and her face was only slightly asymmetric when active but appeared normal at rest. She noted significant improvement in her left face and right hemibody sensation. Her right-sided ataxia had significantly improved.

Case 2 (Fig. 17.2)

A 25-year-old female awoke with headache and progressive blurring of her vision. On examination she was found to have a left homonymous hemianopsia. She had no motor or sensory deficits. This examination correlated with a mass lesion that superiorly displaced the left optic nerve and was most consistent with a CM.

With the patient positioned supine and the head rotated to the left, a modified orbitozygomatic craniotomy was used in which a standard pterional craniotomy was performed, followed by removal of the superolateral orbital wall.

The Sylvian fissure was opened sharply under high magnification. Once the optic apparatus was identified, sharp subarachnoid dissection was used to widen the opticocarotid window. Brain relaxation was gained though patient CSF removal. Next, the exophytic portion of the cavernous malformation was resected and used to create a pathway for internally debulking the lesion. The walls of the cavity were carefully inspected for any residual lesion and the gliotic pseudocapsule was left in place to avoid any unnecessary manipulation of the left optic nerve.

She was discharged home on postoperative day 6. She did well and returned to full time employment. Her left homonymous hemianopsia improved significantly but remained at a 2-year follow-up visit.

Case 3 (Fig. 17.3)

A 26-year-old male originally presented with sudden onset of occipital headaches, nausea, and vomiting accompanied by left face and arm weakness. He suffered two more episodes over the next few months before eventually being referred to our cerebrovascular center. At the time of presentation, his only deficit was numbness in

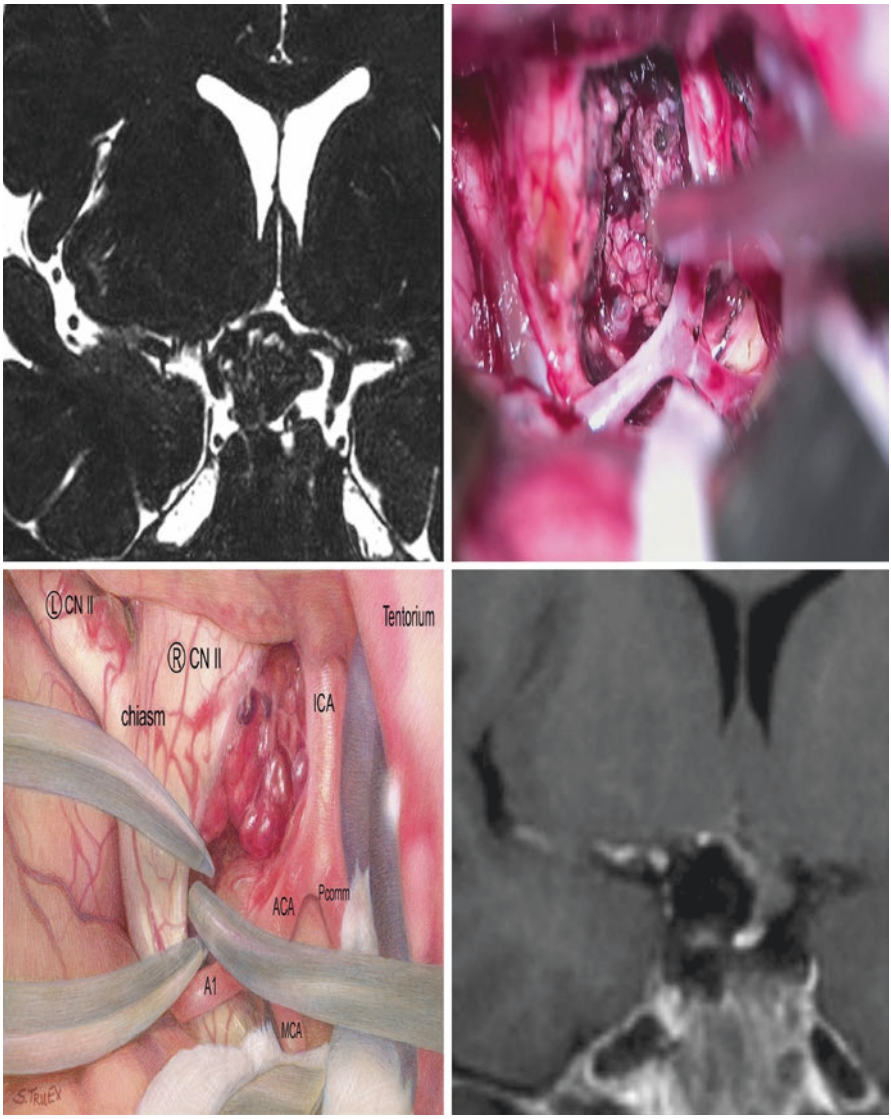

Fig. 17.2 (Case 2) Images clockwise from *top left*: (1) preoperative coronal MRI, (2) intraoperative microscopic view, (3) postoperative coronal MRI, and (4) cartoon of operative view

his left foot. He was hyperreflexic on the left side. His presentation was appropriate for the exophytic pontine cavernoma that was identified on his MRI. A suboccipital far-lateral approach with frameless stereotactic assistance in the lateral position was planned for resection. Neuromonitoring included SSEPs, MEPs, and bilateral CN VII and VIII monitoring.

A generous right far-lateral craniotomy was performed with drilling of the occipital condyle. It was not necessary to mobilize the ipsilateral vertebral artery.

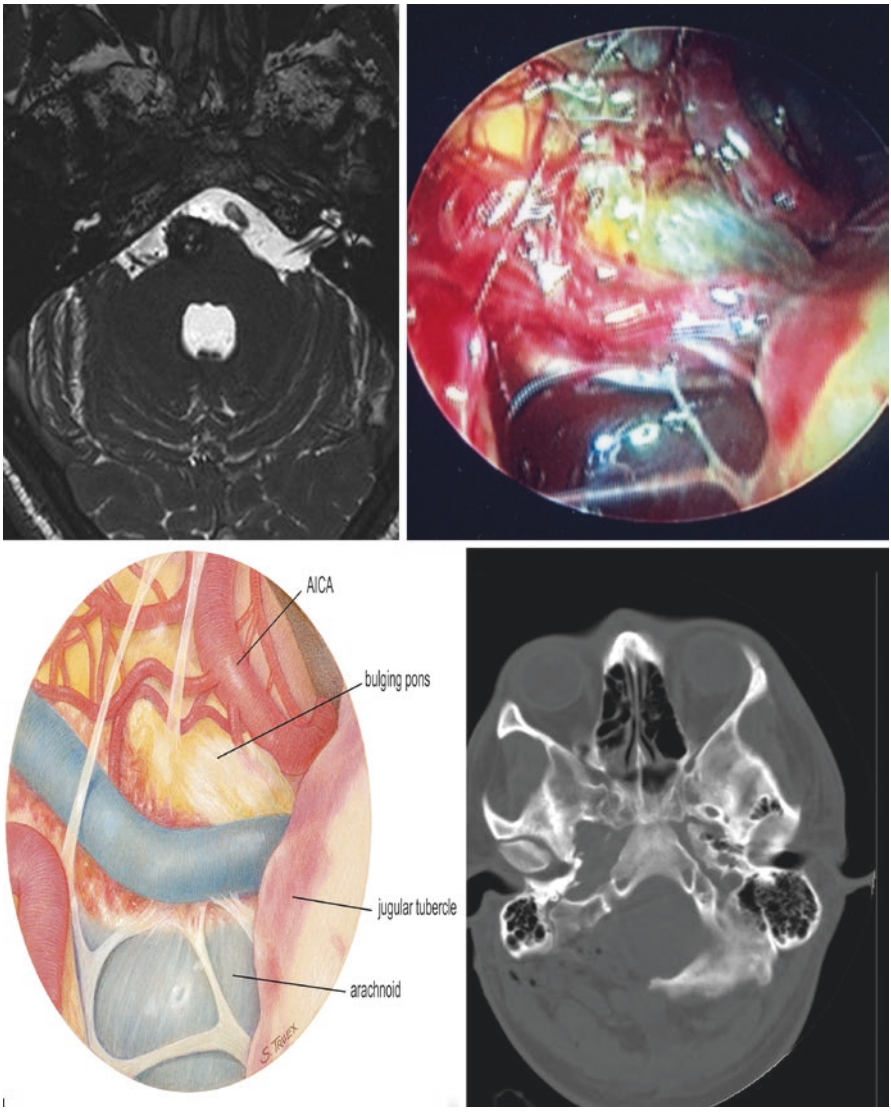

Fig. 17.3 (Case 3) Images clockwise from *top left*: (1) axial MRI demonstrating large exophytic lesion of the left pons, (2) intraoperative endoscopic view of pontine surface with CM visualized as discolored swelling of the pons, (3) postoperative CT demonstrating bony removal for operative approach, and (4) cartoon of intraoperative view

The bony opening was extended to include a retrosigmoid component. The dura was opened in a curvilinear fashion and bisected to allow for maximal lateral exposure. The arachnoid of the cerebellopontine angle was dissected sharply followed by patient CSF drainage to provide relaxation of the cerebellum. The arachnoid dissection then continued medially in order to mobilize the trigeminal nerve and SCA

artery. Venous sacrifice was minimized. The CM was visible on the surface of the pons as a tan protuberance. The capsule was cauterized and entered. Its contents were internally debulked using suction and gentle bipolar cautery. The capsule was left intact, and the cavity was inspected with a 30° endoscope to confirm complete resection.

The patient awoke from surgery with mild left-sided weakness which improved. He failed a postoperative swallow study and required a gastrostomy tube. He was eventually discharged home and had the gastrostomy tube removed 1 month following the surgery. He is neurologically normal and has returned to full-time employment with 5 years of follow-up.

Case 4 (Fig. 17.4)

A 51-year-old female originally presented with severe headaches. She had three episodes of acute decline over the following 4 years with symptoms including blurred vision, right hemibody sensory deficits, and right hemiparesis. She was transferred to our institution from out of state. At the time of presentation, she was no longer ambulatory and somewhat cognitively slowed. Imaging demonstrated mild hydrocephalus in addition to a large CM in the posterior aspect of the thalamus. A supracerebellar infratentorial approach to this region was planned in the sitting position with frameless stereotactic guidance.

With a right frontal external ventricular drain in place, the patient was positioned with careful attention to blood pressure control during her head elevation. Precordial Doppler and a right-sided internal jugular central line were in place for the management of potential air embolism. Neuromonitoring including SSEPs and MEPs was established.

A midline incision extending from above the inion down to C2 with self-retaining retractors was used to expose the suboccipital and posterior occipital bones. A craniotomy was fashioned around the torcular extending above the transverse sinuses and centered to the patient's left side. A persistent occipital sinus was sacrificed during the suboccipital exposure. The dura was opened and retracted toward the transverse sinus and torcular. Two small supracerebellar veins were sacrificed to permit gravity assisted retraction of the cerebellar hemispheres. Following deep subarachnoid dissection, the left pulvinar nucleus of the thalamus was identified and confirmed using stereotaxy. There was a discolored area on the lateral aspect. This region was cauterized and incised with microscissors. Blood of various ages was encountered and evacuated with suction and gentle bipolar cautery. Following this, a 30 ° neuroendoscope was used to fully inspect the walls of the cavity for any residual cavernoma tissue. The cavity was irrigated, and cellulose strips were used to gently tamponade any points of venous oozing from the cavity walls.

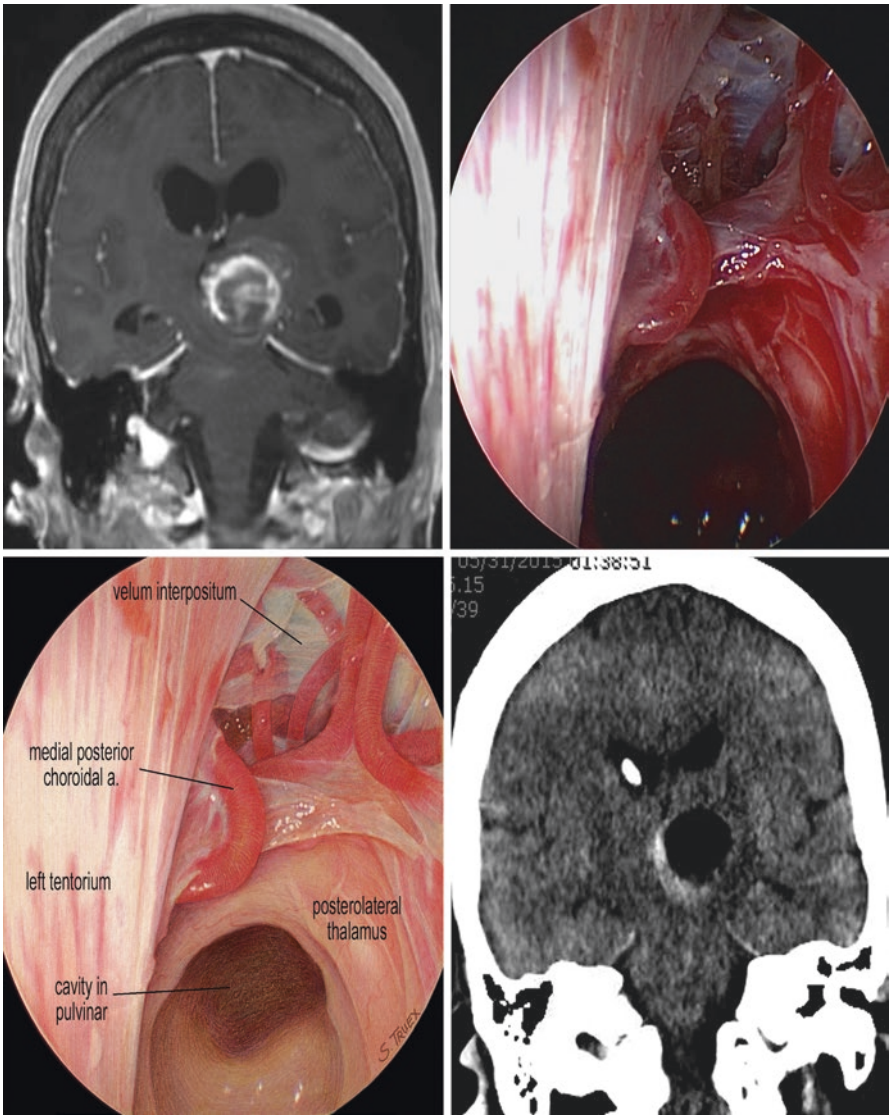

Fig. 17.4 (Case 4) Images clockwise from *top left*: (1) preoperative coronal MRI, (2) intraoperative endoscopic view, (4) postoperative coronal CT, and (5) cartoon of endoscopic view

She was left intubated for 24 h and then extubated. Her right hemiplegia was somewhat worsened postoperatively; however, this improved back to her preoperative baseline left-sided weakness. She was eventually transferred to an out-of-state rehabilitation facility 2 weeks after surgery.

Complication Avoidance

General Considerations

Imaging

The single biggest factor in avoiding complications and mitigating risk when treating patients with CMs lies in patient selection. The majority (70–80%) of CMs are asymptomatic, and thus surgery and its attendant risks are not indicated. The decision to offer surgical treatment should be individualized based on patient factors including mode of presentation, hemorrhage frequency, residual deficit, and lesion location. Any treatment plan should be created to approximate the quality of life that the patient expects using the best information available. In general, without more than one event and presentation to a pial (or ependymal) surface, surgery should be approached with extreme caution or not at all. Once a surgical discussion is held, it is reasonable to discuss temporary postoperative worsening of the patient's deficits. For brainstem lesions the chances of requiring temporary nutritional or ventilator support must be discussed in advance.

The surgical approach to any CM must be tailored to the lesion such that it traverses the least amount of eloquent tissue. Deep-seated and brainstem lesions require more thoughtful consideration. Preoperative permanent neurological deficits should be carefully considered as the approach can be tailored to take advantage of pre-existing deficits and the surgical corridors they may afford. The two-point method, where a straight line connects one point in the center of the lesion and the second point is placed on the pial or ependymal surface closest to the lesion, can be utilized as a guide [6]. The surgeon should be comfortable with the approach and confident that it will ensure adequate exposure of the target (see discussion below).

Usual operative strategies to maximize brain relaxation including intraoperative control of the $PaCO_2$ and the administration of Mannitol remain essential to the approach of CMs. A discussion with the neuroanesthesiology team the day before the case provides an excellent opportunity to anticipate and preemptively address logistical and technical considerations. This discourse should include the use of paralytics such as rocuronium and higher doses of inhalational anesthetics (e.g., sevoflurane) as this may interfere with neuromonitoring during the procedure.

Stereotactic image guidance is essential for all subcortical, deep-seated, and brainstem lesions. Most modern microscopes can be configured such that the focal point of the microscope becomes the stereotactic probe. This can be tremendously helpful for deep-seated and brainstem lesions as the "brain shift" expected during arachnoid dissection and CSF drainage is less, relative to more peripheral structures.

Neurophysiological monitoring is a useful adjunct that increases the safety profile of what is often a relatively high-risk procedure. Brainstem auditory-evoked responses, specific cranial (or spinal) nerve monitoring, somatosensory-evoked potentials, and motor-evoked potentials, along with cortical and deep white matter stimulation and mapping, can all be tailored depending on the location of the lesion

and the specific approach selected. Baseline recordings for noninvasive monitoring techniques should be established before positioning the patient.

Lesions at the end of narrow operative corridors can pose a challenge for the operating microscope, especially when inspecting the walls of the resection cavity. Lighted micro-instruments (suction and bipolar) are commercially available to help illuminate deep cavities. Endoscopes can also be used to augment illumination and visualization in such situations. The availability of multiple angled options can help to look around otherwise obscured corners to evaluate the completeness of any CM resection.

Intraoperative ultrasound can be a useful addition to cranial lesions for identifying subcortical lesions in real time. Such an adjunct can prove very helpful where shift has affected the accuracy of the frameless stereotactic system. As this is an older technology, many of the ultrasound probes are cumbersome, and image acquisition and interpretation are highly user dependent. Intraoperative consultation with a radiologist may be useful. For localizing spinal lesions following a posterior approach, we have found ultrasound to be very useful in planning both the durotomy and localizing lesions which do not obviously present directly to a pial surface.

Specific Considerations

Lobar Cavernous Malformations

Symptomatic lobar CMs are generally safe to resect, but certain principles should be kept in mind especially when dealing with lesions in, or adjacent to, eloquent cortex. The goals of surgery must be clear. Mitigation of hemorrhagic risk necessitates complete lesion resection while the surgical treatment of CM-associated epilepsy may also involve the resection of surrounding brain. Factors that may increase the chances of seizure freedom, particularly in difficult cases, should be evaluated in order to maximize the chances of seizure control but minimize neurological deficit. Many studies report better outcomes when the surrounding gliosis and hemosiderin fringe are removed [10, 11] while some authors have failed to find this relationship [12, 13]. When seizure freedom is a principle goal of surgery, we generally promote extra-lesional resection to include the surrounding gliotic and hemosiderin-stained tissue as dictated by the functional eloquence of the surrounding brain. Surgical adjuncts may include electrocorticography as well as sensory, motor, awake language, and deep white matter tract mapping.

From their review of existing literature encompassing 1226 patients, Englot et al. found that factors associated with seizure freedom following surgery were a duration of seizures less than 1 year, gross total resection, smaller lesion size (<1.5 cm), solitary CMs, and focal seizures without secondary generalization [14]. Hence, surgery for patients with generalized seizures and those with multiple lesions will have a lower chance of seizure freedom. In this meta-analysis, 75% of patients achieved seizure freedom following microsurgical lesion removal.

For those with multiple CMs (familial disease), the correct epileptogenic CM must be resected. Concordance between seizure semiology, EEG, long-term video EEG, and neuropsychological testing can help elucidate the correct seizure generator.

In those with discordant investigations, the chances of postoperative seizure freedom are substantially lower. Consideration should be given to invasive monitoring in order to further delineate the epileptic focus when there is uncertainty. Given that timing is important to achieving a seizure free status with surgery, it may be acceptable to determine a failure of antiepileptic treatment medication sooner than with other forms of epilepsy whose definitions are often more rigorous.

In patients with mesiotemporal CMs and those with concomitant mesial temporal sclerosis, consideration should be given toward resection of the mesial temporal structures (amygdala and hippocampus) in addition to CM resection. On the dominant side, this necessitates interrogation of the functional status of the hippocampus [15].

For supratentorial lesions in non-eloquent regions, the gliotic pseudocapsule can be used as a dissection plane to obtain a complete resection. Often gentle bipolar cautery can shrink the lesion thereby facilitating resection. For resection of CMs in language regions, functional MRI can help plan an appropriate surgical approach to the lesion. Strong consideration should be given to awake craniotomy with mapping of language to help guide resection of the CM (Fig. 17.5).

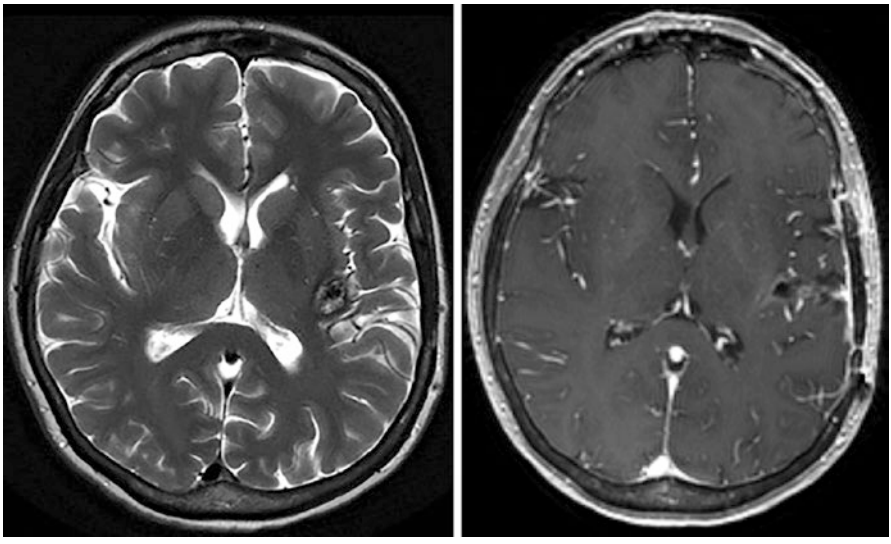

Fig. 17.5 Left pre- and right postoperative MRI of a 37-year-old female with poorly controlled seizures who underwent awake craniotomy with language mapping for resection of this left insular cavernous malformation. Postoperatively she had no language deficits. Her seizures are now well controlled on a single agent

Deep-Seated and Brainstem Cavernous Malformations

Cavernous malformations of the basal ganglia, thalamus, and brainstem represent a surgical challenge. Because the surgical risks in these regions are much higher and the potential for morbidity is greater, careful patient selection is of the utmost importance for these lesions. Relative to supratentorial lesions, the only surgical goal in these deeper lesions is complete resection of the lesion in order to prevent future hemorrhage. The probability of reversing a long-standing neurological deficit is very low, and they do not present with seizures.

The resection of deep-seated and brainstem CMs begins with the localization. Few feelings are worse in neurosurgery than the presumed inaccuracy of frameless stereotaxy during localization of a brainstem CM. Careful attention to image acquisition and merging cannot be overemphasized. Unlike supratentorial lesions, the resection of this category of CM must not include the gliotic pseudocapsule and hemosiderin-stained tissue surrounding the lesion. Bipolar cautery should be used sparingly and only within the gliotic capsule. Excessive bleeding when attempting resection of a deep or brainstem CM should be managed with gentle tamponade.

Most, if not all, deep-seated and brainstem CMs have an associated DVA even if not identified on imaging. Deliberate or inadvertent sacrifice of the associated DVA will increase the risk of venous infarction and elevate procedural morbidity.

Postoperative Management

Long cases involving brainstem CMs in patients who are already at risk for, or already have, respiratory and swallowing difficulty are best kept intubated for 24–48 h in an intensive care setting. Patients who are successfully extubated should all undergo formal swallowing studies before any oral feeding is permitted.

The postoperative blood pressure should be judiciously controlled to protect the resection cavity. We prefer to keep the systolic blood pressure less than 150 mmHg through a combination of titrated short-acting sedatives (dexmetetomodine or diprivan), non-sedating pain medication (such as fentanyl), and short-acting antihypertensive medications (nicardipine, verapamil).

All patients receive perioperative steroids as well as a short postoperative taper to minimize edema and (theoretically) protect neural tissue from damage associated with manipulation.

Postoperative imaging is somewhat variable among practices. Immediate postoperative/intraoperative MRI serves to alert the surgeon to residual CM in the cavity [16]. Many do not take this approach and only image based on clinical changes. Our preference is routine 3-month postoperative imaging with initial close clinical follow-up.

Special Considerations

Spinal cord CMs are rare lesions often grouped together with those of the brainstem. Because of their rarity, the natural history of CMs of the spinal cord is less well defined. They often present with new onset of sensory and/or motor deficits.

A larger percentage of patients in this group (up to 34%) also have associated pain. Any patient with a spinal lesion should be screened with cranial MRI to exclude cerebral lesions which can be found in up to 40% of patients [17].

Presentation to a pial surface, though strongly desired, is a less stringent requirement for spinal lesions. The standard approach for deep spinal lesions is through a posterior midline myelotomy if the lesion does not present to a pial surface. Anterior approaches have also been described and can be utilized when necessary [18].

Neurophysiologic monitoring with SSEPs and MEPs is essential. Signal loss should prompt an immediate cessation of activity. Resection can be restarted at a different location once the signal recovers. Similar to brainstem lesions, the surrounding hemosiderin-stained tissue and gliotic pseudocapsule should not be disturbed.

Outcomes following resection of spinal cord lesions in the literature come from small, single center series. The rate of improvement following resection is variable. Ardeshiri et al. reported a 20% improvement at follow-up while 80% of patients were no worse following resection [19]. Zhang et al. found that 3.4% of patients had a deterioration following surgery while 14.8% of patients in a conservatively managed cohort deteriorated over time [20].

Stereotactic Radiosurgery (SRS)

This treatment modality remains controversial. The utility of SRS is currently unclear and should only be considered for surgically inaccessible, aggressive CMs. Because SRS does not result in radiographic obliteration of CMs, most studies have attempted to demonstrate a decrease in the rate of hemorrhage following SRS [21]. In their series of 103 patients with symptomatic CMs, Lunsford et al. reported a 14% complication rate. The hemorrhage rate was 10.8% per year for the first 2 years and then decreased to 1.1% [22]. Given the known hemorrhage patterns of temporal clustering, the concrete benefits of SRS relative to the natural history of CMs remain uncertain while the adverse events secondary to radiation are clear.

Laser Ablation Treatment

Recently, MR thermography-guided stereotactic laser ablation (SLA) techniques for the treatment of CMs have been proposed based on previous success of this technique for other disease processes. To date, only limited case series and individual case reports have been published [23, 24]. The idea of a minimally invasive stereotactic guided technique for the treatment of CMs is attractive, especially for deep-seated lesions. However, currently there is not enough experience with this technique to advocate for SLA for either the treatment of epilepsy or neurologic symptoms outside of a clinical trial.

Complication Management

From the prior discussion, it should be clear that the best means of avoiding the most common (and most serious) complications associated with CM resection requires a careful approach to the patient before setting foot in the operating room.

New Neurologic Deficit

The key to managing complications lies within the realm of prevention. The following text considers those factors which we feel are associated with a lower likelihood of new postoperative deficits. Patient selection, lesion selection, surgical approach selection, and timing of surgery are all essential to safely resecting the offending lesion while minimizing damage to adjacent tissue. Likewise, functional imaging, accurate integrated neuronavigation tools, and neurophysiologic monitoring can all help to decrease the chances of inadvertently damaging critical structures.

Specific intraoperative pearls include the judicious use of bipolar cautery within the capsule of the lesion. Foci of bleeding should be addressed with patience, irrigation, and gentle tamponade. For brainstem or deep-seated CMs, avoid resecting the gliotic pseudocapsule.

Incomplete Resection

Occasionally, based upon a surgical judgment of risk vs. benefit or changes in neuro-monitoring, part of the CM is purposely left behind. However, inadvertent residual CM tissue is a not infrequent complication associated with long, dark operative corridors combined with a low tolerance for manipulation of eloquent tissue. This can result in an inability to inspect part(s) of the resection cavity appropriately. Once again, preoperative planning, especially with respect to the surgical approach, is essential.

Technical nuances that may assist with visualization include the use of lighted instruments such as bipolar cautery and/or retractors. Some authors have utilized intraoperative (or immediate postoperative) MRI to help define any residual cavernoma tissue. We have found the use of endoscopes to be very beneficial for their superior lighting and visualization of deep and dark cavities and around corners.

Postoperative Hematoma

Blood within the resection cavity is not uncommon following CM surgery. This is not completely unexpected for deep-seated and brainstem lesions given the desire to avoid excessive bipolar cautery and tissue manipulation. The vast majority of the time, this finding can be followed radiographically with close clinical monitoring of the patient in the neurological intensive care unit. Occasionally, the hematoma may be large enough to produce mass effect and clinical change. In equivocal cases this can be a difficult dilemma as new (usually temporary) neurological deficits or worsening is also common following CM resection. Deciding when a patient should return for hematoma evacuation to relieve suspected mass effect on surrounding tissue may be challenging, but erring on the side of hematoma evacuation is probably the best approach. If in doubt, take it out.

Avoiding this complication requires patience, which can be challenging at the end of a long case. Gentle tamponade and carefully placed pledgets of Surgicel or Nu-Knit (Ethicon, Somerville, NJ) are advised. Again, neuroendoscopes may assist with improved visualization of dark corners of the resection cavity.

Persistent Epilepsy

There is always some risk that the seizures are not relieved or even improved following surgical resection of an identified CM. The degree to which this constitutes a true complication is somewhat debatable. Nonetheless, it represents not only an important surgical indication but obviously is also a significant patient expectation. This is a complication that will generally only be discovered postoperatively during the intermediate clinical follow-up period. Avoiding this outcome is heavily dependent on the preoperative workup. Patient and lesion selection can be challenging in those with multiple lesions (see the above discussion regarding discordant seizure investigations).

Certainly, when possible the gliotic pseudocapsule and surrounding hemosiderin stained tissue should be resected. Although evidence is lacking, it would seem reasonable to assume that a more aggressive surgical resection would offer a better chance at seizure freedom, at the cost of increased neurological deficits. To that end cortical and subcortical mapping to direct resection may spare important cortical regions and white matter tracts. Additionally, electrocorticography can be used to focus the resection toward an epileptogenic focus while awake craniotomy can be used to tailor the resection away from critical functions in nearby regions.

Excessive Bleeding During Resection

While operating on deep-seated and brainstem lesions, there are times when the approach, subarachnoid dissection and resection of the CM itself, may prove more difficult than expected. When excessive bleeding occurs, the surgeon should question whether a vascular structure other than the CM was violated (DVA, nearby artery/vein). Although there is always room for persistence in cerebrovascular neurosurgery, knowing when to back away can be just as important. When such bleeding impairs visualization and limits a controlled resection, strong consideration should be given to aborting the procedure. It can often be tackled at a later date when evolution of the lesion may change its consistency and propensity to bleed.

Venous Infarction

Venous infarction following cavernoma resection can have disastrous consequences. As discussed above, DVAs are frequently associated with CMs, and by definition they drain normal regional tissue in a fashion that tends to preclude sufficient venous

collateral pathways from draining the area in the event of their loss. Preservation of an associated DVA is the most direct means of preventing venous infarction and should be taken into consideration at every step of the procedure from planning the surgical approach to resecting the lesion itself.

Postoperative Aspiration

For posterior fossa lesions, a high index of suspicion should be maintained for dysphagia. At our institution, all posterior fossa cases are formally tested by a speech-language pathologist as part of their routine postoperative care prior to any oral intake. Consideration for up-front tracheostomy and/or gastrostomy should be considered in patients with preoperative deficits. This consideration is of added importance when prone positioning is considered best for the resection.

Conclusion

These fascinating lesions run the gamut from benign incidental pathology on neuroimaging to life or quality-of-life threatening. Likewise, surgical resection of CMs extends from routine craniotomies in non-eloquent regions to a complex orchestration of neurosurgical, anesthetic, and electrophysiologic modalities. Complications cannot be entirely avoided in any surgical endeavor; however, they can be minimized and appropriately managed. The vast majority of complications related to CMs can be avoided through careful patient selection, thoughtful planning with attention to detail, appropriate use of surgical adjuncts, and meticulous surgical technique.

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Direct Bypass Surgery: Principles, Nuances, and Complication Avoidance

18

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Checklist: Direct Bypass surgery

Equipment needed	Procedural steps
Neurophysiology • Motor-evoked potentials • Somatosensory-evoked potentials • EEG to guide barbiturate-induced burst suppression Nursing • Confirm patient compliance with medication (e.g., aspirin) • Confirm pre-procedure arterial ultrasound/ Allen's test if radial artery graft planned • Review serum chemistries and blood count • Confirm availability of bypass instruments, suture material, microsuction, and papaverine Anesthesia • Procedure done under general anesthesia; routine preoperative medical clearance • Avoid hypotension, especially during induction • Induced hypertension to augment collateral circulation during temporary occlusion, as directed • Total intravenous anesthesia to facilitate neuromonitoring Neurosurgeon • Review preoperative angiography to plan for bypass and also to establish contingency plan • Operative microscope with mouthpiece and video angiography capability	Graft preparation • Harvest and preparation of donor graft (e.g., superficial temporal artery, radial artery, etc.) • Craniotomy and subarachnoid dissection to the proximal graft site Anastomosis • Temporary occlusion of recipient vessel • Arteriotomy and flushing of vessels with heparinized saline • Suturing with running Prolene • Release of temporary occlusion and reperfusion via opening of donor graft Management • Micro-Doppler confirmation of blood flow through graft and recipient vessel • Video angiography • Digital subtraction angiography postoperatively • Aspirin therapy for life

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Graft occlusion	Anastomotic stricture	Reopen the graft if immediately discovered intraoperatively; reoperation if perfusion imaging suggests territory at risk for ischemia	"Fish-mouth" opening of graft; meticulous suture technique and continuous inspection of suture line; aspirin to prevent delayed occlusion
	Thrombus	Reopen the graft if immediately discovered intraoperatively; reoperation if perfusion imaging suggests territory at risk for ischemia	Aspirin therapy
Perioperative ischemia	Hypotension resulting in decreased cerebral perfusion	Supportive care	Communication with anesthesiologist to avoid hypotension during induction and throughout the case
	Temporary occlusion during anastomosis	Supportive care	Limit time needed for suturing; burst suppression; induced hypertension

Introduction

Cerebral revascularization in the form of direct bypass (artery lumen anastomosis with another artery lumen to permit immediate blood flow) is an important tool in the treatment of a wide range of intracranial pathology. While it has a historically controversial role in the treatment of symptomatic intracranial atherosclerosis [1], few would question the utility of bypass to avert ischemia in other conditions such as complex brain aneurysms or Moyamoya disease [2–7]. The variations of bypass procedures available are diverse, with the workhorse of the superficial temporal artery-to-middle cerebral artery bypass being the most common bypass encountered in clinical practice. Other bypass procedures include extracranial-to-intracranial bypass with interposition graft, aneurysm excision with parent vessel reimplantation, intracranial-to-intracranial bypass without interposition graft, left-to-right hemisphere intracranial-to-intracranial bypass, aneurysm excision with primary reanastomosis, and intracranial-to-intracranial bypass with interposition graft, among others [8, 9]. Each operation can be tailored precisely to the patient-specific anatomy and pathology, with a bias toward simplicity and intracranial-to-intracranial solutions when possible. Even when the procedure appears to be technically sound, perioperative ischemia and graft occlusion can occur and represent the pertinent complications that must be avoided.

Preoperative Evaluation

Preoperative imaging studies are performed to thoroughly define the optimal treatment plan, contingency plans, the collateral circulation present (if any), and the size and location of the intended bypass recipient and donor vessels. This is best accomplished with digital subtraction angiography. For planning purposes of Moyamoya revascularization, the external carotid artery injection gives detailed information about the caliber and quality of the superficial temporal artery, which is the most common donor vessel. In other diseases where vessel sacrifice is planned, a balloon test occlusion can be performed, with single-photon emission computed tomography (SPECT) imaging to improve the sensitivity and specificity of a "negative" test [10, 11]. Vessel sacrifice can be considered in patients with a normal occlusion test, although the risks of a false negative must be weighed against the procedural risk of a bypass. When in doubt, a bypass procedure is favored, as it is a more predictable option than hoping for adequate collateral circulation (Fig. 18.1).

Additional testing with CT angiography can help to define the relationship of the skull base to the arterial tree, as common individual anatomical variations (aerated clinoid process, exposed petrous carotid artery segment, extradural origin of the posterior inferior cerebellar artery, etc.) are best appreciated before entering the operating room. If a flow replacement (high flow) bypass procedure is planned, then radial artery imaging with Doppler ultrasound is performed to determine both size of the radial artery and patency of the palmar arch. A failed Allen's test is a contraindication to using the radial artery as a graft [12, 13], and if both left and right sides are unsuitable, then a saphenous vein or cadaveric specimen can be considered for graft material.

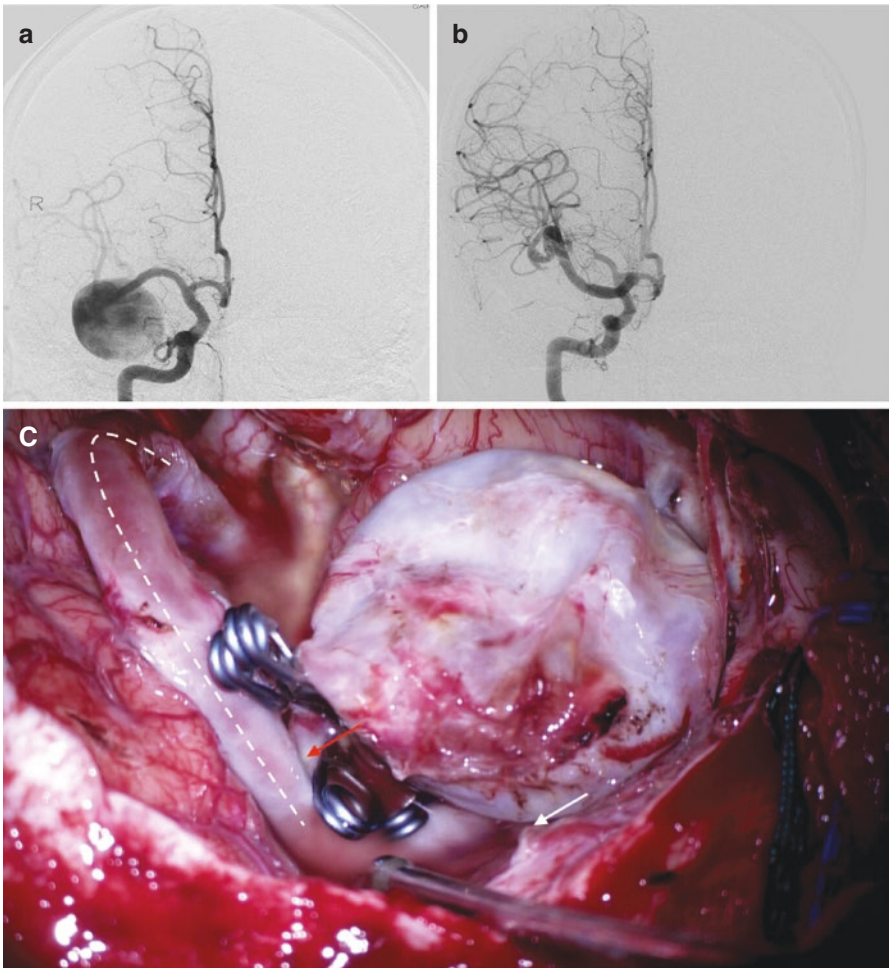

Fig. 18.1 Intracranial-to-intracranial bypass with aneurysm trapping for giant middle cerebral artery aneurysm. A 70-year-old male presented with a giant middle cerebral artery aneurysm that was producing recurrent emboli resulting in small ischemic events. (**a**) Preoperative angiography demonstrated a giant middle cerebral artery aneurysm with the middle cerebral artery trunks coming out of the base of the aneurysm. The aneurysm was not felt to be amendable to direct clipping, and a bypass was planned in order to facilitate safe aneurysm trapping. (**b**) A saphenous vein graft (*dashed line*) was used to connect a donor A1 (end to side), to the frontal M2 MCA branch (side to side, *red arrow*), as well as the temporal M2 MCA branch (end to side, *white arrow*). (**c**) Postoperative angiogram demonstrated cure of the aneurysm with preservation of blood flow in the bypass graft and the MCA branches

Since graft occlusion and perioperative ischemia are two major concerns with any revascularization procedure, patients are placed on antiplatelet aggregation agents either preoperatively or immediately postoperatively, with aspirin being the most commonly used agent. Because aspirin and clopidogrel resistance are relatively common in the general population [14, 15], various point-of-care testing assays for drug resistance may be helpful in personalization of care for these patients [16, 17].

Procedural Overview and Complication Avoidance

Flow Replacement ("High Flow Bypass," e.g., External Carotid Artery–Middle Cerebral Artery)

When a planned operation involves abrupt occlusion of a previously patent carotid artery, a flow replacement bypass is generally needed to support the blood flow requirements of the downstream territory. This type of revascularization involves an interposition graft from the external (or common) carotid artery to the proximal intracranial circulation. The patient is placed under general anesthesia and positioned supine with the head rotated to a position that is similar to what is used for a standard pterional craniotomy. This position allows for subarachnoid dissection of the Sylvian fissure and exposure of the proximal middle cerebral artery, anterior cerebral artery, and internal carotid artery. The arm is extended to the side on a supported table at a 90° angle to the body, allowing for access to the forearm in order to harvest the radial artery.

The craniotomy is performed in the usual manner, and the bone removal can be expanded to meet the specific needs of the tumor portion of the operation. Extensive subarachnoid dissection of the Sylvian fissure, with splitting of the temporal and frontal lobes apart, is helpful in opening the corridor and expanding the working angles to the proximal anastomosis site. The parietal branch of the superficial temporal artery should be preserved in continuity during the craniotomy and can be used as a salvage graft if unexpected circumstances arise during the course of the operation.

Next, the ipsilateral carotid artery bifurcation is isolated in the neck. We prefer to use a horizontal incision that follows a natural crease line of the neck skin to improve cosmetic outcome. The sternocleidomastoid muscle is mobilized laterally, along with the jugular vein. The carotid artery is isolated within the carotid sheath, and the common, internal, and external segments are marked with vessel loops. The external carotid artery is carefully inspected to ensure it is free from atherosclerosis at the planned cervical anastomosis site.

Next, or concurrently with the help of a co-surgeon, the radial artery is harvested from the forearm. Using ultrasound, the surface projection of the radial artery can be marked. An incision is made over this from the wrist all the way to the elbow joint, traversing in a linear path pointing toward the medial olecranon. The artery is bluntly dissected with scissors, and small Weck clips should be placed on the small perforating muscular branches arising from it. Closure of these branches during the dissection increases the likelihood that the graft will be free of leaks. When the full length of the artery is dissected, from the wrist to the elbow crease, temporary aneurysm clips are placed on the ends, the vessel is cut free, and the artery stumps are ligated and cauterized. The graft is marked with ink to indicate the proximal and distal ends. Heparinized saline flushes are used to clear the intraluminal blood contents. Systemic heparin is not used secondary to the high risk of hemorrhagic complications. Next, pressure distension angioplasty is performed by distal occlusion of the graft and injecting it with heparinized saline using manual syringe pressure. This minimizes the risk of graft vasospasm and also identifies occult leaks that can be closed with 10-0 nylon suture. The ends of the graft are cleared of adherent

connective tissue under microscopic vision to prepare for the anastomosis. The distal end of the graft is "fish mouthed" by cutting it at a 60° angle, followed by using scissors to open a few contiguous millimeters along the more proximal portion of the graft. The footprint this creates is a diamond shape, which ensures that the anastomosis site diameter doesn't become smaller than the average graft diameter, even in the setting of sewing.

After identifying the proximal segment of the middle cerebral artery or internal carotid artery where the anastomosis will be performed, temporary clips are then placed on the cerebral vessel to isolate the segment from the circulation. During this period, the amount of time the blood vessel can be occluded without resulting in stroke is highly variable. It appears to be dependent on many patient-specific factors, such as collateral circulation from other vascular territories, although the variability in maximally tolerated ischemia time from patient to patient is not well understood. Patients are closely monitored with somatosensory-evoked potentials and motor-evoked potentials in order to detect the onset of early ischemic changes. Measures to augment blood flow through collateral circulation, including temporary induced systemic hypertension, are thought to be helpful and are routinely used [18]. Alternative strategies to maximize the ischemia window are centered on decreasing cerebral metabolic demand. Studies have examined the use of mild hypothermia [19], although this was not found to be beneficial in patients undergoing surgery for ruptured brain aneurysms. Its potential benefit in patients undergoing elective procedures, or more specifically those undergoing temporary occlusion of cerebral arteries, is not well studied. Another technique frequently used to decrease cerebral metabolic demand is anesthetic-induced electroencephalographic (EEG) burst suppression. Burst suppression is an EEG pattern in which high-voltage activity alternates with isoelectric quiescence. It is characteristic of an "inactivated" brain, is seen with deep levels of general anesthesia, and is thought to be associated with a decrease in cerebral metabolic rate coupled with the stabilizing properties of ATP-gated potassium channels [20]. In clinical practice, the rate of infusion of an anesthetic (typically propofol) can be manipulated by the anesthesiologist based on real-time feedback from continuous EEG monitoring in order to achieve 100% intensity burst suppression. The neuroprotective benefit of this technique to extend the ischemic window is a subject of ongoing investigation. The radial artery is then grafted to the intracranial anastomosis site using continuous nylon suture, usually 9-0 or 10-0. The heel and toe sites are anchored first, and then the needle is passed from extraluminal to intraluminal down each suture line. After all of the passes have been made, forceps are then used to carefully tighten the suture. Alternatively, an interrupted suturing technique can be used. The temporary aneurysm clips are then released, completing the distal portion of the bypass.

The radial artery graft is then tunneled from the craniotomy opening down to the cervical opening through a chest tube passed with a Kelly clamp in order to protect the graft. The external carotid artery anastomosis site is identified, marked, and then isolated with aneurysm clips. An arteriotomy is made in the external carotid artery, allowing for introduction of an aortic punch to create a larger opening. The proximal portion of the radial artery graft is then sewn to this site using 8-0 nylon suture

with a continuous technique. After the temporary aneurysm clips are released, there is usually some amount of bleeding from the anastomosis site. This is controlled with surgical fibrillar (Ethicon) or similar absorbable hemostatic agent. Foam-based hemostatic agents with thrombin additives are avoided. Next careful inspection of the vessels is performed to confirm patency. Micro-Doppler can be used, along with video angiography (indocyanine green or sodium fluorescein). Once satisfied, a permanent aneurysm clip can be placed to proximally occlude the intracranial carotid artery. Alternatively, endovascular proximal occlusion can be performed with intermittent digital subtraction angiography as a gold standard to confirm graft patency. Continuous blood pressure monitoring in the intensive care unit for the first day after the procedure is standard in order to ensure normotension and euvolemia. Postoperative aspirin is administered as soon as the patient is awake and able to tolerate oral intake and is continued indefinitely. It is felt that aspirin decreases the short-term rate of thromboembolism and improves long-term rates of graft patency, drawing on the experience of aortocoronary bypass [21–23].

Flow Augmentation (Superficial Temporal Artery–Middle Cerebral Artery)

In certain cases, such as Moyamoya disease, flow augmentation can restore adequate blood flow and alleviate hemodynamic insufficiency. For this procedure, there is no interposition graft, and the donor vessel is a transposed superficial temporal artery (STA) with its origin left in situ. The patient is placed under general anesthesia and positioned with their head horizontal to the floor. The course of the STA is mapped with ultrasound, and an incision over the surface projection of it, from just above the zygoma to the just above the superior temporal line, is made under microscope magnification. The subcutaneous tissues are dissected bluntly with scissors, and the STA is exposed. The frontal branch of the artery can also be dissected for several centimeters and preserved as a contingency graft. The parietal branch is covered in a rubber sling and moved to the side in preparation for the craniotomy. The exposed temporalis muscle is then incised into four quadrants, and fishhook-style retractors are placed. The temporal craniotomy is then performed directly over the Sylvian fissure, taking care to protect the STA. The dura is opened in a stellate fashion, and the subarachnoid dissection of the exposed middle cerebral artery M3 and M4 segments is performed. A good recipient site is typically one with large caliber, free of atherosclerosis, and has a course that leads most directly to the proximal middle cerebral artery within the Sylvian fissure. There is a balance between selecting a more proximal vessel, which carries the risk of ischemia from temporary occlusion over a greater territory, and selecting a vessel large enough to support blood flow from the STA (Fig. 18.2).

Next, a temporary aneurysm clip is placed on the distal end of the dissected STA, and it is ligated distally, thereby freeing it from its attachment. The vessel is flushed with heparinized saline. The most distal end of the artery to be used in the anastomosis is cleaned of connective tissue and fish mouthed as previously described.

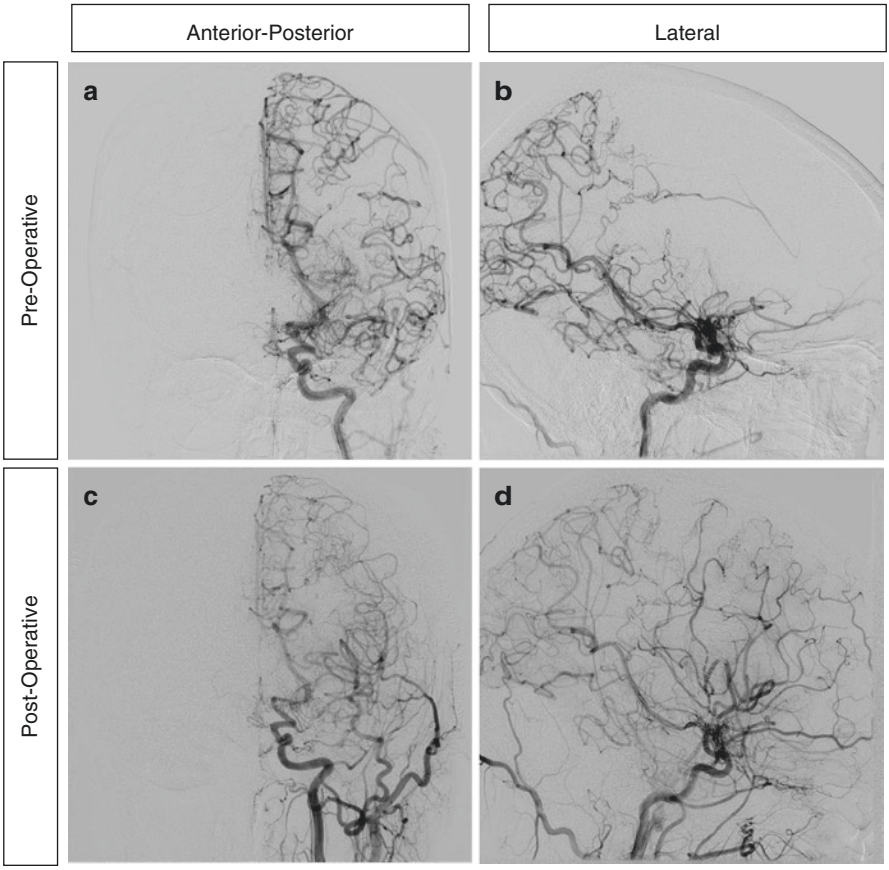

Fig. 18.2 Superficial temporal artery-to-middle cerebral artery bypass for Moyamoya disease. A woman in her 30s presented with Moyamoya disease and a hemorrhagic event. (**a** and **b**) After a period of recovery, preoperative digital subtraction angiography demonstrated near occlusion of her distal carotid artery and a paucity of blood flow through much of the anterior circulation on the patient's left side following carotid artery injection. (**c** and **d**) A superficial temporal artery-to-middle cerebral artery bypass was performed resulting in profound revascularization of the middle cerebral artery territory

Next, the recipient site is isolated with temporary aneurysm clips, and a beveled needle is used to perform an arteriotomy. Microscissors are used to extend the arteriotomy in a line along the MCA that matches the length of the diameter of the prepared STA. The STA is then approximated to the recipient site with heel and toe stitches using 10-0 nylon suture. The suture lines are then completed using these continuous running sutures. Other aspects of the operation, including neuromonitoring, graft inspection, and perioperative management, are similar to those described for flow replacement bypass.

Complication Management

A major complication of direct bypass surgery is graft occlusion with thrombus. This can be detected either at the time of surgery, in the immediate postoperative period, or at some delayed interval. Careful inspection of the graft immediately after the anastomosis and before closing the craniotomy provides an opportunity to detect this complication prior to ischemia. If video angiography and micro-Doppler detect occlusion or inadequate flow, the graft should be reexplored immediately by reoccluding the recipient vessel and opening the suture line. Thrombus can be extracted and the vessel/graft lumen irrigated with heparinized saline. The bypass is then repeated, always taking care to avoid stricture at the anastomosis site. In the immediate postoperative period, if graft occlusion is detected as a result of surveillance angiography, perfusion imaging can be obtained to ascertain whether any mismatch is present between blood flow, blood volume, and transit time in the graft territory. If asymptomatic, or without significant mismatch, the complication can be managed expectantly. If an ischemic penumbra is present, then the graft should be reexplored immediately as described above. Occlusion in the delayed interval (months to years) rarely occurs, and repeated revascularization can be considered in unique scenarios when symptomatic or when significant at-risk territory exists.

Conclusions

Complication avoidance in direct bypass surgery focuses on the prevention of perioperative ischemia and graft occlusion. Patient selection, meticulous microsurgical technique, antiplatelet aggregation agents, and intraoperative neuroprotection strategies are the main tenants needed for successful outcomes.

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Indirect Bypass Surgery

19

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Checklist: Indirect Bypass Surgery

Complication: Injury to the Superficial Temporal Artery

Equipment needed	Procedural steps
Scrub Tech • 10-blade • Gelfoam with papaverine • Gelfoam with thrombin • Small and large Weitlaner retractors • Drill with a 5 mm cutting burr and a B1 craniotome with a footplate • Beaver blade • Microsurgical instruments • 6–0 Prolene sutures • 4–0 Nurolon sutures Nursing • Doppler ultrasound • Bipolar cautery on low power • Monopolar cautery • Microscope draped • Anticonvulsant • Staff pager numbers – Neurosurgery – Anesthesia attending Anesthesia • Attending in the room for induction, intubation, and extubation • Prestated strict blood pressure and pCO_2 goal ranges addressed prior to entering the room • Vasopressors loaded in syringes and ready for injection • Laryngoscope in the room for patients with a difficult airway	Identification of Injury to the STA • Recognize that injury to the artery has occurred. • Identify where along the course of the artery injury has occurred Attempt to Salvage the STA • Apply cold saline, Gelfoam with thrombin, and gentle nonocclusive pressure to the injured segment. • Bipolar only the bleeding region using low power. Convert to an Encephalo-myo-synangiosis • Once the decision has been made to abandon the EDAS, fully cauterize the artery to prevent postoperative bleeding. • Replan the craniotomy to permit isolation of a segment of temporal muscle. This craniotomy is often larger than an EDAS craniotomy Convert to Burr Holes • Once the decision has been made to abandon the EDAS, fully cauterize the artery to prevent postoperative bleeding • Extend the incision as far as needed to permit drilling three to five separate burr holes • Drill burr holes with perforator or high-speed burr • Open dura widely and bipolar the dura back to prevent reclosing • Obtain hemostasis and close the incision

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Injury to the superficial temporal artery	Vessel damage upon dissection	Nonocclusive pressure x 15 minutes; application of cold saline; light electrocautery with bipolar using low power; convert to encephalo-myo-synangiosis; convert to burr holes	Use Doppler to map out the STA path; use blunt dissection and a 10-blade rather than cautery
	Injection of lidocaine with epinephrine in the incision	Wait for epinephrine effect to pass; reverse with topical papaverine	Do not use lidocaine with epinephrine for this operation
Intraoperative hypotension	Complicated Induction	If hypotension was significant during induction, an examination with lightened anesthesia may be necessary prior to beginning the procedure	Emphasize clear blood pressure goals with the anesthesia team prior to OR entry
Intraoperative hypercapnia	Complicated intubation, hypoventilation	Lighten sedation for an examination, obtain CT, and delay procedure in the case of a new deficit	Emphasize importance of continuous oxygenation prior to room entry

Introduction

Moyamoya disease (MMD) is a progressive disease of the cerebrovasculature characterized by unilateral or bilateral large vessel stenosis or occlusion with associated microvascular proliferation. The incidence is highest in Asian populations, with a prevalence in Japan of 3.2–10.5 per 100,000 people [1]. The disease can be congenital with a presentation in children or adults or can be acquired as moyamoya syndrome as a secondary response to a primary vascular occlusion [2]. Options for treatment include direct superficial temporal artery to middle cerebral artery (STA-MCA) bypass or indirect bypass. Direct bypass can have some advantages in certain patient groups and is practiced in specialized centers for patients in whom there are donor and recipient vessels of sufficient size for direct anastomosis. The main benefit to the procedure is that it provides immediate augmentation of flow to the ischemic cortex. Disadvantages of direct bypass include intracerebral hemorrhage secondary to hyperperfusion of anastomotic failure and cerebral infarction.

Indirect bypass is a surgical option that takes advantage of the phenomenon in which ischemic cortex induces angiogenesis from nearby vessels. The procedure takes multiple forms depending on exactly which tissues are placed in contact with the cortex. These procedures include encephalo-duro-arterio-synangiosis (EDAS), encephalo-myo-synangiosis (EMS), and encephalo-duro-arterio-myo-synangiosis (EDAMS). These procedures can also be performed in combination with direct STA-MCA bypass.

There have been no randomized trials evaluating direct versus combined or indirect bypass techniques in the adult MMD population. From single center and multicenter series, the rate of complications in all bypass surgeries ranges from 1.2 to 15.6% [3, 4]. A recent meta-analysis of large series presented an average complication rate of symptomatic stroke, permanent neurologic deficits, and death as 8.3% in patients undergoing direct bypass and 6.7% in patients undergoing indirect bypass [5]. Negative outcomes reported in this meta-analysis include ischemic stroke, transient neurologic deficit, intracerebral hemorrhage, subdural hemorrhage, and surgical site infection. This chapter will address intraoperative strategies to avoid and manage complications that may occur during indirect bypass for MMD in adults.

Procedural Overview

Prior to entry into the operating room, the blood pressure goals and pC02 goals are discussed with the anesthesia team. An arterial line should be placed prior to induction to manage blood pressure during induction and intubation. Induction is carried out with vasopressors drawn for rapid access if needed. Intubation is carried out with a fiber-optic scope in the room and ready if the patient has a moderate to high risk airway. The patient is positioned supine with a bump under the shoulder on the side of interest with the head turned 90° to the opposite side with care not to compress the cervical vessels. The head is positioned on a donut or pinned in a Mayfield head holder. In the ideal position, the head is oriented such that the planned craniotomy is parallel to the floor.

A subset of patients presenting with MMD may already have parasitized blood supply from the external carotid artery circulation. If the middle meningeal artery or other ECA vessels supply cerebral cortex, that area of dura cannot be incised for risk of causing ischemia on the dural opening. This is acritical feature to note on the preoperative angiogram and may dictate operative decision making. MMA supply to the cortex complicates dural opening for a pterional making a direct bypass higher risk. For an indirect bypass, collateral ECA supply to the cortex may dictate where the craniotomy and dural opening must happen to avoid the dural area carrying the critical vessel. Look for the cortical blush on all views of the ECA runs on the diagnostic angiogram.

Using a Doppler probe and marking pen, the course of the superficial temporal artery is mapped out from the zygoma to a point as distal as possible or necessary depending on the cortical area of interest (Figs. 19.1a, b). Often both the posterior and anterior branches are mapped. The branch used depends on the relative size of each branch and the ischemic area of interest. The anterior branch is most often used. Lidocaine with epinephrine is not used to avoid constricting the STA and making it more difficult to identify during dissection.

A skin incision is made along the course of the artery with a scalpel, most often a 10-blade. The soft tissue is dissected using blunt dissection to avoid accidental laceration or cauterization to the STA. Gelfoam with thrombin and light pressure is used to

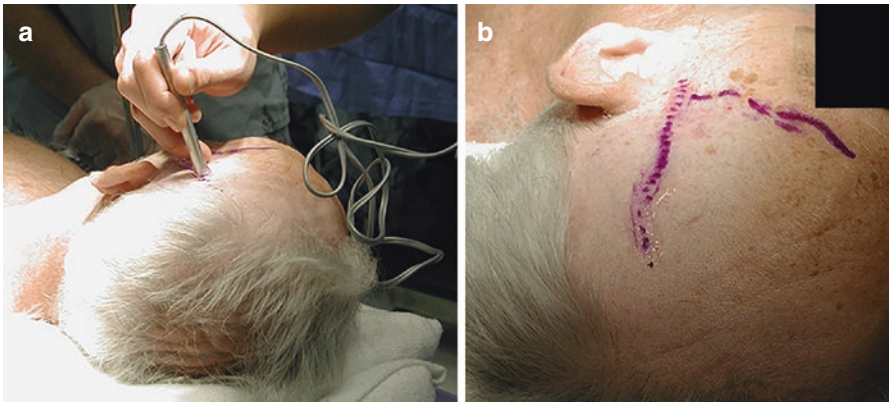

Fig. 19.1 Preoperative Planning. (**a**) The Doppler probe is used to map out the superficial temporal artery, (**b**) clearly labelling the anterior and posterior branches as distally as possible

stop bleeding if possible during the initial stages of the procedure until the artery is clearly identified to avoid vessel injury. Using gentle blunt dissection, the Metzenbaum scissors, and intermittent confirmation with the Doppler probe, the artery is identified along its full course.

The artery itself is not dissected from the surrounding tissue. A strip of galea approximately 5 mm on each side of the artery is delineated and dissected from the surrounding tissue (Fig. 19.2a). Once the full length of the STA has been identified, bipolar cautery and the cutting edge of the Metzenbaum scissors can be used more liberally to stop small bleeding vessels in the galea. Care must be taken to recognize highly tortuous segments of the STA, which may weave laterally and may be injured in the galeal dissection if not recognized. Again, repeated use of the Doppler is key if the artery is not clearly visible throughout its entire course. As the galeal segment is freed from the surrounding tissue, it is increasingly important to prevent twisting or pulling on the STA.

When the galea-STA segment is free from the surrounding tissue, wet cottonoids or vessel loops can be used to gently retract the galea-STA segment either anteriorly or posteriorly to permit unimpeded access to the fascia, muscle, and cranium below (Fig. 19.2b). With the artery and galea-STA segment gently retracted away, the scalpel is used to incise the temporal muscle fascia. The monopolar cautery or scalpel is used to incise the muscle per surgeon preference. A Weitlaner retractor can be used here to retract the temporal muscle. If the galea is free enough, it can be retracted with the muscle, but more often the Weitlaner retractor must be inserted around the galea-STA segment. The periosteal is also used to scrape the cut muscle edges anteriorly and posteriorly.

The high-speed cutting burr is ideal for drilling the burr holes to maximize control and minimize the chance of catching the galea-STA segment (Fig. 19.2c). The burr holes should be 1–1.5 cm in diameter favoring an ovular shape with the long

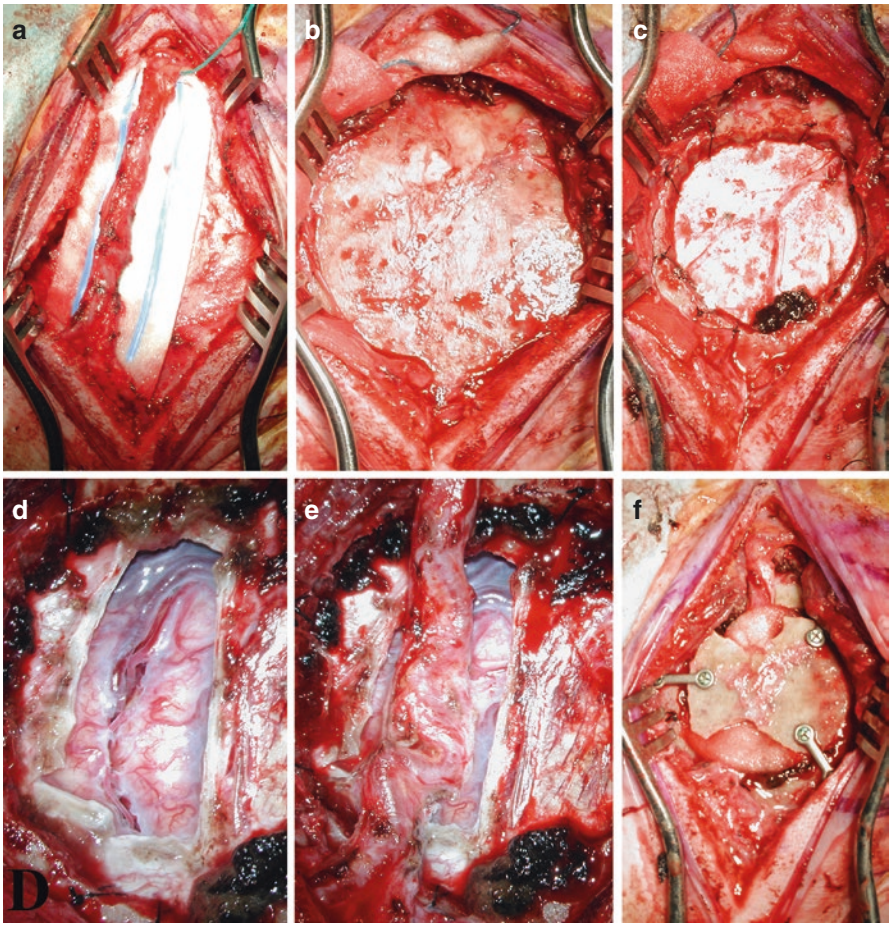

Fig. 19.2 Intraoperative Technique. (**a**) Gently isolate a long segment of STA and the associated galea with care to avoid cauterization unless absolutely necessary. (**b**) Protect the STA and retract it to one side of the incision or the other to expose the bone. (**c**) perform the craniotomy with care to protect the vessel and associated cottoinoids from getting caught in the drill. (**d**) Open the dura linearly from superior to inferior and cut a chevron into the dura at the inferior and superior ends then open the arachnoid. (**e**) Release the STA-galea segment from the retractor, lay it on the surface of the brain, and consider suturing it to the arachnoid. (**f**) Shave the bottom of the bone flap with the drill and cut chevrons into the inferior and superior aspects of the bone flap to permit unobstructed passage of the vessel

axis superior-inferior. One burr hole is inferior in the ovular craniotomy, and the other is superiorly to permit entrance and egress of the artery into the intracranial space. The drill should be well-irrigated to prevent heating the area near the artery. The assistant plays a key role in protecting the galea-STA segment from the drill with gentle retraction and continuous irrigation. The burr holes are connected with the B1 craniotomy with the foot plate. The craniotomy is freed from the dura gently and removed without touching the galea-STA segment.

Hemostasis should be achieved with Gelfoam and cottonoids. The inferior edge of the inferior burr hole and the superior edge of the superior burr hole are flattened down to make a gradual, smooth landing zone for the artery. The craniotomy is thinned down, preserving only the outer lamina in a strip down the middle that will accommodate the galea-STA segment.

The dura is then opened in a vertical incision down the middle of the craniotomy that divides into a three-pointed star (Mercedes logo) at the superior and inferior ends that will remain open after the dura is closed over the implanted galea-STA segment (Fig. 19.2d). At this point the microscope may be brought in to perforate the arachnoid layer and suture the galea to the arachnoid. The subarachnoid can be perforated and cut with the beaver blade and microscissors, respectively. This layer is best-incised over sulci and adjacent to veins where there is clear vessel-free space below the incision site.

The galea-STA segment is then laid on the surface of the cortex. The galea is sewn to the arachnoid in multiple sites using microsurgical instruments and 6-0 Prolene sutures (Fig. 19.2e). This is an excellent opportunity for resident microsurgical training in a controlled environment. The number of sutures varies by surgeon but generally ranges from 4 to 12.

With the galea-STA segment sewn in place, the Doppler is used to confirm flow, and then the dura is closed down the vertical dural incision with 4-0 Nurolon or silk sutures. At this point papaverine can be placed on the STA. The craniotomy is gently placed back with care to check that the artery is not compressed at its entry or exit points. If the artery is compressed, the burr hole sites on the craniotomy flap may need to be expanded to give the artery more space (Fig. 19.2f). The craniotomy is sewn in place with dog bone attachments on the anterior and posterior edges. Burr hole covers are not placed over the burr holes. Once the bone flap is back in place, the Doppler is once again used to confirm proximal flow to and distal flow from the STA.

The muscle fascia and skin are closed with sutures. Extreme care is taken on the closure not to hit the STA with the suture needles. Patients undergoing EDAS are often on aspirin, so hemostasis during closure may be challenging and should be managed with patience, light pressure, and light, targeted bipolar cautery. A strip dressing should be used rather than a headwrap, which can be compressive. Extreme care must be taken to avoid extremes of blood pressure during extubation. The blood pressure parameters should be clearly discussed at the end of the case prior to extubation.

Complication Avoidance

Although a clear step by step procedure, the indirect bypass can be stressful because the entire procedure involves work on and around an artery that must be preserved with adjacent cutting, cauterizing, and drilling. The number one rule in this case is "do not bag the STA." Here is a list of pearls for not injuring the STA:

1. Clearly mark the course of the STA pre-incision using Doppler ultrasound.
2. Do not use lidocaine with epinephrine.

3. Incise to the subcutaneous fat but not beyond on the initial incision.
4. Use gentle blunt dissection with minimal sharp cutting.
5. If cautery is necessary for hemostasis or ligation of branching arteries, use bipolar cautery at a low setting.
6. Use Doppler repeatedly during dissection to clearly understand where the artery is located.
7. Immediately as the galea is freed up, the artery is at most risk for becoming twisted or pulled.
8. Avoid aggressive retraction of the galea-STA segment during craniotomy.
9. Shave the bone down to create a landing zone for the galea-STA segment.
10. Use papaverine at the end of the procedure to "revive" the STA if it goes into spasm after manipulation.
11. Check with the STA with Doppler ultrasound after the craniotomy is secured into place to detect arterial compression if present.

The second most common intraoperative complication is intraoperative hypotension. The most effective armor against this problem is thorough communication with the anesthesia team to convey the importance of blood pressure maintenance within a prespecified range. Here is a list of pearls to avoid intraoperative hypotension:

1. Early and open communication with the anesthesia team regarding MAP goals
2. Placement of a preinduction arterial line
3. Vasopressors pre-drawn to minimize hypotensive time

Intraoperative hypercapnia can also be a problem during the surgery. Again, preemptive and open communication with the anesthesia team regarding the importance of maintaining pCO_2 within a prespecified range is essential. For patients with moderate or severe airways, it is important to have a fiber-optic scope in the room and readily accessible in case intubation is not achievable with a laryngoscope.

1. Early and open communication with the anesthesia team regarding pCO_2 goals
2. Immediate availability of a fiber-optic scope for patients with difficult airways

Complication Management

Injury to the Superficial Temporal Artery

Injury to the STA can occur with varying degrees of severity. If the artery has been damaged, there is a chance it can be coaxed back to life with some simple maneuvers. If the artery goes into spasm and is difficult to detect, apply papaverine to the area and re-Doppler after 2 min. If the artery has been nicked with a sharp instrument and is partially lacerated or there is an avulsed branch, irrigate with cold saline, apply Gelfoam with thrombin, and apply light, nonocclusive pressure for 15 min. The patient will likely be on aspirin, so coagulation will be delayed but will

eventually occur as long as the defect is small. If the defect is too large for pressure to be effective, attempt bipolar cautery at a low setting to cauterize only the defect on the side of the vessel if possible.

If the artery has been damaged beyond saving and the decision is made to proceed without use of the artery, then it should be definitely ligated to prevent postoperative hemorrhage. At this point there are two bailout operations that are both reasonable options that can still benefit the patient. These include encephalo-myosynangiosis and simple burr hole creation.

In EMS, the craniotomy is larger than it is for EDAS. The incision may need to be enlarged to permit a larger craniotomy. The muscle is sharply cut and retracted. Cautery on the muscle is avoided. The craniotomy is made as large as possible in the temporofrontal region with a large inferior burr hole. A segment of muscle is detached distally and laterally but maintains its inferior connection to preserve any small vessel vasculature remaining. Hemostasis of this segment is challenging without cautery but critical as it will remain intracranial. The dura is opened with an inferior chevron as described above. The microscope is brought in, and the arachnoid is cut with a beaver blade and microscissors as described above. The muscle is then laid on the cortex and sutured into place with 4-0 Nurolon or silk sutures. The dura is closed, the craniotomy is fixed into place, the fascia is closed, and the skin is closed as described above.

The second bailout option is burr hole creation, which has shown efficacy in permitting new extracranial to intracranial vasculature to form over time, especially in pediatric cases of MMD. When the decision is made to no longer use the STA, the vessel is definitively ligated. Three to five burr holes are then made in the frontotemporal region. One or two may be placed using the original incision. Two or three will require separate short incisions. These are 1.5 cm burr holes. The dura is opened, reflected back, and cauterized back to keep the cortex exposed. Burr hole covers are placed and the galea and skin are closed as usual.

Intraoperative Hypotension

If significant hypotension occurs during intubation, a management option is to perform a wake-up examination with the patient intubated to verify that the patient has not already suffered irreversible ischemia.

Intraoperative Hypercapnia

The patient is most at risk for hypercapnia during intubation. If there is a problem during intubation causing the patient's O_2 saturation to dip below 85–90%, it may behoove the surgeon to lighten anesthesia to perform an examination to assess if the patient suffered ischemia. If the patient has new deficits, delay of the procedure and a CT of the head are indicated.

Conclusion

Although simpler than direct bypass, indirect bypass procedures have their own set of pitfalls that can be avoided with careful preparation. Basic principles that must be adhered to include avoidance of hypotension, hypercapnia, and meticulous preservation of the superficial temporal artery throughout the procedure.

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Spinal Vascular Malformation Surgery

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Checklist: Spinal Vascular Malformation Surgery

Equipment needed	Procedural steps
Intraoperative EMG and SEEP Neuromonitoring • EMG and SEEP leads • Neuromonitoring transducer • Neuromonitoring computer • Technician • Staff neurologist trained for EMG and SEEP interpretation Neuroanesthesia • General anesthesia • Anesthetic agents compatible with neuromonitoring • Arterial line • MAP regulation for spinal cord perfusion and regulation during AVM manipulation • MAP/SBP management post resection to avoid perfusion injury Neuroangiography Team/Radiology Technicians • Preparation for angiography post resection to verify complete resection while patient anesthetized • Usually done in angiography suite after wound closure for optimal visualization Nursing • Staff pager numbers – Neuromonitoring – Anesthesia attending Spinal Fusion Equipment • Depending on location of AVM and approach, spinal instrumentation should be available. • Operative microscope • Microsurgical instrument set of appropriate length for spinal case • AVM and aneurysm temporary and permanent clips available. • Electrocautery with long microbipolars	Complication: Loss of EMG or SEEG Signals with temporary clip application • Identification of signal change with active EEG/SEEP monitoring requires continual monitoring by the EMG/SEEP technician and temporary clipping prior to resection of artery and then vein • Page/call neuromonitoring staff if question via tech or OR nurse • Verify that anesthesia has not changed • Remove temporary clip and verify return of function • Administer 10 mg of decadron at start of procedure to reduce edema • IC green fluorescent dye can be used to access AVM flow and vessel selection

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Loss of spinal cord function	Resection of artery supplying spinal cord tissue	MAP management during and after procedure	Careful planning from angiogram, intraoperative IC green use, temporary clipping with SEEP/EMG monitoring, neuroanesthesia monitoring/ care
	Edema from spinal cord manipulation	Decadron administration at beginning of procedure and postop	Care to plan spinal approach with intent for minimal cord manipulation (wide exposure)
	Damage of spinal cord from electrocautery	Decadron to reduce edema. Neurontin and/or Lyrica for pain. Symptomatic management, PM&R, spinal rehab	Extreme care with bipolar tips and scissors during resection
	Resection of venous drainage		Consider different microcatheter
Intraoperative hemorrhage	Resection of draining vein prior to arterial removal	Removal of hematoma, resection of additional feeding arteries	IC green use to verify arterial feeder resection, temporary clipping of draining veins prior to cauterization/cutting
CSF leak	Incomplete Dural closure	Careful closure with suture whose needle diameter is not larger than suture material	Watertight closure through diligent suture closure and use of surgeon's preference for sealant (i.e., Tisseel, blood-soaked Gelfoam, muscle, etc.)

Introduction

Unruptured spinal vascular malformations often have a slowly progressive course as venous hypertension increases leading to progressive myelopathy, muscle weakness, numbness, and bladder and bowel dysfunction [1]. This slow progression can be insidious for years prior to diagnosis [1]. When progressive venous hypertension occurs leading to necrotic myelopathy, this is called "Foix-Alajouanine syndrome." Foix-Alajouanine was initially described in France when two young men were followed for progressive neurologic decline and paralysis. Succumbing to complications of paraplegia, they were found to have pathologic changes that were then attributed to an aberrant arteriovenous malformation on autopsy with findings of necrotic myelin changes. The role of venous thrombosis, often attributed to the diagnosis, has since been discredited from translation of the initial transcripts [2].

Compressive myelopathic symptoms from a large AVM may present initially as presumed spinal stenosis. In some cases, patients present with a cranial and spinal subarachnoid hemorrhage and, during workup, have a negative cerebral angiogram. After magnetic resonance imaging of the brain, the cervical and thoracic spine demonstrates blood lower in the spinal canal than expected; spinal angiogram then demonstrates a spinal AVM. If these patients state that they had sudden severe back pain during the onset of the hemorrhage, they have the condition called "coup de poignard rachidien" first described by Michon in 1928 [3].

Classification of Spinal Vascular Malformations

As outlined in Perry Black's article, the classification of arteriovenous malformations has gone through numerous iterations historically starting with Virchow in 1958; Elsberg in 1916; Cushing and Bailey in 1928; Bergstrand, Olivecronna, and Tonnis in 1936; and Wyburn-Mason in 1944 [4]. More modern classification schemes include but are not limited to the Borden classification of dural AV fistulas (1995) [5], Anson and Spetzler classification in 1992 [6], and the modified Spetzler classification system for vascular malformations [7].

For the purpose of this chapter, we will outline the modified Spetzler and the Borden classifications systems.

The modified Spetzler classification system divides spinal vascular pathology into neoplasms, aneurysms, and arteriovenous lesions. Neoplasms consist of hemangioblastomas and cavernous malformations. Spinal arteriovenous lesions consist of arteriovenous fistulas and arteriovenous malformations. From here, AVFs are divided into intradural and extradural. Intradural are either ventral or dorsal. AVMs are divided into extradural-intradural and intradural malformations. Intradural lesions can be divided into intramedullary, intramedullary-extramedullary, and conus medullaris (Table 20.1).

Table 20.1 Modified Spetzler classification

Modified Spetzler classification	
Neoplasms	Hemangioblastomas, cavernous malformations
Aneurysms	
Spinal arteriovenous malformations	
Dural AV fistulas	Intradural
	Ventral
	Dorsal
	Extradural
Arteriovenous malformations	Extradural-intradural
	Intradural
	Intramedullary
	Intramedullary-extramedullary
	Conus medullaris

Table 20.2 Borden classification

Borden classification of dural arteriovenous fistulous malformations (cranial and spinal)		Subtype
Type I	Direct drainage into dural venous sinus or meningeal vein	A: single fistulous connection
Type II	Drainage into dural venous sinuses or meningeal veins + retrograde flow into SA veins	B: multiple fistulous connections
Type III	No drainage into dural sinus or meningeal veins + retrograde flow in SA veins	

The Borden classification system (Table 20.2) defines both cranial and spinal dural arteriovenous fistulous malformations (AVFMs) into three types. Type I consists of dural AVFMs that drain into dural venous sinuses or meningeal veins directly. Type II drains into dural sinuses or meningeal veins but has retrograde flow into subarachnoid veins. Type III drains into subarachnoid veins and does not have dural sinus or meningeal venous drainage. Meningeal arteries are the major blood supply, and there are subtypes of either subtype A being a single fistulous connection or subtype B being a multiple fistulous connection. Types II and III, as there is retrograde flow, have a higher hemorrhage rate and are at higher risk of early rebleeding [5].

Procedural Overview

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) is an important modality usually used as a screening tool for patients presenting with spine-attributed symptoms. Cord signal changes, cord edema, and flow voids may be observed that help the physician discern a potential vascular etiology for the patient's symptoms. Pulsation artifacts can sometimes be confused for abnormal vessels.

High-resolution MRAs with the TWIST sequence have been more recently used at our institution to look at specific suspected spinal levels which help narrow spinal angiography target areas to reduce radiation and contrast administration (Fig. 20.1).

Spinal Angiogram

Selective spinal angiography is the gold standard for imaging spinal vascular malformations (Fig. 20.2). Introduced by Di Chiro in 1965, the angiographer selects each radicular branch of the aorta and observes for signs of early drainage or a vascular malformation nidus [8]. Use of three-dimensional rotational spinal angiography has been described as a method to get a more detailed view of vascular malformation characteristics [9]. Care must be taken when reading a spinal angiogram as completeness of the study includes injection of the iliac arteries, the median and lateral sacral arteries, and the superior intercostal arteries.

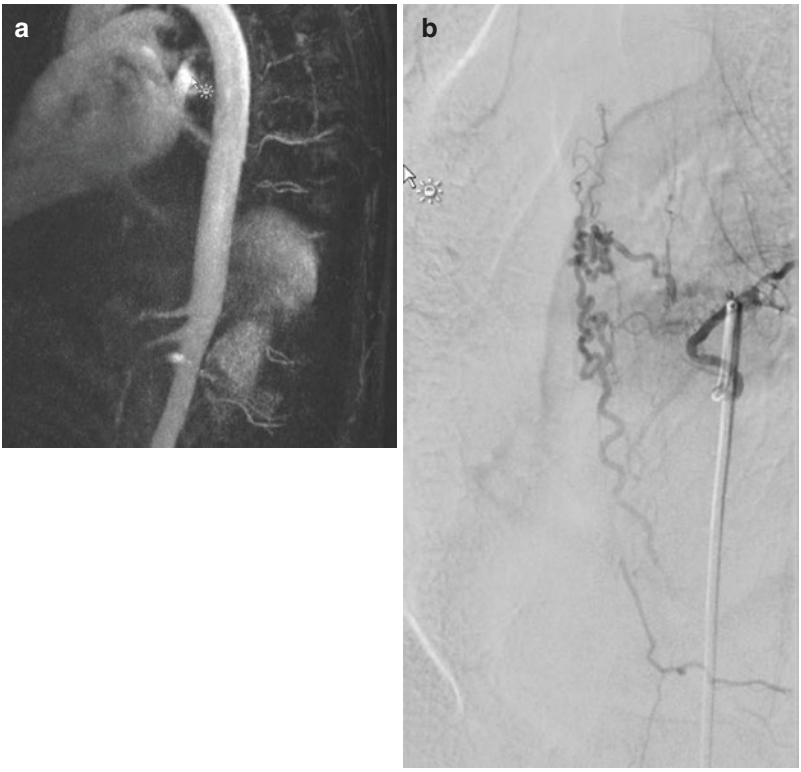

Fig. 20.1 **(a)** Magnetic Resonance Imaging TWIST Sequence Demonstrating an early draining vein at T7. **(b)** Anterior Posterior Spinal Angiography View of Same Patient at the Left T7 Radicular Artery with a Type I Dural Arteriovenous Fistula

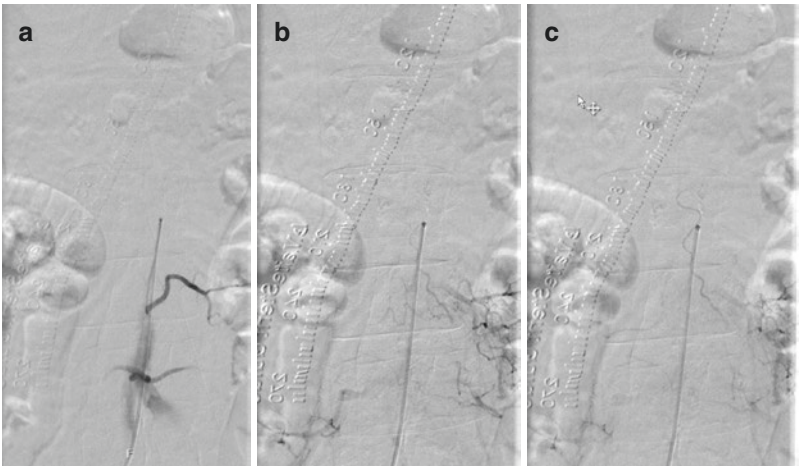

Fig. 20.2 Spinal Angiogram of Type 1 Dural AV fistula. Sequential images **(a–c)** demonstrating sinusoidal curve of early spinal draining vein

Intraoperative Tools and Techniques

The use of intraoperative microscope equipped with fluorescence imaging capabilities is now a standard of surgical resection [10].

Neuromonitoring

Neuromonitoring for spinal vascular malformations can be a useful tool particularly in resection an intramedullary lesion [11]. Fast changes from somatosensory-evoked potentials (SSEPs) can be seen with temporary clip placement on feeding arteries. Motor-evoked potentials (MEPs) and SSEPs should be monitored together to avoid "false negatives" [12].

Anesthesia

For neuromonitoring purposes, total intravenous anesthesia (TIVA) comprised of propofol and fentanyl is often used to maintain evoked potentials. Volatile anesthetics are known to suppress evoked potentials [13]. Remifentanil is less suppressing of MEPs in animal models but has been found in humans to have a dose-related response to suppression of MEPs and SSEP signals [14]. Precedex in addition to remifentanil and propofol does not appear to affect MEPs or SSEP signals [15].

Neuronavigation

Use of neuronavigation systems is often not needed for resection of spinal vascular malformations. Care must be taken, however, to verify from the spinal angiogram how the level of the vascular malformation was determined. This level count can be determined from the lowest rib being considered T12 from an anterior-posterior view or from the lateral determination of what is considered L5. If a transitional segment is seen with L5/S1, then the level should be agreed upon before localization is performed in the operating room to mitigate the risk of wrong level surgery.

Indocyanine Green Fluorescence

Indocyanine (IC) green fluorescent technology that is incorporated into the operating microscope has proven to be a valuable tool to establish feeding and draining vessels in cerebrovascular neurosurgery [16] and particularly in spinal vascular malformation operations [17]. Used at the beginning of the vascular malformation resection, the arterial feeding vessels and the early draining veins will sequentially appear followed by the normal draining veins. This gives real-time information for the surgeon in planning where to start cauterizing feeding vessels. The ability to identify normal draining veins and the major contributing arteries may help

preserve spinal cord function where previously determining the anatomy of the vascular malformation may have been more difficult [18]. In some cases, angiographic occult fistulas can be identified using IC green in areas that demonstrate MRI and clinical changes requiring exploratory surgery [19].

Intraoperative Angiogram

Though the intraoperative angiogram is possible in the prone position, at our institution, we often elect for transfer of the patient to the angiography suite after IC green angiography has demonstrated resection of the AVM or dural AV fistula. The surgical site is often closed, and necessary spinal closure or fusion is performed.

Intraoperative Doppler

Intraoperative ultrasonography and color Doppler is a tool that can be used to target intramedullary vasculature during resection [10]. The benefit of the tool is that even if the surgical field changes, ultrasound provides real-time feedback, does not require contrast or fluorescent dye administration, and gives a spatial orientation for the vasculature.

Surgical Approaches

The surgical initial approach will change depending on the location of the dural AVF or AVM. For lesions that are ventral to the dentate ligament in the cervical spine, an anterior approach to the vascular malformation could be chosen which consists of a corpectomy and post resection interbody graft and fusion [20]. In the cervical, thoracic, or upper lumbar spine, the approach may require a lateral exposure. Facet and rib resection with muscle flap elevation to minimize spinal cord retraction can be needed in the thoracic spine. Resection of spinal structural components often requires post resection fusion. Prior to removal of bone, a localizing x-ray should be done to confirm the location with particular care to verify that the technique used to identify the level on the spinal angiogram is also used in localizing the appropriate level in surgery.

Careful hemostasis should be performed to optimize visualization prior to dural opening. In some scenarios, opening the dura and egress of CSF will cause a fair amount of epidural venous bleeding. Tamponade with Gelfoam with thrombin, a cotton patty, and sometimes a foam clotting agent can help as well as dural tack-ups with 4.0 braided nylon suture. In cases where spinal cord retraction is needed, the dentate ligament may need to be cut to allow for gentle cord rotation. Arachnoid sutures or clips can be used to help elevate the cord.

Once the anatomic location of the fistula or AVM has been exposed, IC green fluorescence can be used to determine the main feeding arteries and early draining veins (Fig. 20.3). At this point, careful arachnoid dissection should be performed to allow for very accurate cautery of feeding arteries.

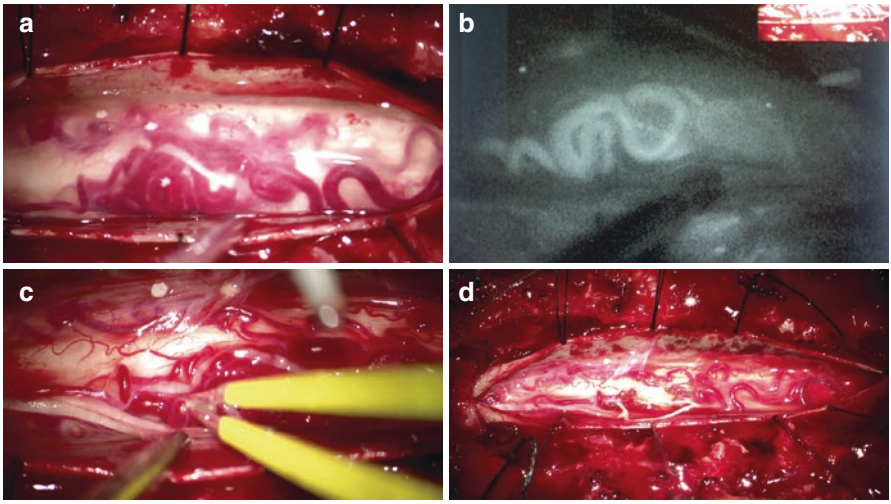

Fig. 20.3 Surgical Resection of Spinal AVM with Intramedullary Component through a Lateral Thoracolumbar Approach. **(a)** Demonstrates intraoperative microscopic view of dural sutures and a clean operative field with exposure of the AVM. **(b)** IC green run demonstrating the early filling of feeding vessels of the AVM. **(c)** Stepwise coagulation of feeding arteries using bipolar forceps and suction. **(d)** End of surgical resection with remaining un-involved spinal vessels left intact

Dural Arteriovenous Fistulas

In dural AV fistula, the arterialized draining vein should be skeletonized to allow for cautery and division. The arterialized radicular vein can usually be traced back to the nerve root foramen under the pedicle. If uncertain of the contribution of the vessel, a temporary aneurysm clip can be placed on the vessel to verify that the draining veins return to normal venous color and another IC green run can be performed.

Arteriovenous Malformations

Extradural-Intradural

Extradural-intradural AVMs, particularly the "juvenile" form, can be a formidable challenge. To decrease the risk of intraoperative bleeding, preoperative embolization of selected feeding arteries has been a successful technique used to resect these AVMs [21].

Intramedullary

Intramedullary lesions can be resected more successfully when the patient has a small compact nidus (glomus). There is greater difficulty and more likelihood of postoperative neurologic decline with multifocal or diffuse nidus [22]. In the thoracic spine and lumbar spinal cord, there is less redundant arterial circulation, so the risk may be greater with intramedullary AVM nidal resection [23]. Additionally,

incomplete resection may be elected if the risk of neurologic impairment is too great. There are limited studies as to the comparative long-term outcome of residual AVMs. In situations where there has been an intraspinal cord hemorrhage, the timing of surgery may be best when the patient is allowed to "cool off" from the hemorrhage but still operate early enough that the patient will not lose recently gained neurologic functional progress from surgery.

Conus Medullaris

Successful reports of treatment of conus medullaris AVMs have been published using a multidisciplinary approach of preoperative embolization and microsurgical resection [24].

Recovery from Surgery

Spinal Dural AV Fistula

Surgical resection has been found to be a definitive treatment of dural arteriovenous fistula which, in comparison, has been found to be more durable than endovascular embolization [25, 26]. Chibarro et al. retrospectively looked at 30 patients with surgically resection dural AV fistula and found that 83% had clinical improvement and there were no recurrences [26]. In the Steinmetz et al. study, all patients that had undergone treatment for their fistulae were evaluated. Of the patients that had surgery, 98% had complete obliteration of their fistula after the initial treatment compared to 46% with embolization. 89% of these patients demonstrated improvement or stability in their neurologic symptoms with surgery [25]. Other institutions have quoted higher success rates with embolization obliteration of the fistula and recommend either surgical or endovascular treatment of the fistula with significant improvement in outcomes with treatment [27]. In yet another study, Rosenblum et al. found that 88% of their patients who underwent surgery for their dural AV fistulas had good outcomes compared to 49% of patients with intramedullary AVMs [28].

Spinal AVM Outcomes

Results vary depending on anatomic pathology, patient selection, and combination of treatments. Yasargil found that with surgical resection of intramedullary AVMs that approximately 48% improved, 32% were unchanged and 20% worsened after 3 years postsurgery in 41 patients [29]. In an examination of 16 patients that underwent conus AVM resection with or without embolization initially with a mean follow up of 70 months, 43% of patients neurologically improved, 43% were stable neurologically, and 14% worsened. Of these patients, three recurred which included the two patients that had worsened. 75% of the patients that were initially nonambulatory regained the ability to walk, and those that presented able to walk did not lose that function unless there was a recurrence [24].

Complication Avoidance and Management

Spinal vascular malformations' surgical complications can include loss of spinal cord function in the form of sensory loss, bladder or bowel incontinence, and motor weakness below the level of the lesion and, additionally, the levels of the spinal cord supplied by the vasculature at the levels of the lesion. Additionally, intraoperative rupture of the vascular malformation leading to blood loss or intraspinal hematoma can occur. CSF leak and infection are risks of any intradural or spinal procedure. Spinal instability can occur in patients where the approach to the vascular malformation required the resection of important structural components of the spine.

Avoiding Loss of Function

Careful discussion with patients regarding the risks of surgery should be done prior to surgery. In patients with already significant loss of function from either spinal cord edema or hemorrhage from their lesion, discussion of preventing further loss of function and potentially allowing for permanent gains of return of function with physical therapy after successful complete resection of their vascular malformation can be done. In patients with relatively quiescent lesions, the potential for causing upfront loss of function in the hope of preventing future catastrophic events should be carefully weighed and discussed.

The surgeon should plan their approach to the lesion very carefully using appropriately detailed spinal angiography images. Neuromonitoring, IC green, and temporary clipping should be performed to verify intraoperatively that the vessels in question do not contribute to the normal spinal cord and are involved in early drainage in the vascular malformation. The surgeon will need to weigh the risk versus benefit of arterial sacrifice in the setting of complicated vascular malformations. Careful discernment of the neuromonitoring signals must be performed with good communication between neuromonitoring and neuroanesthesia. MAP and SBP goals need to be discussed prior, during and after surgery with the anesthesia team. Arterial monitoring is essential for managing cord perfusion.

Avoiding Intraoperative Hemorrhage

Intraoperative hemorrhage can occur in multiple scenarios. Aggressive dural opening and inadvertent rupture of the AVM can occur. In this scenario, the surgeon must be ready to quickly obtain hemostasis, be in communication with the anesthesia team regarding blood loss and blood pressure, and work systematically to carefully obtain control of the bleeding without jeopardizing neural function. Hemostasis can be done using temporary AVM clips, bipolar cautery, and temporary tamponade. Premature occlusion of the draining vein can lead to intranidal hemorrhage. The surgeon must be watchful for enlargement of the spinal cord as with intramedullary AVM; the hemorrhage may occur within the spinal cord and be enclosed in neural tissue. Care must then be taken to evacuate the hematoma and obtain hemostasis while attempting to maintain the integrity of the neural tissue. Temporary clipping of the draining vein when all arterial feeders are felt to have been ligated is a way to test the resection prior to ligation of the draining vein. Postoperative angiogram

should be performed to verify complete resection of the AVM to prevent future hemorrhage potential. Additionally, careful blood pressure monitoring should be done in the perioperative time period to prevent risk of perfusion-related hemorrhage or ischemia within the spinal cord.

Avoiding CSF Leak and Infection

As with any dural closure or, for that matter, spinal procedure, CSF leak can be a risk. Careful closure of the dura, usually with a running dural suture, should be performed. The suture should match the diameter of the suture needle. A larger needle may lead to leakage around the suture puncture sites if the suture is not picked carefully. Additionally, the surgeon can choose to use sealants, blood-soaked Gelfoam, muscle patches, etc. to reinforce their suture line. Care must be taken to avoid compression of the spinal cord with aggressive sealant, patches, or inadequate hemostasis. Copious irrigation, careful watertight closure, systemic glucose management, and perioperative antibiotics can help enable wound healing and prevent CSF leak and infection. Additionally, some surgeons consider CSF drainage system (i.e., subarachnoid drain) placement perioperatively to help aid in wound closure as well as a period of lying flat (usually 24–48 h) to prevent increased pressure on the dural closure.

Avoiding Spinal Instability

Whether done solely by the vascular neurosurgeon or in collaboration with another surgeon who specializes in spinal stability, care must be taken to appropriately expose the vascular malformation as well as plan for spinal stabilization if needed. Appropriate instrumentation should be available for the surgical case in the event that it is needed.

Conclusion

Surgical treatment of spinal vascular malformations requires careful planning and detailed imaging and can be made more successful with the use of the aforementioned intraoperative tools. Patient expectations must be managed preoperatively with a realistic informed consent of the possible outcomes given the fragile vascular supply to the spine. Postoperative imaging and close follow-up should be performed to watch for recurrence as recurrence or incomplete resection can cause continued neurologic decline.

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Part III

Endovascular Procedures

Access and Closure

21

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Checklist: Arteriotomy Access and Closure

Equipment needed	Procedural steps
Neurophysiology • None Nursing • Confirm patient medication list (e.g., antiplatelets/anticoagulants) • Assess and document distal pulses • Confirm pre-procedure arterial ultrasound/Allen's test if radial artery access planned • Review serum chemistries and blood counts Anesthesia • Local anesthesia with 2% lidocaine. Bicarbonate can be added to decrease pain • Analgesia/sedation during puncture • IV antihypertensive medications for SBP <185 (to decrease the risk of dissection during access) Neurointerventionalist • Review anatomic landmarks for access • Judicious use of pre-puncture fluoroscopy/ultrasound to confirm positioning	Access • Marking anatomic/fluoroscopic/US landmarks • 18-gauge/21-gauge needle access followed by dilation as needed • Advance the appropriately sized sheath using Seldinger technique • Attach to heparinized saline flush line • Post-arteriotomy fluoroscopy/angiography to assess arteriotomy Closure • Manual compression >15 min, based on medication history, sheath size, and heparin administration. • Check ACT as appropriate if anticoagulation administered. • Closure device if warranted. Management • Post-procedure evaluation of arteriotomy site • Distal pulse, capillary refill, vital signs, and neuro checks for Q15 min × 1 h, Q30 min × 2 h, and then Q60 min × 4 h • Monitoring for a potential retroperitoneal hemorrhage: assessment of flank pain, hematuria, and limited urine output • Outpatient instructions for care of the arteriotomy site and daily activity

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Vasospasm	Excessive wire manipulation Smaller arteries with high sheath: artery ratio	Intra-arterial calcium channel blockers/ vasodilators Time	Careful wire manipulation under fluoroscopic guidance Using the smallest sheath necessary
Hematoma	Poor primary closure of the vessel Persistent anticoagulation after interventional procedure	Extended manual compression Fixed, extended compression device	Extended compression time Good closure device techniques Adequately assessing compression time with the use of an pre-closure ACT
Retroperitoneal hemorrhage	High puncture above the inguinal ligament with inadequate closure of an arteriotomy	Low threshold of suspicion, with urgent CT abdomen/ pelvis Urgent surgical consultation for potential repair	Avoiding arteriotomies above the inguinal ligament Judicious use of ultrasound/ fluoroscopy pre-puncture Assessing puncture site on fluoroscopy prior to closure
Pseudoaneurysm	Dissection of arterial wall during access or during closure with a device	Manual compression Direct thrombin injection Endovascular coiling stenting Surgical repair	Good arteriotomy access and closure techniques
Limb ischemia	Dissection or flow-limiting thrombosis at the arteriotomy site	Surgical repair Heparin	Avoiding punctures below the common femoral artery bifurcation Avoiding using closure devices in small arteries Serial puncture site and distal pulse/capillary fill time assessments
Dissection	Difficult arteriotomy access or wire advancement Traumatic sheath insertion Damage during closure device placement	Antiplatelet medications vs. heparin Stenting/bypass Surgical reconstruction	Judicious use of ultrasound/ fluoroscopy pre-puncture Good arteriotomy access and closure techniques

Introduction

When addressing endovascular procedures, complication avoidance is often aimed at the critical portions of a procedure where the risk for a catastrophic outcome is the highest, for example, when deploying a framing coil in a ruptured aneurysm or delivering a liquid embolic to a potential area of eloquent cortex adjacent to an AVM. A perfectly framed aneurysm can be a satisfying result for both the interventionalist and the patient, but this success is easily belittled when access site complications occur at the beginning or end of an endovascular procedure. Formidable complications, such as the loss of a limb, or even the need for unplanned rescue procedures or surgeries required to treat the complications, are avoidable with prudent preparation from the interventionalist. This chapter will address complication avoidance in arteriotomy site access and closure, as well as management when these unfortunate outcomes manifest.

Procedural Overview

Arteriotomy: Access

Several arteriotomy sites can be used for neuroendovascular procedures, which include the common femoral artery, the radial artery, the brachial artery, or even the carotid artery. The right common femoral artery is typically a preferred access site because of patient positioning and straightforward access compared to other sites, and it is easier to close with manual compression against the femoral head. This site can also afford larger-bore arterial sheaths than other peripheral sites, such as the radial artery. Using fluoroscopy to identify the access site at the level of the femoral head (below the inguinal ligament and above the common femoral artery bifurcation) or using an ultrasound to localize the common femoral artery may be helpful, if clinical landmarks are difficult to delineate. A single-wall puncture should be attempted using a 21-gauge needle (micropuncture kit) in case of coagulopathy; otherwise an 18-gauge needle can be used. Pulsatile blood flow and a left-sided projection of the guide wire into the aorta can confirm arterial versus venous access (Fig. 21.1). Using a long sheath is advisable in cases of tortuous iliac arteries; otherwise a 10 cm sheath can be used. A flush line of heparinized saline should be connected to the sheath to prevent thrombus formation within or around the sheath. The size of the sheath should be tailored to the goal of the endovascular procedure. The majority of diagnostic procedures can be performed through the use of a 5 French catheter delivered through a 5 French sheath (Fig. 21.2). Pediatric cases often utilize a 4 French sheath so that the arteriotomy is smaller when compared to the vessel diameter. Interventional procedures typically require larger access ranging from 5 to 10 French sheaths. If arterial transduction is necessary, a line can also be connected to the sheath for continuous blood pressure monitoring, though a slightly larger sheath is necessary (1 French larger than the guide catheter).

Using alternative access sites, such as radial, brachial, axillary, and common carotid arteries, can be helpful in case of inaccessible femoral sites or tortuous/

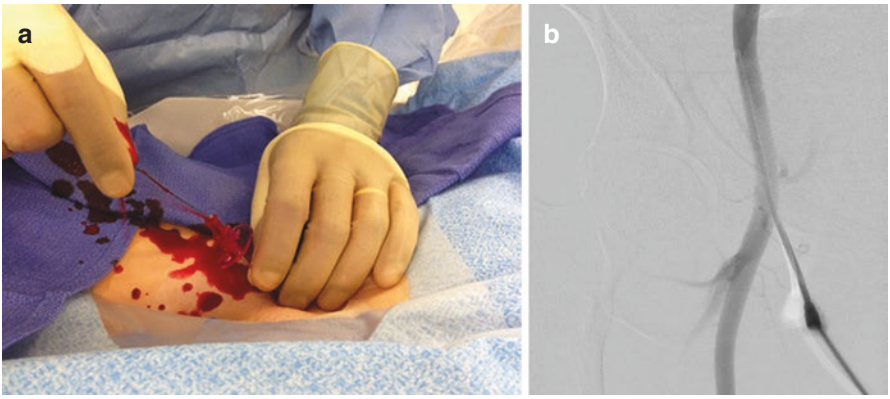

Fig. 21.1 (**a**) Common femoral arteriotomy: the pulse is palpated 2 finger widths below the inguinal ligament. The needle is advanced along the course of the artery, at 45° from the skin, and between two fingers. A J-shaped guide wire is introduced after noticing pulsatile blood flow. (**b**) Right common femoral angiographic run demonstrating the puncture site above the artery bifurcation and below the inguinal ligament, with no evidence of complications

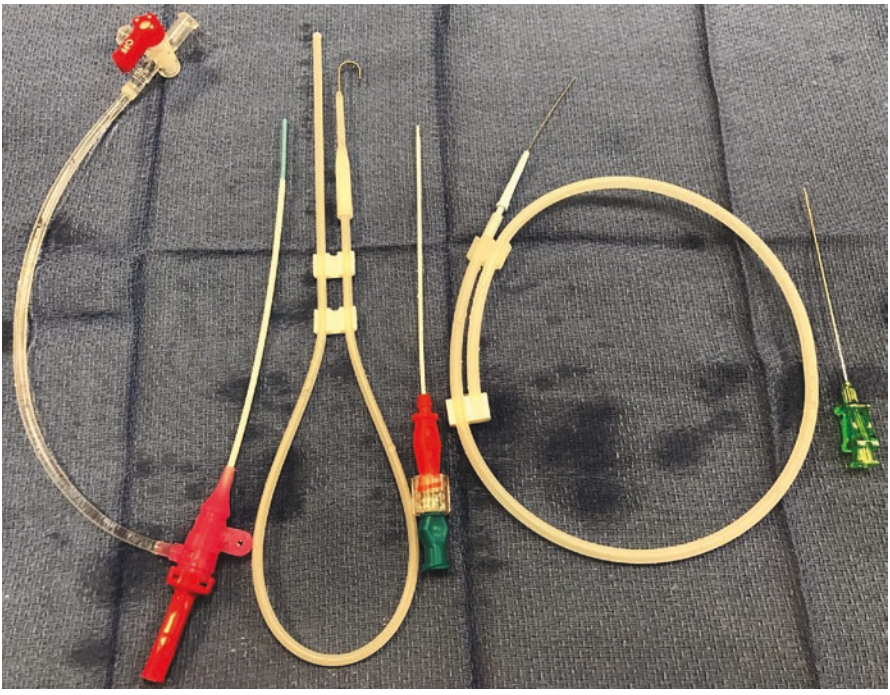

Fig. 21.2 5 French arteriotomy micropuncture kit. From *left* to *right*: 5 French sheath with introducer, J-wire, MicroSheath, 21-gauge microwire, 21-gauge needle

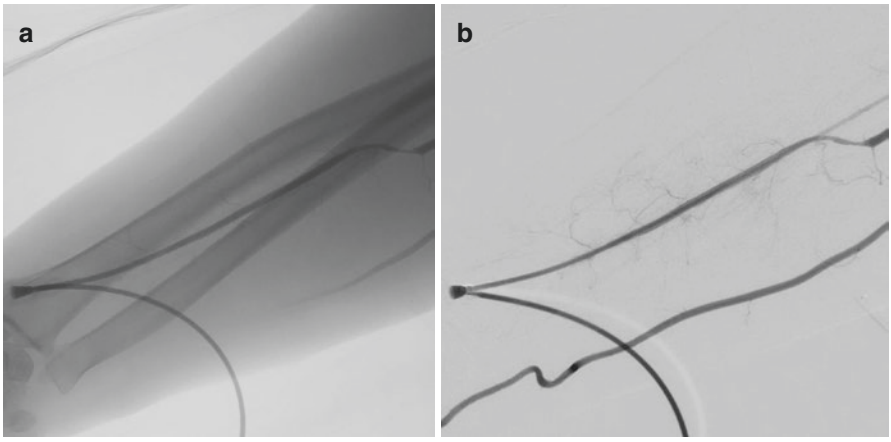

Fig. 21.3 (**a**) Radial access sheath, unsubtracted image. (**b**) Subtracted image demonstrating spasm just distal to the sheath

diseased thoracic aortas. These alternative sites have the advantage of early post-procedure ambulation and the disadvantages of difficult access to the contralateral carotid and vertebral arteries and a higher risk ofvasospasm or occlusion (in radial access) [1–3] (Fig. 21.3).

Arteriotomy: Closure

Closing the arteriotomy site can be achieved by manual compression, placing an external compression device, or inserting an arteriotomy closure device. In the majority of diagnostic procedures where patients are not on an intensive antiplatelet regimen or anticoagulation and heparin is not bolused, manual compression of the arteriotomy is a standard technique. Near occlusive manual compression should be applied for approximately 15–20 min for a 5 French arteriotomy to ensure hemostasis, followed by the patient lying supine for at least 5 h. Placing a knee immobilizer can help ensure that the patient does not flex his/her leg during this time period. Additional compression time is warranted for larger arteriotomies or if the patient takes antiplatelet or anticoagulant medications and compression is chosen as a closure technique. Noninvasive external compression devices such as FemoStop™ (balloon) or CompressAR™ (clamp) can also achieve hemostasis while saving the operator's time (and hand cramping), but the data favoring these devices over manual compression is debatable. Invasive arteriotomy closure devices such as Angio-Seal™ (collagen plug, Fig. 21.4), StarClose™ (clip device), and ProGlide™ (suture device) are useful in cases with larger arteriotomies or in the presence of a coagulopathy, when manual compression would take a longer time to achieve hemostasis. Patients can ambulate earlier after using an arteriotomy closure device, but the same arteriotomy site should not be used for 90 days until the collagen plug completely dissolves. Studies have shown similar complication rates comparing arteriotomy closure devices to manual compression [4–13].

Fig. 21.4 6 French Angio-Seal™ closure device™ with collagen plug

Complication Avoidance and Management

Despite a seemingly straightforward arterial access and adequate closure, complications can still arise. The interventionalist must be aware of potential arteriotomy complications such as development of a hematoma, pseudoaneurysm, retroperitoneal bleed, arteriovenous fistula, vasospasm, dissection, or limb ischemia. These complications occur in less than 2% of the cases [14]. The incidence of these complications can be reduced by practicing safe arteriotomy techniques such as using a 21-gauge needle when needed, achieving a single-attempt single-wall arteriotomy, connecting the sheath to a flush line, performing confirmatory angiography/fluoroscopy, using alternative access sites if needed, and following cautious postoperative arteriotomy site care. Immediate arteriotomy complications such as vasospasm or dissection can be assessed by performing an angiographic run or fluoroscopic loop (Fig. 21.4). This post-arteriotomy imaging can also assist in determining the use of closure techniques discussed above.

Vasospasm

Vasospasm is a not uncommon complication that is more prevalent in smaller vessels without atherosclerotic disease. Arteries with a higher percentage of smooth muscle, such as the radial artery, are more predisposed to spasm. Vasospasm at access sites can arise from excessive wire manipulation, difficult advancement of a sheath, or when a sheath abuts or irritates the wall of the vessel being accessed. Judicious wire placement and post-arteriotomy angiography are helpful in preventing and monitoring for spasm. When observed, it is prudent to slightly retract the sheath away from the wall of the artery and reassess flow within the vessel. Significant, persistent vasospasm requires administration of vasodilators, e.g., verapamil or nitroglycerin, until there is resolution. Dosing of vasodilators is dependent on the degree of vasospasm, but the authors of this text typically use 2.5–10 mg of verapamil and/or 50–200 mg of nitroglycerin. In radial arteriotomies, the incidence of vasospasm is higher, so it is prudent to prophylactically administer an intra-arterial "cocktail" including verapamil and/or nitroglycerin during sheath insertion.

Hematoma

Hematomas can occur from incomplete closure of an arteriotomy secondary to inadequate duration of compression, inadequate inability to form a platelet plug, or failure of a closure device. They can occur acutely or they can be delayed in onset.

A detailed history with dedicated questions regarding bleeding diatheses and antiplatelet/anticoagulant use can help the interventionalist plan for the appropriate duration of manual compression. Serial arteriotomy site/distal pulse checks, as frequent as every 15 min for the first hour and every 30 min for the second hour, can help detect early hematoma formation. Education regarding immediate level of activity and bed rest to both the patient and the supervising nurse can also help avoid delayed hemorrhage. Arteriotomy hemorrhagic complications are usually primarily managed by applying extended manual compression, though in case of large hematomas, vascular compromise may require urgent surgical treatment from vascular surgery.

Retroperitoneal Hemorrhage

A low threshold of suspicion should always be present for retroperitoneal hemorrhages, as these can be life threatening. Pain radiating into the abdomen, flank, and back, reduction in urine output, or new hematuria should raise concern. Tachycardia and hypotension can often be delayed, as several liters of blood can pool in the retroperitoneal space prior to hemodynamic compromise. CT angiography of the abdomen and pelvis as well as a general surgery consultation should be performed emergently when appropriate to deem whether surgical repair of the arteriotomy is necessary.

Pseudoaneurysm

Access site pseudoaneurysms occur in approximately 0.1% of procedures. The percentage is increased when closure devices are used, but good closure techniques can decrease the risk of vessel injury. Small pseudoaneurysms under 2 cm can be treated successfully with manual compression or direct thrombin injections, but larger lesions may require surgical/endovascular treatment. Evolution of pseudoaneurysms into arteriovenous fistulas has been described, and the interventionalist must be vigilant of this potential outcome.

Dissection

Vessel dissection is observed in approximately 0.3% of arteriotomies. It can result in limitation of flow leading to limb ischemia, pseudoaneurysm formation, hematoma, or retroperitoneal hemorrhage. We advocate the use of a single-wall puncture whenever possible and judicious use of micropuncture kits when appropriate. Visualization with post-arteriotomy angiography or Doppler ultrasound is useful in making the diagnosis. Treatment can range from antiplatelet medications to endovascular stenting or open vascular repair [15].

Limb Ischemia

Both the upper and lower extremities have good collateral arterialization, but limb ischemia can still result if there is a significant diminution in overall blood flow through the blood vessels distal to the arteriotomy. Clinically, it can present with decreased distal capillary refill times, a reduction of distal pulses, or a cold extremity. A low threshold of suspicion must be present to preserve an extremity, and an urgent consultation from vascular surgery is recommended. Avoidance is achieved by good puncture techniques to prevent dissection and limiting the use of closure devices in smaller vessels.

Conclusion

Arteriotomy access and closure are often overlooked as potential areas of complication avoidance due to their routine practice in all endovascular cases. Correlating anatomical, ultrasonic, and fluoroscopic landmarks prior to an arteriotomy as well as angiographic confirmation of successful access can assist in mitigating these complications. Meticulous perioperative and postoperative care is crucial in the prevention, early detection, and management of peripheral complications. It is critical to evaluate the puncture site and distal pulse frequently for the complications discussed in this chapter. Standardized order sets should be utilized for regimented monitor of adverse events, and clear discharge instructions regarding puncture site care, activity level, and follow-up plan should be provided to the patient to ensure that there are no delayed-onset issues with the arteriotomy.

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Iatrogenic Large Vessel Injury

22

Jay Ashok Vachhani, Adam Stephen Arthur, and Daniel Alan Hoit

Checklist: Iatrogenic Large Vessel Occlusion

Aortic dissection
• Extremely rare complication of angiography (quoted 0.06% during coronary angiograms)
• Cardiology literature suggests close monitoring and early surgical consultation
Injury during cerebral angiography
• True incidence of dissection unknown, but quoted to occur in 0.1–0.6% of cerebral angiograms
• Optimal management is controversial and remains unclear. Early anticoagulation with heparin and eventual transition to aspirin, clopidogrel, and/or warfarin has shown good outcomes
• Aspirin and clopidogrel have a lower risk of hemorrhagic complications and warfarin has a lower risk of ischemic complications
• Stenting is typically reserved for patients with clinically significant stenosis despite maximal medical management
Injury during spine surgery
• Uncommon injury that usually occurs during instrumented fusion of the upper cervical spine
• Optimal management depends on the extent of injury and collateral blood supply. Options include medical management with blood thinners, primary vessel repair, vessel sacrifice, or stenting
Injury during central venous catheter insertion
• Estimated to occur in 0.5–11.4% of internal jugular vein central venous catheter insertions
• Practice guidelines recommend use of real time ultrasound to achieve a higher first insertion attempt success rate, reduced access time, higher overall successful cannulation rate, and decreased rate of arterial puncture

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Radiation induced injury
• Recommend medical management with antiplatelet medications
• Cerebral revascularization is reserved for patients that fail maximal medical management
• Carotid stenting is recommended for symptomatic radiation induced cervical carotid stenosis due to the high risk of surgery
Injury during cranial surgery
• Even if the injury can be primarily repaired with suture, the patient should be monitored with serial non-invasive imaging to watch for thrombus or pseudoaneurysm formation
• If primary repair is not possible, options include vessel sacrifice with or without bypass or endovascular repair with stenting or coiling
Chiropractic injury
• Significant controversy exists on the true incidence of chiropractic injury to the vertebral and carotid arteries due to under-reporting and lack of large studies
• Estimates on the incidence of symptomatic vertebral artery dissection from chiropractic manipulation range from 1 per 228,000 and 1 to 2,000,000 manipulations

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Aortic dissection	Tortuous anatomy Poor visualization of the descending aorta during catheter advancement Excess load in the system	Conservative management Early surgical consultation Potential heparinization	Fluoroscopy during initial catheter introduction
Carotid/vertebral dissection	Tortuous anatomy without 1:1 manipulation of wire to catheter Poor visualization of the catheterized vessel Excess load in the system	Antiplatelet agents, e.g., ASA, clopidogrel, dipyridamole, or ticagrelor, vs. anticoagulation Stenting if >70% narrowing/poor collaterals	Assess need of catheter-based angiography vs. noninvasive imaging Liberal use of road maps Continuous/frequent heparinized saline flush Careful guide wire manipulation Remove load from the system after catheter advancement
Dissection/stroke during spinal surgery	Transarticular/pedicle screw fixation Prolonged retraction	Depends on extent of injury Conservative management with neuromonitoring and imaging Antiplatelet agents Primary vessel repair Vessel sacrifice Stenting	Visualization of arterial structures on CT angiography of the neck Careful placement of retractors. Limit retraction time/ strength Intraoperative monitoring

Complication	Cause	Remedy	Avoidance
Dissection during cranial surgery	Poor visualization of arterial structures during transsphenoidal surgery Underlying tortuous/ calcified vasculature	Initial treatment with cottonoids/Gelfoam Conservative management with neuromonitoring and imaging Primary vessel repair Vessel sacrifice Stenting/bypass	3D visualization of arterial structures on CT angiography of the head Intraoperative monitoring
Perforation/ dissection during central venous catheter insertion	Lack of imaging guidance Arterial structures overriding the veins	Manual compression Surgical repair Endovascular Stenting/balloon tamponade	Follow guidelines for using a real-time ultrasound in all central line insertions
Radiation-induced injury	Radiation doses to affected area> 50Gy	Antiplatelet medications Stenting/bypass Surgical reconstruction	Limit total radiation dose/field

Introduction

Iatrogenic large vessel injuries are an uncommon, usually benign, but potentially catastrophic complication of cerebral angiography and a variety of surgical and nonsurgical procedures. While it is impossible to completely avoid this complication, the risks of it occurring and potential harm to the patient can be minimized through appropriate patient selection, careful preparation, and correct identification and management once a complication has occurred. This chapter will briefly review the causes and treatments of iatrogenic large vessel injury.

Procedural Overview

A 57-year-old male presented with right-sided neck pain, facial pain, and trismus. He had no significant past medical history. Two weeks prior to presentation, he underwent a dental procedure in which a local anesthetic needle was fractured in his oropharynx without an attempt at retrieval. A computed tomography (CT) scan (Fig. 22.1) demonstrated a 2 cm by 1 mm foreign body consistent with a needle fragment penetrating the right internal carotid artery with the proximal and distal ends outside of the lumen.

Initially, he underwent a transoral exploratory surgery by vascular surgery and otolaryngology. This procedure was aborted due to the inability to identify the needle. A second CTA showed the needle had migrated further into the jugular foramen as a result of the surgical manipulation (Fig. 22.2). The proximal end of the needle was now entirely within the cervical internal carotid arterial lumen making an attempt at endovascular retrieval possible.

Under general anesthesia, an 8 French FlowGate (Stryker Neurovascular, Fremont, CA) balloon guide catheter was deployed in the right internal carotid artery through a 9 Fr short femoral sheath (Fig. 22.3). A 4 mm GooseNeck Microsnare

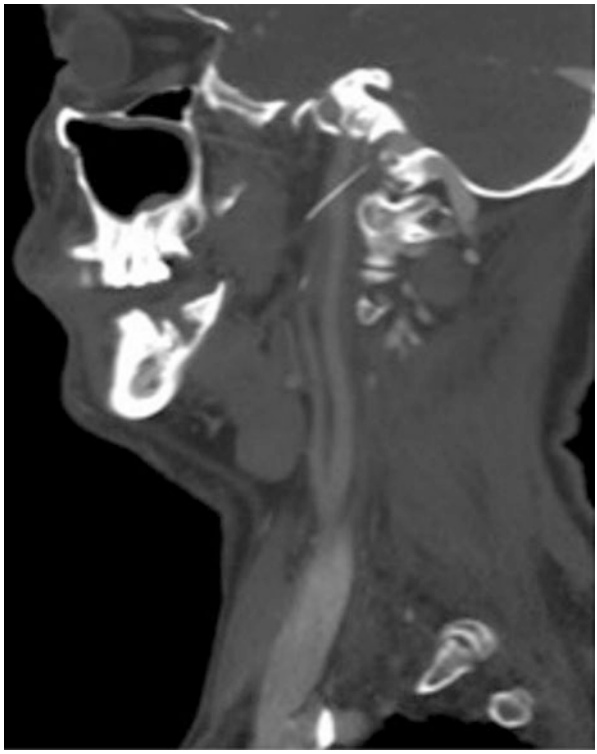

Fig. 22.1 CT scan showing needle fragment adjacent to the right internal carotid artery extending into the jugular foramen

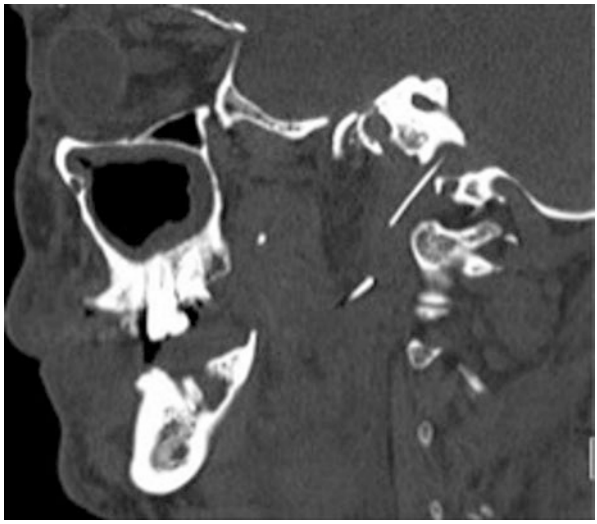

Fig. 22.2 CT scan following exploratory surgery showing metallic fragment entering the jugular foramen

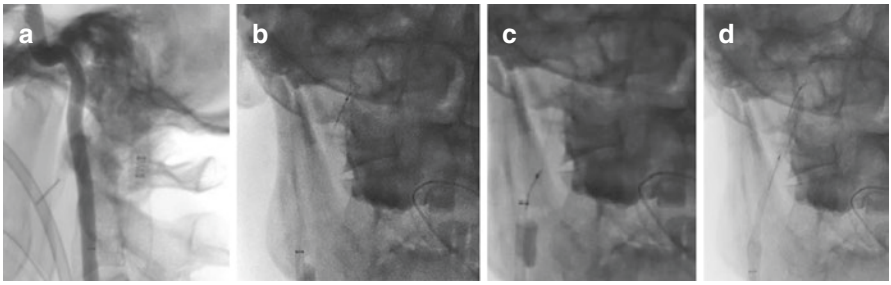

Fig. 22.3 (**a–d**) Endovascular retrieval of needle using a GooseNeck Microsnare and FlowGate balloon catheter

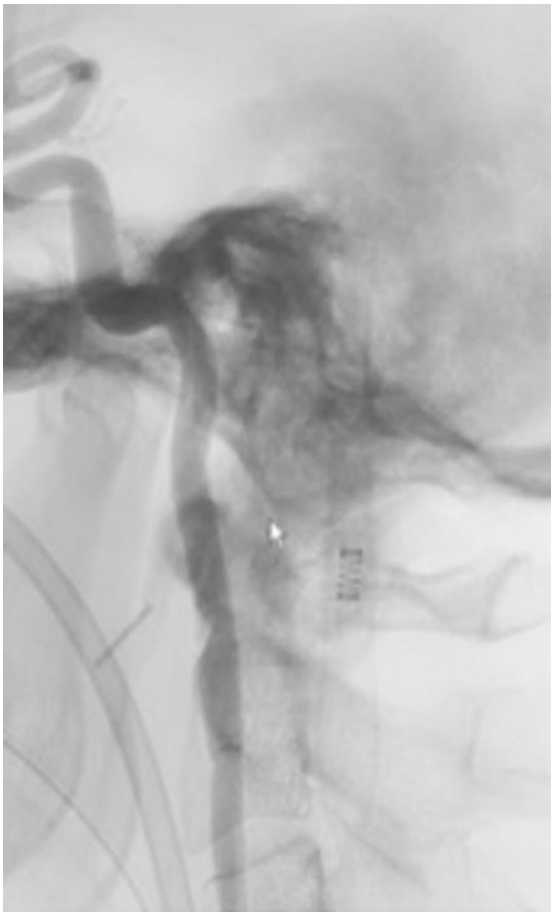

Fig. 22.4 Grade 1 dissection of the distal right cervical ICA after removal of needle

(ev3 Endovascular Inc., Plymouth, MN) was used to capture the proximal portion of the needle within the arterial lumen. Proximal flow arrest was accomplished by inflating the balloon on the guide catheter. The needle was slowly pulled proximally within the carotid artery until the needle was oriented longitudinally. In this orientation, however, the proximal needle end became embedded in the intima. We were unable to withdraw it into the guide catheter. A second snare was then used to capture the distal end. This enabled the manipulation of the needle using the two snares, and the needle was advanced forward into the cervico-petrous junction, freeing the back end from the intima and allowing the needle to be pulled into the guide catheter. The FlowGate balloon was deflated, and the catheter was removed with the two snares and the needle in the catheter lumen. Angiography showed a retrograde non-flow-limiting grade 1 ICA dissection with no contrast extravasation (Figs. 22.4, 22.5, and 22.6).

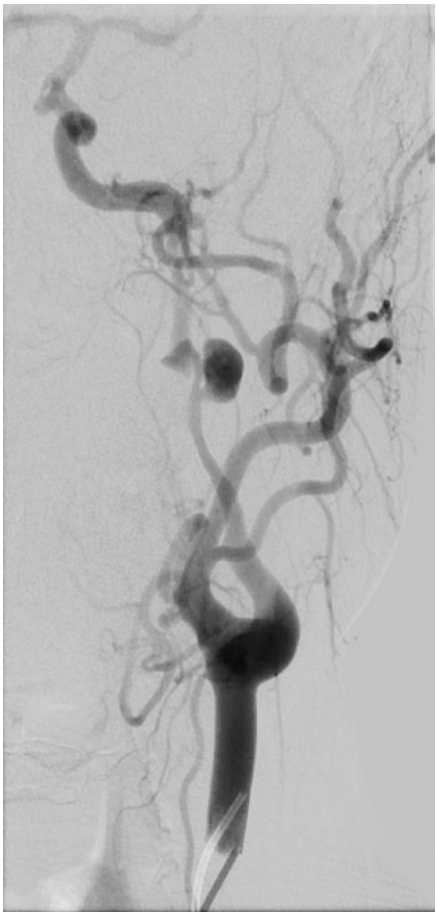

Fig. 22.5 Grade 3 dissection of the left internal carotid artery causing 95% stenosis. Patient presented with acute-onset aphasia and right upper extremity weakness and has a history of chronic chiropractic neck manipulation

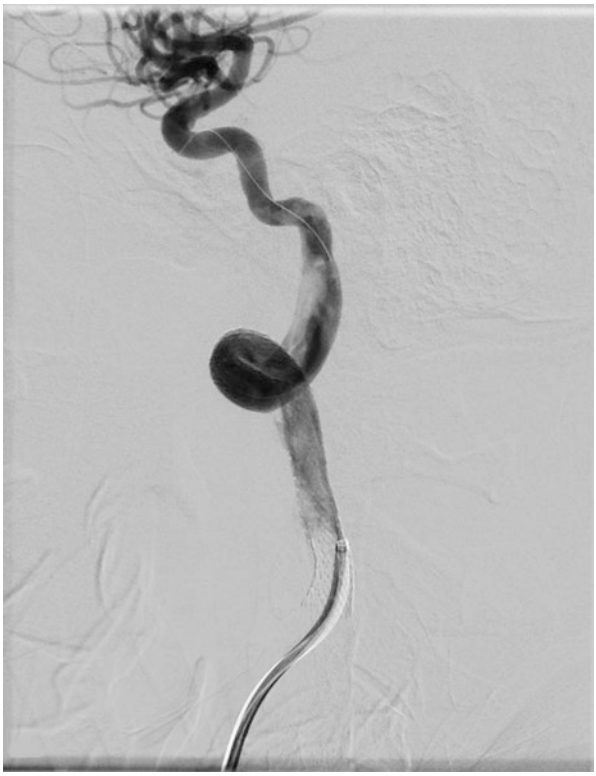

Fig. 22.6 Patient was treated with a left internal carotid artery stent due to persistent waxing and waning symptoms on maximal medical management. After stent placement, the patient remains asymptomatic with a National Institutes of Health Stroke Scale score of 0 and modified Rankin Scale score of 0

Iatrogenic Aortic Dissection

Iatrogenic aortic dissection is not well described in the neurointerventional literature. Although the complication is exceedingly rare, the majority of the published literature comes from case studies and case series from interventional cardiology. In their multicenter retrospective review, Nunez-Gil found an aortic dissection incidence of 0.06% during cardiac catheterization. Of the 74 patients with dissection, 36 were managed conservatively, 35 with angioplasty and stenting, and 3 with cardiac surgery. Two patients died of cardiogenic shock, and none of the remainder suffered any complications as a result of the dissection. The authors advocate a conservative approach with close monitoring and early surgical consultation [1].

Injury During Cerebral Angiography

Although the risk of dissection from cerebral angiography is low, it does occur. Prior to obtaining consent, the most important factor to consider is the utility of the test and risk of the procedure. Increasing age and medical comorbidities have been found to be associated with an increased rate of complications with cerebral angiography [2]. While catheter-directed angiography remains the gold standard, recent advances in computed tomography and magnetic resonance imagining technology have made cerebral angiography less necessary. The clinician must first ask whether the information that is needed can be obtained through noninvasive studies. Catheter-directed angiography of the cervical and cerebral vessels is thought to have a 0.1–0.6% risk of dissection [3–5]. However, the true incidence of vascular injury is likely higher as many of the infarcts may be silent. Bendszus and colleagues performed a prospective study of magnetic resonance imaging of patients before and after cerebral angiography. None of the patients suffered any neurologic deficits, but 23 out of 91 patients had bright lesions on diffusion-weighted imaging consistent with embolic infarcts [6].

Careful guide wire manipulation, liberal use of road mapping, and continuous or frequent flushing of catheters with heparinized saline are thought to reduce the risk of complications. Some studies have found neurologic complications to be more common in patients with cardiovascular disease and age greater than 55 years old and when fluoroscopy times were 10 min or longer [7]. Some have found a lower complication rate in the hands of more experienced angiographers [8], while others have not found significant differences between experienced and inexperienced angiographers [9]. Unfortunately, due to the retrospective nature of the studies and the low incidence of complications, the patient and procedural risk factors seem to vary from study to study. A thorough discussion of the risks and benefits of cerebral angiography is necessary for all patients when obtaining informed consent.

The optimal management of iatrogenic carotid or vertebral dissections remains unclear. No randomized controlled trial exists, and all treatment guidelines are based on small case series or expert opinion. Some authors advocate heparinization in the acute phase followed by aspirin, clopidogrel, or warfarin, with stenting reserved for patients with greater than 70% luminal narrowing with poor

intracranial cross circulation [5]. Groves et al. managed their iatrogenic dissections with no treatment in 29% of cases, aspirin alone in 35%, aspirin and clopidogrel in 25%, anticoagulation in 8.8% of patients, and stenting in one patient (1.5%). The majority of the patients that underwent no treatment did so because of a recent intracranial hemorrhage [4]. Both groups demonstrated a good neurologic outcome in greater than 90% of their patients [4, 5]. Early detection of injury and prophylactic medical treatment are both important to limiting neurologic morbidity from dissection.

Significant controversy exists regarding the optimal medical management for iatrogenic cervical carotid or vertebral dissections. Although not specifically designed to evaluate iatrogenic dissections, the Cervical Artery Dissection in Stroke Study was a randomized controlled trial to determine if anticoagulation or antiplatelet medications were superior in treating extracranial carotid or vertebral dissections. A total of 250 patients were randomized to receive anticoagulation (heparin followed by warfarin or warfarin alone) or antiplatelet medications (aspirin, dipyridamole, or clopidogrel alone or in combination) within 7 days of symptoms onset for 3 months. Overall, stroke occurred only in four patients (2%), three in the antiplatelet group and one in the anticoagulation group. Although there was no statistically significant difference in the rate of stroke between the two groups, the one patient that suffered a stroke in the anticoagulation group had a subarachnoid hemorrhage from a vertebral artery dissection with intracranial extension. No patients in the antiplatelet group suffered a hemorrhagic stroke, and no patients in the anticoagulation group suffered an ischemic stroke [10].

Injury During Spinal Surgery

Due to the proximity of the carotid and vertebral arteries, iatrogenic injury to these vessels is a rare but well-documented complication of cervical spinal surgery [11–17]. While the most common scenario resulting in dissection is vertebral artery injury during instrumentation of the upper cervical spine, cervical decompression via the anterior or posterior approach has been shown to place the carotid and vertebral arteries at risk [18]. Although the exact incidence is unknown, some reports have documented a rate of up to 8.6% during atlantoaxial transarticular screw fixation [19]. In a meta-analysis of the literature examining C2 pedicle screws versus transarticular screws, Eliott and colleagues found vertebral artery injury during 0.72% (26 of 3627) of transarticular screws versus 0.34% (10 of 2939) of C2 pedicle screws [20]. In a survey of 847 active members of the American Association of Neurological Surgeons/Congress of Neurological Surgeons Section on Disorders of the Spine and Peripheral Nerves by Wright and Lauryssen, the risk of vertebral artery injury was reported to be 4.1% per patient and 2.2% per screw inserted [21].

Injury to the internal and common carotid artery during spinal decompression is less common than injury to the vertebral artery. Recent studies have demonstrated that the average distance between the internal carotid artery and the C1 anterior arch is 3.7 mm on radiographic studies [22]. While exceedingly uncommon, injuries to

the internal carotid artery from posterior cervical screw fixation at C1 have been documented [23, 24]. Although dissection has not been documented from use of retractor blades during anterior cervical decompressions, an ischemic stroke due to thrombus formation from prolonged retraction of the common carotid artery has been documented. In order to prevent this devastating complication, the authors recommend careful placement of the retractor and adequate maintenance of cerebral perfusion pressure throughout the procedure [25].

Optimal management of carotid and vertebral artery injury during spinal surgery is controversial and depends on the extent of injury and the collateral blood supply. Options include medical management with blood thinners, primary vessel repair, vessel sacrifice (either endovascular or surgical), and stenting.

Injury During Central Venous Catheter Insertion

Inadvertent puncture of the common carotid artery is estimated to occur in 0.5–11.4% of internal jugular vein central venous catheterizations. In most instances, the patients remain asymptomatic after manual compression of the puncture site. More serious complications such as stroke, retropharyngeal hematoma, and arteriovenous fistula have been reported to occur, but the incidence is unknown [14]. Inadvertent vertebral artery puncture has also been reported but is significantly less common than inadvertent carotid puncture. Of the 45 cases of symptomatic vertebral artery injury after central venous catheter insertion, the majority occurred in the V1 segment, followed by the V2 segment. Patients who had symptoms immediately after the procedure presented with acute ischemic infarcts, whereas patients who presented in a delayed fashion usually had an arteriovenous fistula and/or pseudoaneurysm [15].

Optimal management of central venous catheter-associated carotid and vertebral artery injuries remains unclear. The majority of the evidence focuses on the use of ultrasound to reduce the risk of vascular injury during central venous catheter insertion [26]. Current practice guidelines published by the American Society of Anesthesiologists Task Force on Central Venous Access found category A1 evidence from meta-analysis of multiple randomized controlled trials for the use of real-time ultrasound to achieve a higher first insertion attempt success rate, reduced access time, higher overall successful cannulation rate, and decreased rate of arterial puncture [27].

Radiation-Induced Injury

Radiation-induced vasculopathy can affect the intracranial as well as the extracranial arteries of both children and adults. Intracranially, children are at highest risk of developing occlusion of large- or medium-sized vessels and possible development of moyamoya syndrome when receiving radiation younger than 7 years of age with a total radiation dose of greater than 50 Gy. Adults, on the other hand, usually present with stenosis or occlusion of major vessels without development of moyamoya

syndrome. Extracranially, radiation causes intimal damage and periadventitial fibrosis, which leads to arterial wall thickening and stenosis. Doppler sonography is the most common screening test, but conventional angiography is considered the "gold standard" for diagnosis. The incidence of stenosis greater than 50% to the carotid arteries after radiation treatment ranges from 11.7 to 78.9%. Spontaneous rupture of the carotid arteries is a rare but potentially fatal complication of radiation-induced damage that requires emergency endovascular occlusion [14]. In contrast, radiation-induced damage to the vertebral arteries has been documented but is far less common. Subclavian artery stenosis is a more common presentation of patients who have undergone radiation for breast or lung cancer. Patients will often present with vertebrobasilar insufficiency or ischemia to the upper extremity [15].

Management of intracranial radiation-induced damage focuses on medical management with antiplatelet medications, with cerebral revascularization reserved for patients who fail medical management. The management of extracranial radiation-induced arterial damage is more difficult because the natural history of radiation-induced stenosis is not well known. Due to the high risk of surgery, carotid stenting is recommended for symptomatic radiation-induced carotid artery stenosis [14]. Stenting of the vertebral artery is much more controversial due to its uncertain efficacy [28]. Surgical reconstruction using transposition and grafting has been described, but the optimal management remains uncertain [15].

Injury During Cranial Surgery

Inadvertent injury to the internal carotid artery during skull base surgery can be difficult to manage. Although the injury may be amenable to primary suture, such cases still need to be followed with serial noninvasive imaging to watch for thrombus or pseudoaneurysm formation. In cases where primary repair is not possible, vessel sacrifice with or without bypass may be necessary. Particular attention must be paid to the tortuosity of the cavernous internal carotid artery during transsphenoidal surgery. Careful inspection of the preoperative imaging may prevent this complication. Once bleeding is encountered, it should initially be treated with packing with cottonoids or Gelfoam. If primary repair is not possible, endovascular repair with stenting or coiling is preferred [14].

Chiropractic Injury

Significant controversy exists on the incidence of chiropractic injury to the vertebral and carotid arteries. Due to under-reporting and lack of large studies, definitive conclusions regarding the incidence of carotid and vertebral artery injury from chiropractic injury remain unresolved. There has been no clear causal relationship established between internal carotid artery dissection and chiropractic manipulation [29]. The relationship between vertebral artery injury and chiropractic manipulation is slightly stronger but still not clear. Estimates on the incidence of symptomatic

vertebral artery dissection from chiropractic manipulation range from 1 per 228,000 to 1 to 2,000,000 manipulations [15]. Until a concerted and cooperative study between chiropractors and physicians is performed, patients should be warned of possible vascular injury to the carotid and vertebral arteries from chiropractic manipulation of the cervical spine.

Conclusions

Medical and surgical advancements in patient care have had the unintended consequence of increasing the possibility of iatrogenic injury to the blood vessels of the body. Thankfully, most of these injuries are benign and are unlikely to result in significant harm. Aside from being able to recognize and treat these complications if they occur, physicians must have a thorough discussion of the risks and benefits of all medical and surgical treatments, so the patient is truly informed prior to giving consent.

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Stenting of the Great Vessels

23

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Abbreviations

CAS	Carotid artery stenting
CCA	Common carotid artery
CEA	Carotid endarterectomy
CTA	Computed tomographic angiogram or angiography
DSA	Digital subtraction angiography
ECA	External carotid artery
Fr	French [scale]
ICA	Internal carotid artery
IVUS	Intravascular ultrasound
NIHSS	National Institutes of Health Stroke Scale

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Checklist: Stenting of the Great Vessels

Equipment needed	Procedural steps
Radiology technicians • Balloons (4, 6 mm diameter) • Additional rotating hemostatic adapter and tubing • Dyna-CT protocol Nursing • Heparin • Protamine • Verapamil/nicardipine • Additional heparinized saline bag for line flush • Staff pager numbers – Neurosurgery – Anesthesia attending Anesthesia • Pressure monitoring equipment for mean arterial pressure • Propofol • Endotracheal tube (if not under minimum alveolar concentration) Neurointerventionist • Choice of balloons • Choice of multiple stents • Distal protection device • Proximal protection device	Identification • Recognized occlusion and inability to pass wire across lesion • Recognized migration of stent • Device failure • Recognized vessel dissection Initiate and Engage • Determine if alternative access needed • Anesthesia: vital signs • Anesthesia: additional assistance • Nurses and technologists to page for additional assistance • Technicians to open additional stents, wires as requested Repair • Angioplasty stenotic segment • Calcium channel blockers for vasospasm • Stent deployment over dissection • Additional imaging as needed

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Embolus	Inadequate anticoagulation	Re-bolus heparin	Check activated coagulation time is 2–3× baseline prior to lesion manipulation
	Nontherapeautic antiplatelet agents is adequate	*IV Gp IIb/IIIa inhibitors* *Re-bolus antiplatelet medications*	Preprocedure aspirin and Plavix effect assays, re-dose if needed
	Plaque microemboli	Close observation	Distal protection device
	Dissection	Prolonged heparin, antiplatelet therapy	Hydrophilic guidewire for vessel selection. Judicious advancement of microcatheter
Femoral hematoma	Groin closure failure	Pressure	Closure device, dilation of entry tract, prolonged compression, checking the ACT prior to closure
Hemorrhage	Vessel perforation	Balloon occlusion, possible stenting, consider heparin reversal	Careful wire or catheter manipulation

Introduction

The great vessels leading to the cerebrovascular circulation include the vertebral and carotid arteries, as well as their parent vessels, the subclavian and innominate arteries. Pathologies involving these vessels and requiring treatment may include atherosclerotic disease, spontaneous dissection, radiation injury, trauma, or iatrogenic injury from another procedure (surgical or endovascular).

Before delving into the nuances of great vessel stenting, interventionists should recognize that despite the "gold standard" role of digital subtraction angiography (DSA) in obtaining a diagnosis, the treatment of vascular disease does not come without risk. Therefore, an understanding of vascular anatomy and anatomical variants is paramount prior to any stenting of the great vessels. Complication avoidance must be advanced to the forefront of procedural planning because vessel perforation, iatrogenic stroke, and dissection are potential adverse outcomes any time the vasculature is accessed endovascularly. The reported rate of extracranial artery dissection from diagnostic DSA ranges from 0.07 to 0.3% and is higher for the vertebral artery than for the carotid artery [1, 2]. The mechanism of dissection is most commonly subintimal injection of contrast media. Most angiographically significant dissections remain clinically asymptomatic and resolve spontaneously with a 48 h course of anticoagulation therapy. Further treatment is with prolonged antiplatelet therapy or, in some instances, stenting of the dissection.

Carotid artery stenting (CAS) for atherosclerotic disease has been demonstrated to have long-term morbidity and mortality equivalent to that for carotid endarterectomy (CEA). The rate of perioperative stroke from cerebral embolism is reported to be higher with CAS than CEA [3–6]. Associated procedural risk factors for CAS include carotid tortuosity, distal landing zone, concentric calcification, pseudoocclusion, National Institutes of Health Stroke Scale (NIHSS) score > 10, femoral artery access difficulty, and renal disease.

Comparatively, a series of 87 brachiocephalic angioplasty and stent procedures included postprocedural complications consisting of brachial hematoma in 3.4% of cases, arteriovenous fistula requiring operative repair in 1.1%, brachial pseudoaneurysm requiring operative repair in 1.1%, femoral hematoma requiring operative repair in 1.1%, embolism to the brachial and left internal mammillary arteries each in 1.1%, congestive heart failure in 1.1%, renal failure in 1.1%, stent covering the left vertebral ostia in 2.3%, common carotid artery (CCA) dissection in 3.4%, and stroke in 2.3% [7].

Meanwhile, a series of 110 subclavian artery angioplasty and stenting procedures included eight failures due to atherosclerosis [8]. In this series, seven patients had complications including three with groin hematoma, two with peripheral emboli, and two with amaurosis fugax.

Another center reported 48 consecutive stenting procedures for occlusive lesions of the subclavian and innominate arteries [9]. They reported four complications: two cases of entry site hematomas, one of distal hand ischemia, and one cerebral ischemic event.

Patients with head and neck cancers who undergo surgical tumor resection and radiation to the neck are at risk for post-irradiated carotid blowout syndrome [10, 11]. In such patients, carotid pathology can be categorized based on risk of bleeding (threatened, impending, or active extravasation) or vessel irregularity on imaging (1, no disruption; 2, focal irregularity; 3, pseudoaneurysm; or 4, active extravasation) [10, 12]. Vessel reconstruction with stent placement or embolization is necessary to prevent extravasation in those at risk or to achieve hemostasis in those with active extravasation. Technical success of quelling active hemorrhage was achieved in all patients in both stenting and embolization groups. Complication rates of acute infarction for stenting and embolization are reported as 11.1% and 10.5%, respectively [10].

Trauma presents a unique challenge for great vessel stenting, both immediately with vessel integrity and on a delayed basis with the possibility of pseudoaneurysm development. A review of studies in the literature from 1995 to 2007 found reports of endovascular graft repair of the following great vessel injuries: 179 carotid artery, 13 vertebral artery, 7 innominate (brachiocephalic) artery or trunk, and 91 subclavian artery [13]. Blunt carotid injury, at 137 cases, was by far the most common reported injury followed by penetrating 39 and iatrogenic 7. Blunt injury is often easy to overlook because of distracting injury (traumatic brain injury, spinal cord injury, or torso injury) or patient intoxication. A grading scale has been developed to classify blunt trauma: I, luminal irregularity or dissection of the vessel with <25% to 50% narrowing; II, luminal irregularity or dissection with >50% narrowing; III, pseudoaneurysm; IV, occlusion; and V, extravasation [14]. Management involves a stepped treatment with anticoagulation as the basis for grade I injury, stenting for grades II and V, and coil embolization with stenting of grade III [13, 15, 16].

Patients with vertebral artery injuries most commonly present with tinnitus and pain, and the management involves conservative management with anticoagulation or intervention with vessel sacrifice via embolization. Dissection, although uncommon, may involve the basilar circulation and necessitate treatment via stenting or vessel sacrifice.

Subclavian and innominate injuries are also often quiescent in their presentation, though if symptomatic, upper extremity claudication is the most common finding. Again, conservative management is undertaken with antiplatelet agents or anticoagulants. However, there is debate concerning lesions that require treatment in the trauma population. The patients tend to be younger and more prone to being lost to follow-up. Thus, the choice between a bare-metal stent, requiring a longer course of anticoagulation, and a covered stent, which endothelializes more rapidly, is uncertain.

Procedural Overview

Great vessel stenting is fraught with potential perilous pitfalls at various stages throughout the intervention. Careful study of the preprocedural noninvasive vessel imaging (CTA/MRA) is paramount for success. An understanding of the arch type, location, and grade of vessel pathology and anomalous anatomy helps the intervention proceed without complication.

First, the creation of a vascular access site is required for endovascular angioplasty and stenting. At our institution, most interventional procedures are performed under conscious sedation. Femoral artery access is obtained >90% of the time. However, utilization of the smaller-caliber radial artery or brachial artery may be necessary for patients with poor femoral access or unfavorable aortic arch anatomy. Furthermore, in the cardiac literature, these approaches have been shown to have lower risk of access site bleeding and major complication [17, 18]. Also, upper limb approaches allow for direct access to subclavian or innominate pathology and may incur less risk of infection [19]. We will refer to these approaches as retrograde throughout this chapter.

Vascular access is achieved either through surgical cutdown or percutaneous exposure and dilation. The latter confers easier closure via a closure device. Either access site may be closed with suture and adequate hemostasis. Following the introduction of a sheath (6–9 French [Fr]) into the access site, a vessel run (angiogram) is obtained to verify arterial placement and the absence of access site dissection. A total of 70 units/kg bodyweight of heparin is administered intravenously for systemic heparinization.

Then, the guidewire is advanced to the aortic arch, and a diagnostic catheter is advanced. We use a 0.035-inch hydrophilic glidewire over which we advance the diagnostic catheter to climb the arch. A diagnostic angiogram is obtained to better characterize the vessel, lesion pathology. Three-dimensional reconstructions of the angiogram may be utilized for a better understanding of anatomical considerations, such as branching arteries, true lumen, and pseudolumen. Reconstructions from these noninvasive imaging studies are compared with the physiological live view provided by the DSA, and any variations are taken into account.

For lesions involving the brachiocephalic (innominate), common carotid (CCA), or left subclavian arteries, a retrograde approach is often required. The CCA or brachial artery is surgically exposed, and micropuncture of the artery is performed (Fig. 23.1). The microcatheter is advanced retrograde into the aortic arch.

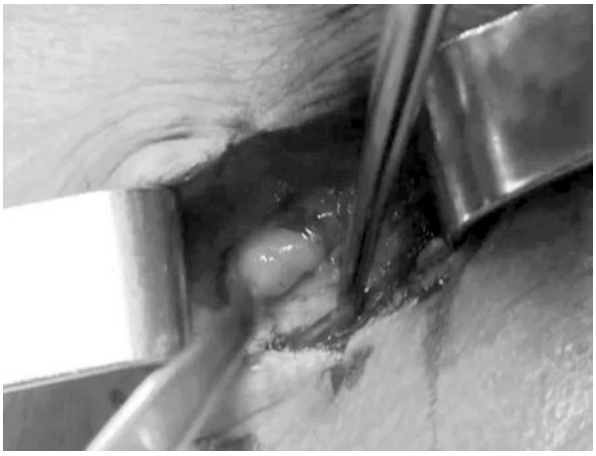

Fig. 23.1 Intraoperative photograph. Surgical cutdown access of the common carotid artery for retrograde access

Stenotic segments are often predilated with balloon angioplasty before deployment of the stent. This helps prevent poststent placement stenosis or premature separation of the balloon from the stent. Stent placement is undertaken with a balloon-expandable stent device or, alternatively, by a self-deploying/self-expanding stent.

Several variations of carotid artery stenting may be performed. To reduce the risk of thromboembolic complications, multiple distal embolic filters are available. Additionally, proximal protection devices, such as the Mo.Ma proximal protection device (Medtronic), can be deployed to prevent thromboembolic complications. Determinations of the selection of an embolic protection device are based primarily on provider preference, proceduralist comfort with use of the device, and degree of stenosis within the internal carotid artery (ICA). We favor distal protection as well as make every attempt to ensure that the filter time is minimized (<5 min in total) as well as avoidance of crossing the lesion (Fig. 23.2). For symptomatic carotid arteries with mobile plaque, the Mo.Ma device is utilized to prevent anterograde blood flow and, in essence, perform an "endovascular" carotid endarterectomy. The balloons on the Mo.Ma device occlude the external carotid artery (ECA)

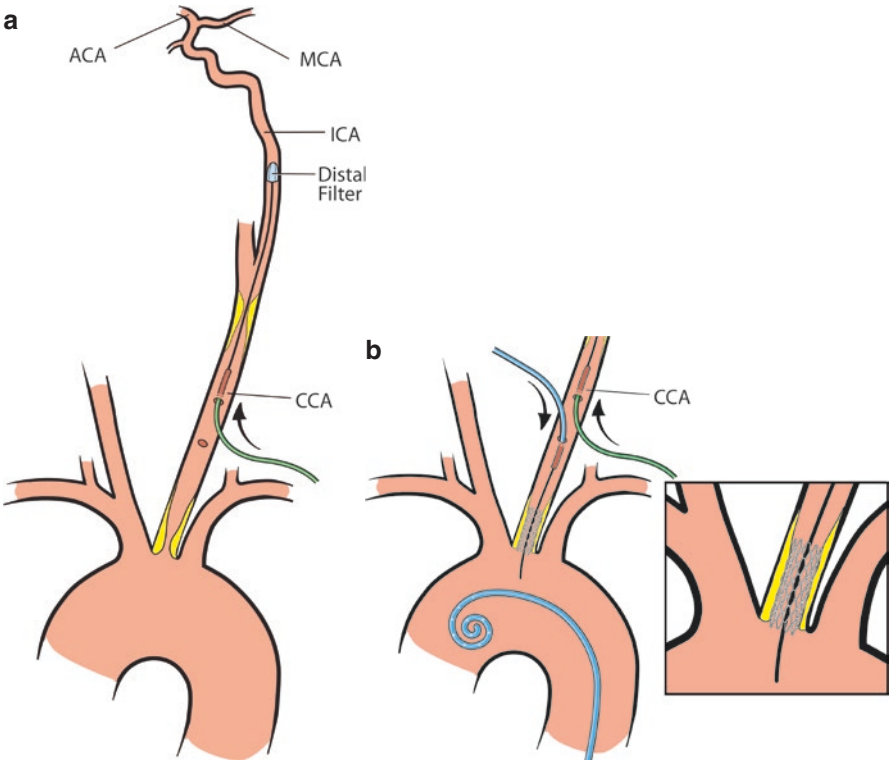

Fig. 23.2 Schematic illustrations. (**a**) Placement of a distal protection device from the surgical cutdown site. (**b**) Retrograde stent placement with distal carotid protection device

and then the ICA, allowing for complete anterograde flow arrest. Furthermore, should concern exist for thrombus or mobile plaque, we use the Wallstent (Boston Scientific) as it is a closed-cell system, which has a greater likelihood of trapping the thrombus or mobile plaque, as opposed to an open-cell stent design, which may cause "cheese grating" of soft contents through the stent. For most of our cases, which involve patients with asymptomatic, straightforward arch anatomy, we typically use a 6 French guide catheter like an Envoy XB (Codman). If there is any concern with navigating a difficult arch or a need for more support because of anticipated difficulty pushing a stent through the catheter, a Cook Shuttle (Cook Medical) may be used.

After the CCA has been engaged with the guide catheter, we focus on crossing the lesion with a distal embolic protection filter. Several filters are available on the market; our preferences are the NAV6 (Abbott) and the EZ Filter (Boston Scientific). Once the filter is deployed, usually anterior to the C1 arch, close attention is given to the amount of time the filter is engaged in the distal ICA (filter time). Prestent deployment plasty versus poststent deployment plasty is a decision made by the surgeon. Selection of the stent is determined by the degree of vessel stenosis, length of the stenotic segment, consistency of the plaque, and the size of the vessel.

Examples of the stents and indications for their use in our practice are as follows: iCast balloon-expandable covered stent (Atrium Medical) for subclavian stenting (Figs. 23.3 and 23.4), Xact (Abbott) for CAS, Express Stent or REBEL bare-metal stent (both Boston Scientific) for vertebral artery origin stenting (Fig. 23.5), and the Xact, Precise (Cordis), or Wallstent for CCA or carotid bifurcation stenting (Fig. 23.6). Each stent has specific advantages and disadvantages that should be taken into consideration when selecting a stent for each indication. The more proximal the lesion is to the vessel origin, the more likely we are to use a balloon-expandable stent, whereas for more distal lesions we may use a self-expanding stent.

Additional stents may be necessary if the initial stent does not cover the entire length of the lesion, if there is persistent stenosis, or if persistent intraluminal thrombus is apparent on intravascular ultrasound (IVUS) imaging obtained after stent placement. If the proximal stent overhangs into the lumen of the parent vessel, we flare the stent open with a Flash Ostial Dual Balloon Angioplasty (Ostial Corp.) [20, 21]. Angiographic success is determined by visualization of brisk flow through the stenotic segment, with no evidence of thrombosis, endoleak, or dissection.

Pre-and posttreatment measurements of the blood pressure across the lesion demonstrate the physiological success of the treatment. A value of <5 mmHg for the pressure gradient across the stent is considered physiologically successful.

We routinely use IVUS imaging following stent placement. Unlike the two-dimensional perspective of DSA, IVUS allows for intra-arterial imaging of vessel anatomy. The IVUS findings can be compared to the luminal diameter of the CTA and the arterial wall pathology identified immediately. This proves especially useful for plaque thrombus and intraluminal thrombus that may cheese grate through a porous stent and require removal by aspiration or pinning against the vessel wall by the placement of a second stent.

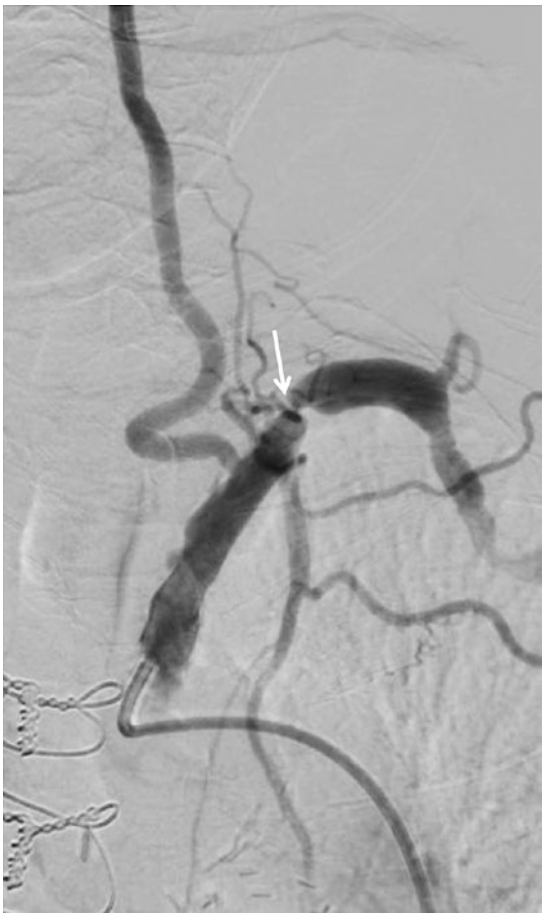

Fig. 23.3 Digital subtraction angiogram. Left subclavian artery in anteroposterior view demonstrating severe stenosis (*arrow*) of the subclavian vessel distal to the vertebral artery (VA) origin

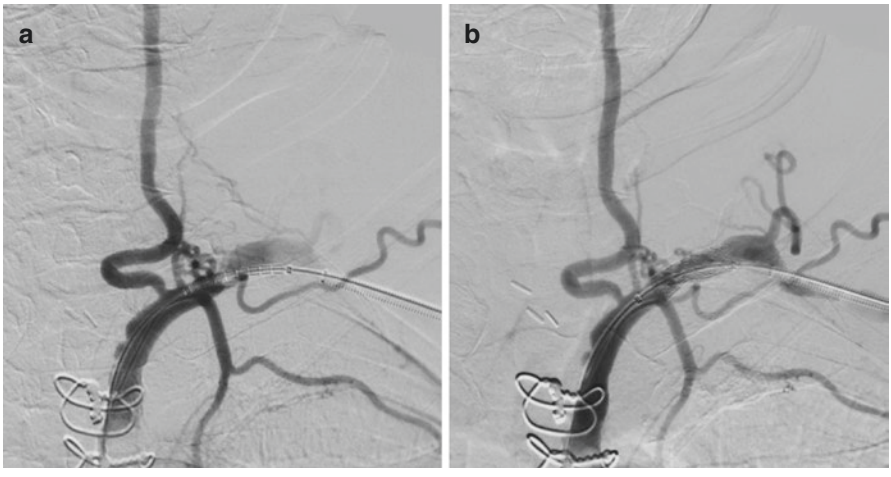

Fig. 23.4 Digital subtraction angiograms. Pre (**a**)- and post (**b**)- deployment of an Atrium balloon-expandable stent (Atrium Medical). Notice that the stent begins well distal to the origin of the VA to avoid any complication

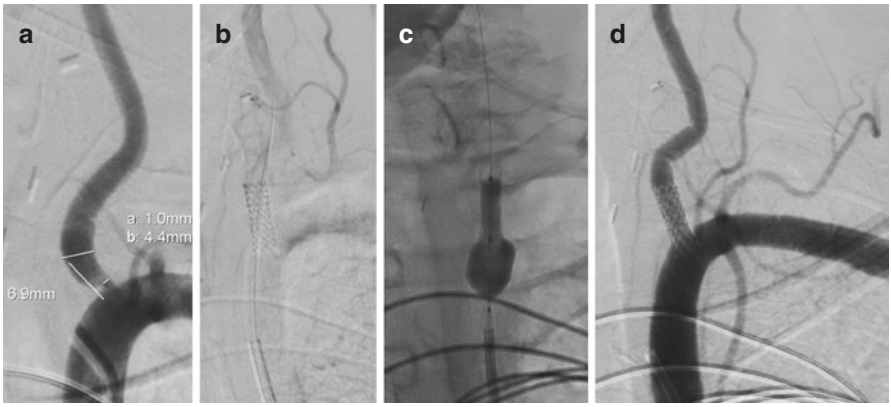

Fig. 23.5 Digital subtraction angiograms (from *left* to *right*): (**a**) VA ostia stenosis and preprocedure measurements. (**b**) REBEL stent (Boston Scientific) deployment. (**c**) Flash Ostial dual-diameter balloon (Ostial Corporation) angioplasty of proximal stent. (**d**) Poststenting remodeling

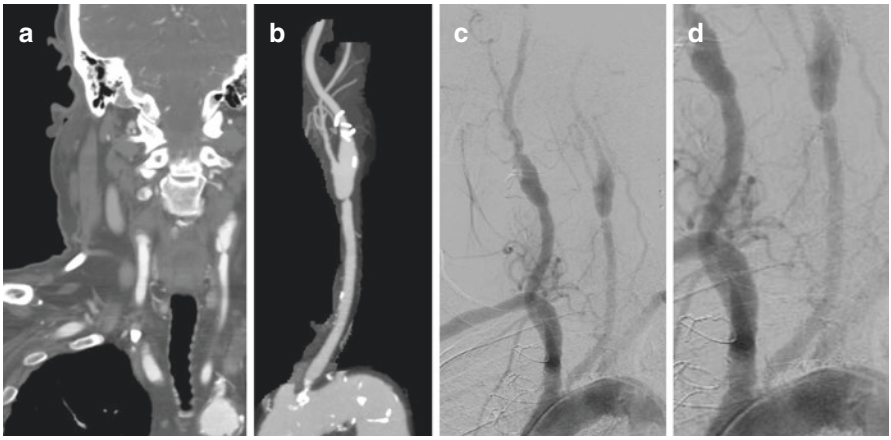

Fig. 23.6 From *left* to *right*: (**a**) coronal and (**b**) sagittal reconstructions of the left carotid artery consistent with stenosis at ostia and bifurcation. (**c**) Pre- and (**d**) postprocedure angiograms following surgical cutdown and stenting with Wallstent (Boston Scientific) and iCAST covered stent (Atrium Medical)

Complication Avoidance

Complications associated with stenting of the great vessels are uncommon. The most frequently encountered complications include access site hematoma, distal peripheral vascular embolism, central nervous system embolism, vessel intima dissection, and in-stent thrombosis [22].

The advent of percutaneous access site closure systems has significantly reduced both the time required for access site closure and the risk of an associated access site hematoma. These devices typically integrate suturing the vessel wall closed or placement of a hemostatic sealant over the access site. We utilize the Angio-Seal

Vascular Closure Device (St. Jude Medical), in which a sealant is delivered into the extravascular space. If oozing of blood is noted after delivery of the sealant, pressure is held manually until hemostasis is achieved. The patient lays flat with a leg immobilizer for 6 h after the procedure. Dilation of the subcutaneous tissues above the vessel, after the initial skin incision is made at the beginning of the procedure, allows for efflux of hemorrhage out of the skin, rather than trapping it in the subcutaneous space.

Embolism to distal arteries of the peripheral or central nervous system can cause significant morbidity and even mortality. Careful selection of a stent of an open- or closed-cell design for the pathology being treated can minimize procedural embolic risk. Likewise, in-stent thrombosis can shower emboli or cause ischemic injury in distal vessels. To minimize embolic risk, we ensure the effectiveness of preprocedural antiplatelet therapy by checking an aspirin effect (platelet function) assay as well as a Plavix (Bristol-Myers Squibb/Sanofi Pharmaceuticals) effect (CYP2C19) assay. Further, for all interventional procedures, we administer a bolus of heparin intravenously and ensure that the activated coagulation time is $2 \times -3\times$ the baseline value. Finally, for carotid vessel disease, we utilize the aforementioned embolic protection techniques, either with a filter or with balloon occlusion of the ICA and aspiration of vessel debris (thrombus or particulate matter) following stent deployment [5]. More recently and if the vessel pathology is favorable, we utilize both proximal and distal protection with the Mo.Ma proximal protection device, which allows for complete flow arrest. For use of the Mo.Ma device, a stiff wire is placed in the guidewire, which is then placed in the ECA, after which the device is advanced. Flow arrest is achieved by inflating the ECA occlusion balloon, followed by the proximal CCA balloon. The microguidewire and stent delivery system are then navigated across the stenotic segment of the vessel, and angioplasty and stenting are performed. The delivery system is removed and the ICA is aspirated to remove any embolic debris. The distal balloon and then the proximal balloon are deflated and circulation is resumed.

Complication Management

Access Site Hematoma

Hematoma at the access site can occur from inadequate hemostasis during access site closure. Management is with additional manual pressure to the vessel puncture site to ensure hemostasis. Placement of a 10 lb sandbag on the leg following hemostasis can prevent further swelling. We also perform frequent neurovascular checks of distal pulses during the next 24 h. Although an access site hematoma is typically self-limiting, an expanding hematoma may require surgical exploration and repair. The brachial artery access site has been reported as having a higher incidence of bleeding than the femoral artery access site, necessitating surgical repair [7]. Radial artery access has been associated with a decreased risk of complications compared with femoral artery access [17].

Anterograde Access Difficulty

Following advancement of the guidewire and microcatheter to the aortic arch, the vessel with the lesion of interest is selected. Inability to advance the guidewire across the lesion may be encountered. If the guidewire cannot be advanced after several attempts have been made, retrograde access may be necessary. For carotid vessel disease, surgical exposure of the carotid artery distal to the lesion allows for retrograde passage of the guidewire. The brachial artery in the ipsilateral arm can be used for access in cases of subclavian or innominate vessel disease. The distance from the retrograde entry approach to the lesion is closer than that from the standard femoral artery access site, lessening the bending action through the wire when attempting to cross severely stenotic lesions.

Dissection

Dissection seen during the procedure or detected on postprocedural imaging is managed conservatively. Continuation of anticoagulation for 24–48 h after the procedure and use of antiplatelet agents prevents asymptomatic lesions from showering emboli. For symptomatic or delayed symptomatic lesions, an increase in the antiplatelet agent or the addition of another antiplatelet or anticoagulant can prevent further progression. Likewise, the placement of a stent across the dissection prevents further embolic events. The "no-touch" technique, or avoidance of contact of the guidewire with the lesion, has been reported to decrease the risk of embolic complication [23]. Complete occlusion of the subclavian artery or the inability to successfully advance a stent across that artery may warrant surgical transposition of the artery onto the carotid artery [24].

Embolism

Distal vessel embolism is often undetected during the vessel stenting procedure. In the initial perioperative period, signs of peripheral ischemic changes include change in skin pallor, cold extremities, and loss of pulses if a larger, more proximal vessel is involved. Intracerebral artery embolus may go undetected or manifest as neurological changes such as amaurosis fugax, vision changes, visual field deficit, sensory changes, or motor weakness. Confirmatory diagnostic imaging via ultrasound imaging or CTA for peripheral vessels and CTA or magnetic resonance imaging with diffusion-weighted imaging or fluid-attenuation inversion recovery for cerebral vessels is necessary. Continuation of anticoagulation and antiplatelet agents prevents further propagation of embolic lesions. The administration of intravenous or intra-arterial tissue plasminogen activator for small vessel embolus or embolectomy for large-vessel occlusion allows for reperfusion.

Stent Thrombosis

In-stent thrombosis following a procedure can be a source of embolic events or ischemic perfusion injury. Prevention is undertaken via dual antiplatelet therapy. If thrombosis is detected clinically, diagnostic imaging is obtained via CTA or, preferably, DSA. The latter confers the ability to intervene immediately by revascularization with mechanical embolectomy. Conversion to surgical thromboendarterectomy may also be required. When diagnosis and treatment via thrombectomy or endarterectomy are performed in a timely fashion, clinical sequelae may be minimized.

Conclusion

Stenting of the great vessels is an increasingly common procedure for myriad indications. Careful procedural technique and use of preventative care allow for a diminished risk of complication.

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Complications in the Coiling of Cerebral Aneurysms

24

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Checklist: Complications in the Coiling of Aneurysms

Equipment needed	Procedural steps
Neurophysiology • ICP monitoring, EVD • Consider SSEP and MEPs for unruptured aneurysms Nursing • Confirm patient medication list (e.g., antiplatelets/anticoagulants) • Assess and document distal pulses • Review serum chemistries and blood counts • Baseline ACT Anesthesia • General anesthesia • EVD monitoring • IV antihypertensive medications prepared • IV heparin prepared • Protamine sulfate for urgent heparin reversal prepared Neurointerventionalist • Review CT angiography for access catheters, coil sizing, and potential necessity of adjunctive tools • Judicious use of pre-puncture fluoroscopy/ultrasound to confirm positioning	Pre-embolization • Assessment of proximal tortuosity • 3D-imaging pre-embolization for sizing of coils • Reassess the need for adjunctive devices, e.g., stents/balloons • Heparinization for unruptured aneurysms. Weigh risk-benefit of heparinization in ruptured • Administer antiplatelets beforehand in stenting likely required Coiling • Selection of appropriately sized framing coil (avoiding both over- and underframing) • Resetting of road maps to ensure accurate coil placement and avoiding prolapse • Monitor for increased tension/load in the microcatheter system • Recheck ACT periodically and redose heparin as needed Post-embolization • Ensure no thrombosis of the aneurysm neck or distal vasculature on follow-up angiography • Check ACT as appropriate if anticoagulation is administered • Closure device is recommended if ACT elevated Management • Post-procedure evaluation of arteriotomy site • Distal pulse, capillary refill, and vital signs, for Q15 min × 1 h, Q30 min × 2 h, and then Q60 min × 4 h • Neuro checks with same frequency as site checks for delayed thrombosis of parent vessel • SAH/ICP management

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Intraoperative perforation	Arterial tortuosity Excessive tension/ load in the system	DO NOT remove the microcatheter: Coil through the rupture point and complete the aneurysm embolization Balloon inflation (if located in primary vessel) EVD placement/open EVD Heparin/Antiplatelet reversal Acute SBP reduction ICP Management	Alleviation of tension within microcatheter prior to coiling Use of intermediate/ distal access catheters Frequent resetting of roadmaps
Thromboembolism	Thrombosis already present in large aneurysms Intrinsic hypercoagulable state in SAH Use of thrombophilic devices, e.g. stents, balloon used as adjuvants Coil prolapse into primary vessel	Administer Gp IIb/IIIa Inhibitors (intra-arterial or intravenous) as opposed to fibrinolytics Limited evidence for use of stentrievers for embolectomy	Load with antiplatelets prior to embolization if adjuvant therapy suspected. Heparinization prior to embolization Continuous flush lines on the microcatheter Appropriately size framing coil to avoid prolapse
Coil prolapse	Poor framing of aneurysm Over-packing of aneurysm	Rescue stent/balloon assistance to push the coil back into the aneurysm or support the coil against the wall of the parent vessel Administer Gp IIb/IIIa Inhibitors (intra-arterial or intravenous) as opposed to fibrinolytics	Use of a 3-dimensional framing coil appropriately sized for the aneurysm Use of adjunctive devices, e.g. balloon/ stent when needed Frequent re-roadmapping during embolization
Coil migration	Premature detachment/fracture of a coil Coil prolapse without appropriate anchoring	Retrieval with stentriever/snare devices Long term antiplatelet therapy	Use of a 3-dimensional framing coil appropriately sized for the aneurysm Use of adjunctive devices, e.g. balloon/ stent when needed
Contrast induced encephalopathy	Excessive contrast extravasation through a compromised blood-brain-barrier Multiple angiographic runs within the same artery	IV Hydration Time May need antiepileptic medications during contrast resorption	Limit overall contrast administration Avoid overuse of 3-dimensional angiography post-procedure

Introduction

While endovascular treatment of intracranial aneurysms is now established as a safe and effective treatment option, it is not without its complications. In general, complication rates related to endovascular treatment of intracranial aneurysms range from 1 to 5% depending on both aneurysm characteristics (i.e., size, location, morphology, and rupture status) and the technique used (i.e., simple coiling, stent-assisted coiling, flow diversion, etc.). With the advent of new techniques and indications for endovascular treatment of intracranial aneurysms, the type and frequency of complications have changed as well. For example, the advent of improved microcatheter technologies and softer coils has been associated with reduced complication rates in the treatment of tiny intracranial aneurysms [1].

It is important for the endovascular neurosurgeon to be aware of the various complications which occur during or immediately after endovascular treatment of intracranial aneurysms including their causes, techniques to avoid complications, and how to manage complications once they occur. In this chapter, we cover issues related to the management of complications which occur during or immediately after endovascular treatment of intracranial aneurysms.

Intraoperative Perforation

Incidence, Outcomes, and Risk Factors

Intraoperative perforation during endovascular treatment of intracranial aneurysms occurs in up to 5% of cases depending on the series [1]. Risk factors for intraoperative perforation include small aneurysm size, treatment of a ruptured aneurysm, location in the anterior communicating artery region and posterior circulation, and aneurysms with daughter sacs or teats [2]. Arterial tortuosity is another potential contributing factor due to decreased control of the microcatheter during embolization procedures. Prior studies suggested that intraprocedural perforation is associated with high rates (~30–40%) of permanent disability or death; however, more recent series have suggested that perforation-related morbidity and mortality rates are on the order of 10% or less [2, 3].

Intraoperative perforation can result from the microcatheter, the coil, or the microguidewire. In general, outcomes associated with microcatheter or coil perforation are significantly worse than that of microwire perforations. This is expected given the fact that the diameter of a typical microcatheter or coil is between 0.5 and 1.0 mm. Furthermore, coils have a secondary wind which can range in size from 2 to 20 mm which could result in a much larger hole within the aneurysm dome. Studies on the outcomes of intraoperative perforation have found that a vast majority of cases of morbidity and mortality related to intraoperative perforation occurred following microcatheter or coil perforation, whereas adverse neurological outcomes rarely occurred following wire perforation [3–6].

Complication Management

In general, intraoperative perforation is a complication that can be avoided. Microguidewire and microcatheter perforation can generally be prevented by being conscientious of the amount of tension that exists within the system and close monitoring of the behavior of the wire and catheter as they approach the aneurysm. Watching the microcatheter closely as one pulls the microguidewire out to make sure it is not advancing is particularly important. Microcatheter perforations can also occur during the coiling phase as the microcatheter is often difficult to visualize once coils have begun to be placed within the aneurysm. For this reason, functions that allow for resetting of the road map image are particularly useful as the operator is able to better visualize the microcatheter and the coils. Coil perforations can be avoided by not packing the aneurysm too densely as well as by not trying to force the coil into the aneurysm. The availability of modern distal access guide catheters which can be safely navigated in proximity of aneurysm sites also provides increased microcatheter stability, and it is likely to reduce the incidence of this complication.

The key to managing an intraoperative perforation is prompt recognition that a perforation has occurred. The more common and consistent physiologic sign of an intraoperative perforation is a sudden increase in arterial pressure parallel to the sudden increase in intracranial pressure that accompanies an aneurysm rupture. Angiographically, a perforation should be suspected when the device extends beyond the confines of the aneurysm on the road map. A perforation can then be confirmed by injecting the guiding catheter. A change in the color and an increased rate of drainage of the CSF collected through the EVD are other signs that a perforation has occurred in patients with ruptured aneurysms who had gone placement of an EVD before coil embolization [7]. DynaCT can be used intraoperatively to gauge the amount of hemorrhage and its associated effects.

Once a perforation is identified, several interventions, both pharmacologic and procedural, need to take place simultaneously. From the procedural standpoint, the operator needs to decide whether to withdraw the offending device or leave it in place. Because microguidewire perforations are generally very small and result in minimal, if any, bleeding, slowly withdrawing the microguidewire and proceeding to coil the aneurysm are reasonable (Fig. 24.1). In the setting of a microcatheter perforation, immediate withdrawal of the microcatheter can make matters worse. In this case, it may be better to introduce a second microcatheter and start coiling the aneurysm with the original microcatheter in place and slowly withdraw the offending microcatheter once the aneurysm is secured [3, 7, 8]. Placing a balloon at the aneurysm neck or in the parent artery more proximally to promote hemostasis is another commonly reported technique [2, 3, 7]. Some authors have advocated the use of NBCA glue in addition to coils to seal the hole within the aneurysm sac [9, 10].

In addition to sealing the aneurysm, a plan should be made for prompt management of the elevated ICP that can result from a perforation. The best case scenario is that the external ventricular drain (EVD) has already been placed and is working properly. However, in cases where an EVD has not yet been placed (i.e., unruptured aneurysm) or is not working properly, an emergent EVD should be placed in the

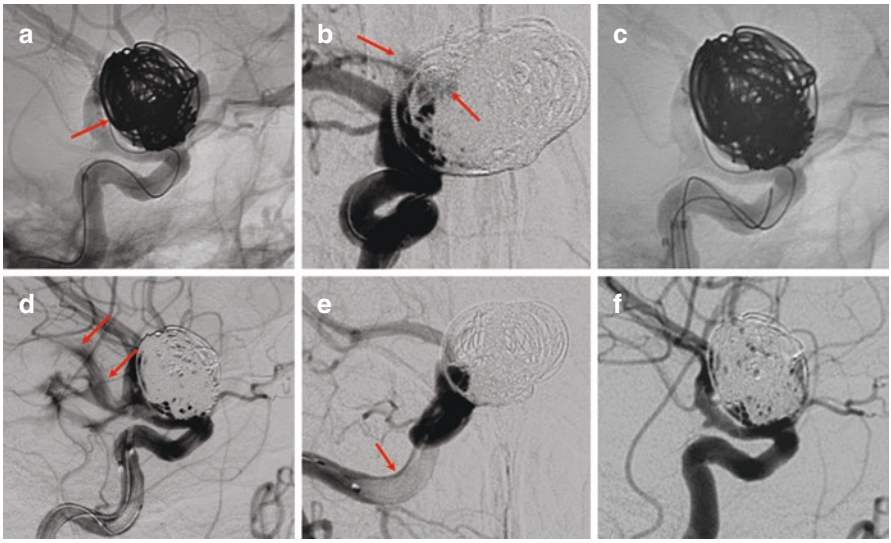

Fig. 24.1 Wire perforation. (**a**) During attempted repeat embolization of a residual large carotid ophthalmic aneurysm, the microguidewire was found to be beyond the confines of the vessel wall. (**b**) Angiographic run shows active contrast extravasation from the perforation site. The patient had stable vital signs. (**c**) The wire was left in place, and a second microcatheter and balloon were introduced to complete the coiling. (**d**) The wire was then removed and active extravasation was again noted. (**e**) The balloon was then inflated in the petrocavernous segment for several minutes. (**f**) Final angiographic run shows no additional extravasation of contrast

angiography suite in patients with increased intracranial pressure from a severe extravasation [2, 3, 7]. In one systematic review of intraoperative rupture, the authors found that one of the main variables associated with poor outcome following intraoperative perforation was delayed placement of an EVD [3].

Pharmacologically, the first intervention that should be performed is immediate reversal of heparinization if heparin has been given. In general, 1 mg of protamine is administered for every 100 U of heparin up to 50 mg. If the patient has been placed on aspirin and clopidogrel preoperatively, platelets and desmopressin can be administered. Blood pressure should be controlled to achieve a systolic blood pressure below 160 mmHg. Mannitol and hyperventilation can be employed to reduce intracranial pressure [7].

Intraprocedural Thromboembolic Complications

Incidence, Outcomes, and Risk Factors

Periprocedural thromboembolic complications during endovascular treatment of intracranial aneurysms can occur in up to 15% of patients [7, 11, 12]. In general, these complications are asymptomatic or result in transient ischemic attack or minor strokes, and patients often make a complete recovery. In a recently published

systematic review and meta-analysis of patients receiving rescue treatment for thromboembolic complications occurring during endovascular coiling, only 11% of patients receiving GP IIb/IIIa inhibitors suffered perioperative morbidity or mortality from stroke or hemorrhage, and recanalization rates were well over 70% [12].

A number of factors, both technical and nontechnical, can predispose a patient to developing a thromboembolic complication. Regarding aneurysm characteristics, treatment of large or giant aneurysms, partially thrombosed aneurysms, and aneurysms with wide necks is a potential risk factor for thromboembolic complications during endovascular coiling [7, 11–13]. In addition, endovascular treatment of ruptured aneurysms is associated with a higher thromboembolic complication rate than treatment of unruptured aneurysms. This is likely due to a combination of the proinflammatory, and thus hypercoagulable, state of aneurysmal subarachnoid hemorrhage and the fact that many operators do not use heparin at all during endovascular treatment of ruptured aneurysms in the acute phase.

Regarding technical risk factors, the use of adjunctive devices such as stents or balloons is thought to be associated with higher rates of thromboembolic complications. In general, the more foreign bodies one introduces into the cerebrovascular system, the higher the likelihood of a thromboembolic complication [7, 11–13]. Coil prolapse into the parent artery lumen is also a risk factor due to the prothrombotic nature of platinum.

Complication Management

There are several pre- and intraprocedural variables that the endovascular neurosurgeon can control to mitigate the risk of periprocedural thrombus formation. First, if there is any chance that the patient might require or benefit from stent-assisted coiling, then the patient should be loaded with aspirin and clopidogrel prior to embolization. In some practices, all elective patients are loaded with aspirin and clopidogrel prior to treatment, and pretreatment with single or dual antiplatelet therapy in preparation for elective coiling of unruptured aneurysms has been demonstrated to decrease the incidence of periprocedural thromboemboli [14]. Heparinization during the procedure to keep the activated clotting time between 250 and 300 s is generally recommended during the embolization of unruptured aneurysms. Regarding treatment of ruptured aneurysms, a variety of strategies for intraprocedural heparinization are currently employed. In some practices, most ruptured aneurysm patients are heparinized at the start of the procedure, before any coils are placed. In other practices, practitioners wait until the framing coil is in place prior to administering heparin, while in many practices, no heparin is administered at all. There are currently no studies comparing various heparinization strategies employed during treatment of ruptured aneurysms.

Technical considerations that are helpful at avoiding intraprocedural thromboembolic complications include reduction of vasospasm, use of continuous flush, and avoiding coil-related complications such as coil prolapse into the parent artery. The combination of a large-bore distal access catheter and catheter-induced vasospasm creates stasis in the parent vessel which is a known risk factor for thromboembolic

complications. Dense aneurysm packing to the point that a portion of the finishing coil is protruding into the parent artery lumen should be avoided due to the prothrombotic nature of the platinum coils [7].

Because patients are typically under general anesthesia during aneurysm embolization procedures, the operator generally is forced to rely on angiographic images alone in the detection of thrombotic events. Angiographically, the detection of distal emboli or a focal filling defect around the aneurysm neck is the most common finding in the setting of a thromboembolic event. Special attention should be paid to the aneurysm neck, particularly any prolapsed coils. Thromboembolic complications are often recognized during the final control angiographic run with the presence of filling defects in smaller PCA, MCA, and ACA branch vessels. For this reason, operators should focus not only on the appearance of the aneurysm on the final control run but should pay particularly close attention to the distal vasculature. Comparison with baseline, pre-coiling angiograms of the intracranial circulation is helpful to confirm the filling defect related to intraprocedural emboli. Treat the post-embolization runs as you would a stroke case [7].

A number of pharmacological options have been studied for treating intraprocedural thromboemboli. The key factor to consider is that during coiling procedures, platelets are the primary component of thromboemboli. For this reason, the use of fibrinolytics such as tPA is strongly discouraged [7, 11, 12]. One large meta-analysis found that the use of fibrinolytic therapy for treatment of intraoperative thromboembolic complications was associated with significantly higher rates of perioperative stroke and hemorrhage when compared to patients receiving GP IIb/IIIa inhibitors (29% vs. 11%) [12]. Furthermore, fibrinolytic therapy was associated with significantly lower recanalization rates (50% vs. 72%). The benefit of intravenous versus intra-arterial GP IIB/IIIa inhibitors is not well established (Figs. 24.2 and 24.3). Some authors contend that intra-arterial therapy may be superior due to the notion that local administration would provide better thrombolysis and because local administration mitigates the risk of systemic complications from IV administration.

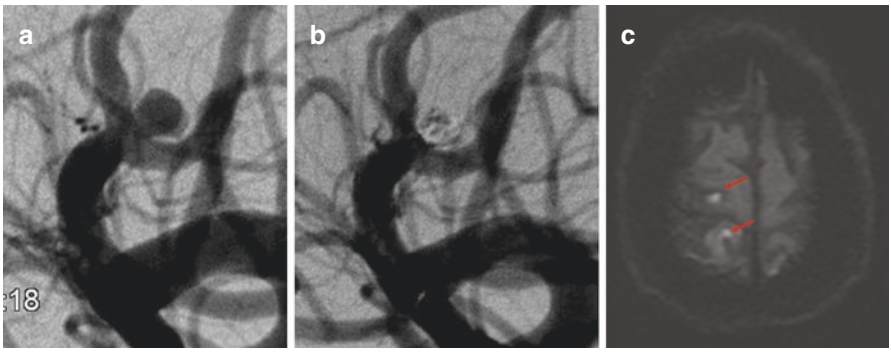

Fig. 24.2 Postoperative stroke treated with abciximab. A 60-year-old female undergoing coil embolization of an unruptured anterior communicating artery aneurysm (**a** and **b**). Following the procedure, she had transient left leg weakness. DWI showed infarcts in the right ACA territory. The patient was treated with an intravenous infusion of abciximab and made a complete recovery

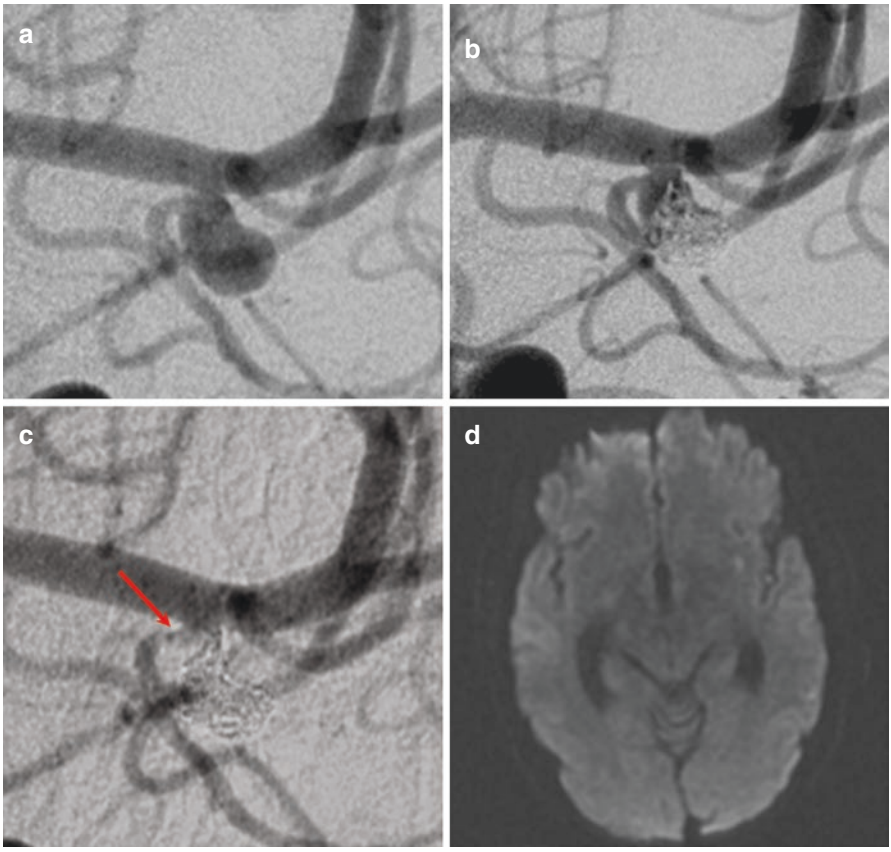

Fig. 24.3 Anterior temporal artery thrombus treated with intra-arterial abciximab (**a** and **b**). Coil embolization of an aneurysm at the origin of the anterior temporal artery in a 58-year-old female. During the coil embolization procedure, a focal thrombus was noted at the origin of the anterior temporal artery (**c**). The patient was treated with intra-arterial abciximab. There was incomplete recanalization of the vessel; however, postoperative MRI did not demonstrate any large associated stroke

However, one recently published systematic review found no difference in outcomes between IA and IV administration. There are some data to suggest that tirofiban and eptifibatide result in improved recanalization rates when compared to abciximab. The standard intravenous dose for abciximab is a bolus of 0.25 mg/kg followed by 0.125 μg/kg/min for 12 h not to exceed an infusion rate of 10 μg/min. The standard intra-arterial dose is 2 mg boluses up to 10 mg [12].

More recently, several groups have reported the use of mechanical thrombectomy with stent retrievers for treatment of intraoperative thromboembolic events. This has been shown to be safe and effective with recanalization rates close to 100% and complication rates close to 10% [15]. There are some potentially unique risks to using a stent-retriever device, particularly when treating local thrombus in the parent artery of the aneurysm including (1) catching the coils on the stent-retriever

device and (2) migration of the thrombectomy device into the aneurysm neck or sac. This treatment should be considered a rescue therapy only after pharmacological therapy preferentially with GP IIb/IIIa inhibitors has failed or in the setting of a large intraoperative thrombus occluding the parent artery [15].

Other Complications

Coil Prolapse

Prolapse of part of the coil ball into the parent artery is a well-known complication of endovascular aneurysm treatment. In a majority of cases, this is considered a minor technical complication that requires no additional invasive measures and has no impact on patient morbidity or mortality. The main problem associated with coil prolapse is the risk of local thrombus formation and associated thromboembolic events acutely. In the long term, there is the risk of gradual occlusion of the parent vessel or any branch vessels that the protruding coil loops could be obstructing the parent vessel [16].

The best way to prevent this complication from occurring is avoiding dense packing at the aneurysm neck. Using a 3D framing coil that configures to the shape of the aneurysm neck could be helpful in preventing prolapse of filling and finishing coils into the parent artery. In the situation of a wide-necked aneurysm or wide-neck bifurcation aneurysm, the use of balloon or stent assistance should be strongly considered [16]. If coil prolapse does occur, the operator has a few options. First, if the prolapse is large and looks like it will definitely compromise parent artery flow, consideration should be made for rescue stent assistance or balloon assistance to push the coil back into the aneurysm sac. If the prolapse is small (i.e., a loop of coil) and the procedure is finished, the operator should closely inspect control angiographic runs for any thrombus formation. If there is local thrombus formation, GP IIb/IIIa inhibitors should be administered. If not, the patient can typically be managed with either single or dual antiplatelet therapy (Fig. 24.4).

Coil Migration

Coil migration, stretching, and fracture are rare complications which require quick thinking. The effects of these complications range from minor local flow alterations without associated thromboembolic event to large vessel occlusion resulting in large ischemic infarcts. Migration of a coil into the parent artery can occur due to premature detachment or fracture of a coil (usually a manufacturing error which should be reported to the company) or from a coil that seemed to be well placed in the aneurysm sac “falling into” the parent vessel. The latter could potentially be avoided through the use of 3D framing coils and appropriate sizing of the filling coils.

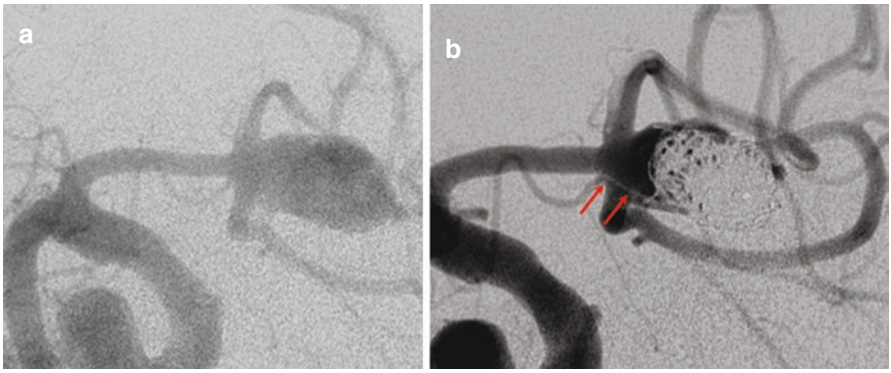

Fig. 24.4 Coil protrusion. (**a**) A 63-year-old male undergoing treatment of a large anterior communicating aneurysm. (**b**) Following coil embolization, there was some stretching of the final coil and protrusion of the coil loop into the parent artery. There was no associated thromboembolic complication. The patient was discharged home the next day on dual antiplatelet therapy with clopidogrel and aspirin. He was taken off of clopidogrel after 4 months and told to continue aspirin for life

These complications are rare enough that the primary literature on addressing them is published in case reports and small case series only [15]. Techniques that have been employed to retrieve migrated coils include stent retrievers, microguidewires, and snare devices. Wire techniques that have been reported include the simultaneous use of two microguidewires to "capture" the coil and essentially wrap the coils around the microguidewires as well as the creation of a microsnare to hook onto the coils. More conventional techniques include the use of a gooseneck snare or a stent retriever to capture migrated coils. In cases where the coil cannot be retrieved or there are adequate collaterals to take over the flow of the vessel occluded by the coil, long-term antiplatelet platelet therapy is recommended (Fig. 24.5) [16].

Contrast-Induced Encephalopathy

Contrast-induced encephalopathy is a poorly understood complication of neuroendovascular procedures which likely is the result of blood-brain barrier breakdown from large volumes of contrast injected into one cerebral hemisphere [17]. This complication most commonly occurs in the setting of multiple angiographic runs in the same artery during and following endovascular embolization. Common clinical manifestations include encephalopathy, seizure, and focal neurological deficits. This can present within 24 h of treatment and is usually self-limiting. The typical non-contrast CT finding in CIE is high attenuation of the cerebral sulci which is often interpreted as cerebral edema. However, with the use of dual energy CT and iodine subtraction, it becomes clear that the high attenuation of the cerebral sulci is due to iodinated contrast rather than blood or edema [17]. MRI can help in differentiating edema from pseudo-edema as well. Accurate, prompt diagnosis is important so that further contrast administration with serial diagnostic tests (e.g., repeat CTA and angiography) can be avoided. Management is generally conservative (Fig. 24.6).

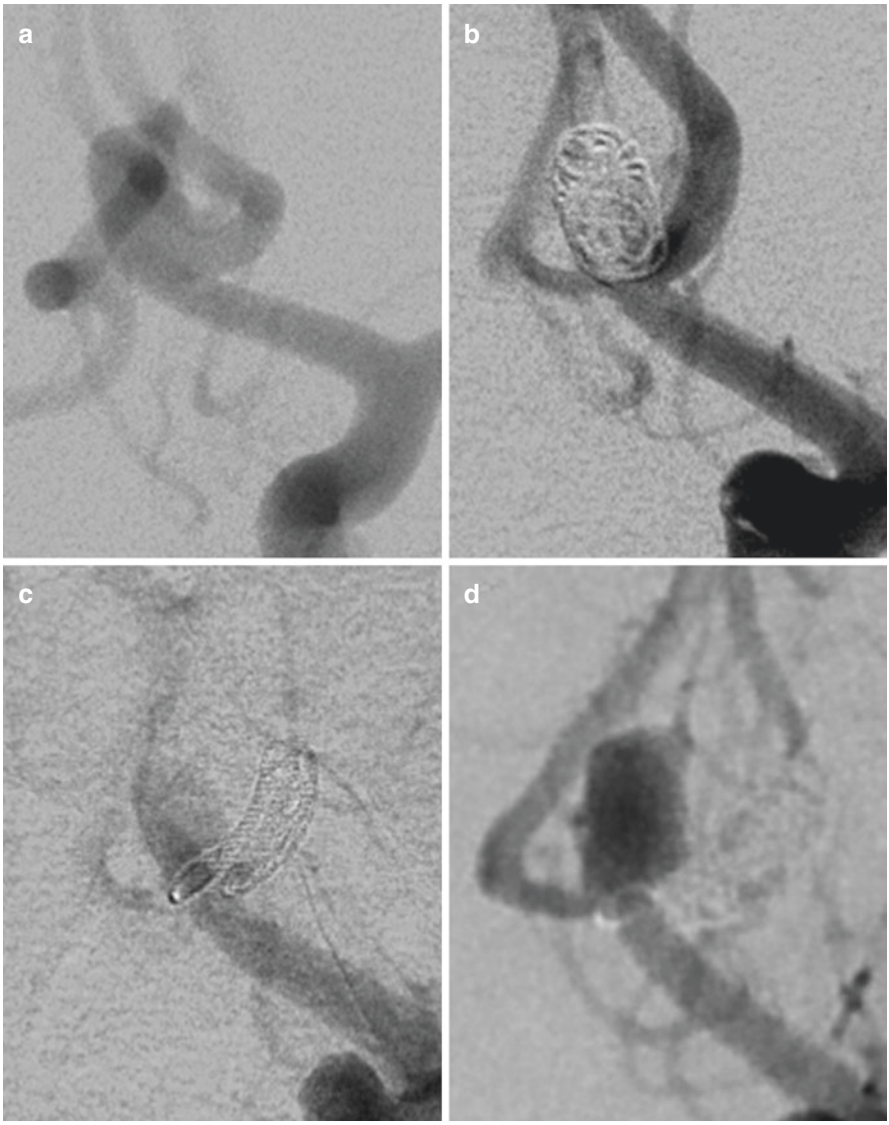

Fig. 24.5 Coil migration. A 63-year-old male undergoing coil embolization of an anterior communicating artery aneurysm (**a**). The aneurysm was nearly completely occluded with coils, and there were no immediate intraoperative complications during the coiling procedure (**b**). As the patient was emerging from anesthesia while still intubated, he was noted to have weakness in the right side of his body, particularly his leg. Repeat cerebral angiography demonstrates migration of the coil mass into the left A2 and out of the aneurysm (**c**). He was immediately administered abciximab which resulted in recanalization of the A2 around the coil mass. He was then transitioned to warfarin which he was already taking preprocedurally because of a history of pulmonary emboli (**d**). Repeat cerebral angiogram 2 years later shows the persistent coil mass in the left A2 with antegrade flow. Patient made a complete recovery

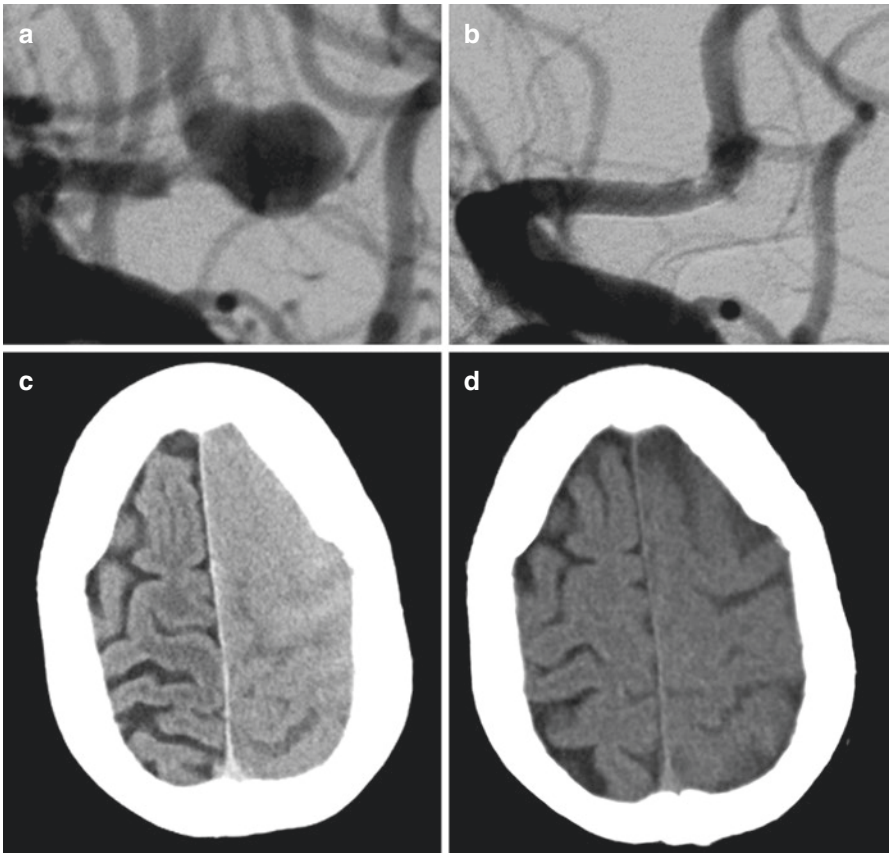

Fig. 24.6 Contrast-induced encephalopathy. A 72-year-old female with an anterior communicating aneurysm (**a**). Following placement of a single flow diverter, there was a significant reduction of blood flow within the aneurysm (**b**). One hour postoperatively, the patient was found to have mixed aphasia which progressed over the rest of the day, and she also developed progressive right hemiparesis (**c**). CT demonstrated hyperdensity in the cerebral sulci and apparent sulcal swelling. However, following iodine subtraction, it became apparent that the gyral and sulcal hyperdensity were due to iodinated contrast (**d**). There was no infarct on MRI to correspond with her neurological findings. She was managed conservatively and recovered complete function by the time of discharge a few days later

Conclusion

Understanding various complications that can occur during endovascular treatment of intracranial aneurysms is important so that measures can be taken to prevent these complications from occurring. Having a standard plan or checklist for managing complications that occur during or following neuroendovascular procedures is important to decrease the risk of neurological deficits resulting from these complications. The best way to learn about management and prevention of complications is through open discussion among colleagues in the workplace and during complication meetings so as to benefit from the collective experience of neuroendovascular specialists.

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Balloon- and Stent-Assisted Endovascular Occlusion of Intracranial Aneurysms

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Checklist: Aneurysm Treatment with Adjuvant Devices

Administrative and pre-procedural nursing assessment
- Confirm patient identity, procedure, and consent
- Inquire about contrast allergies and pregnancy status if applicable
- Creatinine level
- Ensure intensive care unit inpatient bed availability

Technologist
- RHV
- Tubing
- Choice of balloons, coils, and stents
- Microcatheters
- Guidewire
- Dyna-CT protocol

Nursing
- Heparinized saline
- Protamine
- Active type and screen
- Platelets on call to the interventional suite
- Desmopressin
- Glycoprotein IIb/IIIa receptor inhibitor—abciximab or eptifibatide
- Mannitol
- Anticonvulsants
- Call numbers to anesthesiology attending, neurosurgery resident on call, and CT scanner

Anesthesia
- Endotracheal intubation equipment
- Intracranial pressure monitoring equipment

Neurosurgery
- External ventricular drain kit

Neurointerventionalist
- Pre-procedural neurological exam
- Ensure all equipment is available prior to start of procedure
- Identify contrast extravasation from the aneurysm fundus
  - Ask nursing and anesthesia teams to reverse anticoagulant/antiplatelet agents
  - Tell technologist to prepare for possible Dyna-CT
  - Keep microcatheter in place
  - Deploy and inflate balloon via an additional RHV
  - Rapidly coil ruptured aneurysm
  - Post-op neurological exam and CT scan
- Identify coil migration or prolapse into the parent artery
  - Deploy balloon or SEIS through additional RHV to trap prolapsed coils in aneurysm fundus
  - Consider use of retrieval devices to remove migrated coil
- Identify stent misplacement or migration
  - Consider placement of a second stent
  - Evaluate functional neck size and consider coil embolization
  - Consider staging the procedure to allow for endothelialization
- Identify local thrombus formation
  - Evaluate antegrade flow in parent and branching vessels
  - Ask the nursing or anesthesia teams to determine the activated clotting time
  - Administer local infusions of GP IIb/IIIa
  - Post-op neurological exam
  - Post-op platelet inhibition testing
  - Consider a post-procedural heparin or GP IIb/IIIa drip

Complication Avoidance Flowchart

Complication	Cause	Management	Avoidance
Intraprocedural Aneurysmal Rupture	1. Iatrogenic—Injury secondary to microcatheter, guidewire, or coils 2. Morphological features of the aneurysm, e.g., the presence of a small basal outpouching, smaller aneurysms, may increase intraprocedural rupture risk 3. Previous aneurysm rupture	1. Reverse antiplatelet/anticoagulants administered prior to or during the procedure 2. Keep systolic blood pressure less than 140 3. If present, inflate a balloon within the parent vessel to obtain hemostasis 4. Rapidly coil the ruptured aneurysm with coils 5. Open surgical management 6. CT scan to evaluate for hydrocephalus 7. Standard subarachnoid hemorrhage management	1. Careful positioning of the microcatheter into the fundus 2. Avoid overpacking the fundus during coil embolization 3. Consider staged embolization/leaving a neck remnant for recently ruptured aneurysms
Coil migration/malposition	1. Inappropriate positioning of the microcatheter 2. Premature coil deployment 3. Deployment of undersized coils	1. Coil retrieval using Merci devices, stent retrievers, alligator clips, or microwires 2. Administer intra-arterial abciximab if coil migration has led to thrombus formation	1. Stabilize microcatheter within the fundus to prevent kickout and possible coil malposition
Coil herniation	1. Displacement of the first coil after subsequent embolization 2. Excessive embolization	1. Deployment of a SEIS within the parent vessel to trap the prolapsed coils 2. Inflation of a balloon across the aneurysm neck	1. The use of longer and stiffer coils to form a stable initial basket 2. The use of shorter and softer coils in the later stages of endosaccular embolization
Stent misplacement/migration	1. Unstable delivery catheter position 2. Trans-stent manipulation of microcatheters, additional stents, etc. through the deployed stent 3. Tortuous anatomy of the parent vessel	1. Deployment of a second stent across the aneurysm neck to provide adequate neck protection 2. Coil embolization of the aneurysm if the misplaced stent reduces the functional neck size 3. Stent retrieval	1. Staged deployment of multiple stents or coil embolization to allow for stent endothelialization 2. Stable distal microwire access

(continued)

Complication	Cause	Management	Avoidance
Thromboembolic complications with intracranial stenting	1. Non-responders to first-line antiplatelet treatment 2. Medication noncompliance	1. Administer intra-arterial abciximab until the thrombus has dissolved or stabilized and antegrade flow in parent and branching vessels has resumed	1. Patients are loaded with dual antiplatelet medication prior to intervention 2. Full heparinization during the procedure with a goal ACT of 250–300 s 3. Preoperative platelet inhibition testing

Introduction

Endovascular approaches to the management of intracranial aneurysms have been employed since the early 1960s and usually involved the use of free coils or detachable balloons which were technically challenging and had limited safety and effectiveness in comparison to open surgical clipping of the lesion [1]. This remained the case until early 1990s, when two watershed moments would form the impetus for the development and widespread use of endovascular techniques for the treatment of intracranial aneurysms.

The first of these was the FDA approval of the Guglielmi detachable coil (GDC) in 1995. Unlike devices employed prior to its introduction, the GDC allowed for both the retrieval and repositioning of the coil in order to achieve complete occlusion of the fundus, while maintaining patency of the parent vessel [2, 3]. The second was the results of the international subarachnoid aneurysm trial (ISAT), a multicenter, prospective, randomized controlled trial that compared the results of open surgical clipping and endovascular coiling for patients with ruptured intracranial aneurysms. This trial was stopped ahead of schedule after a planned interim analysis demonstrated a better outcome for patients treated with endovascular therapy, with the rates of death or dependency at 1-year follow-up being 23.5% for the endovascular group and 30.9% for the surgical group [4].

While these results led to the increased use of coil embolization for intracranial aneurysms, interventionalists soon realized that the presence of a wide neck, dome to neck ratio less than 2.0, large-size tortuous vessels, and bifurcation aneurysms posed a greater challenge and were associated with a higher risk of incomplete fundus occlusion and recurrence. This has necessitated the development of several adjuncts to conventional endovascular therapy including balloon remodeling techniques, stent-assisted coiling, and flow-diverting stents. These techniques have simultaneously increased the armamentarium of the modern interventionalist and expanded the range aneurysms amenable to endovascular treatment. In this chapter we discuss the development, indications, safety, and efficacy of balloon remodeling and stent-assisted endovascular occlusion of intracranial aneurysms.

Procedural Overview

Balloon Remodeling Technique

Moret et al. described the balloon remodeling technique in 1997, and at that time, it was the first adjunct capable of facilitating the successful endovascular treatment of intracranial aneurysms with an unfavorable neck-to-dome ratio [5]. During this procedure, a nondetachable balloon is placed within the parent vessel across the neck of the aneurysm, while a second microcatheter is positioned within the fundus of the lesion. Following balloon inflation, coils are placed within the aneurysmal sac; the balloon is then deflated in order to test the stability of the coil within the lesion prior to coil detachment. The temporary inflation of the balloon results in obliteration of the neck and thus allows the coils to assume the shape of the lesion and ultimately prevents prolapse of the coil mass. Following the satisfactory occlusion of the aneurysm, the balloon is removed from the parent vessel.

Balloon remodeling offers several advantages: it prevents herniation of the coils, it forces the coils to assume the three dimensional shape of the aneurysm, thus increasing the density of the coil mass, and it provides a means of tamponade in the setting of intraprocedural aneurysm rupture [6, 7]. It does not require pre- or post-procedural dual antiplatelet therapy, which is particularly advantageous if this technique is pursued in patients who present following subarachnoid hemorrhage or suffer an intraprocedural rupture. Finally it conforms to the shape of the parent vessel, and in doing so, it delineates both the neck of the lesion and any adjacent vessels that protect them during the procedure [6].

Early adopters of the balloon remodeling technique employed low-compliance nondetachable balloons glued onto microcatheters or balloon microcatheters with a guidewire running through it [5, 8]. Catheterization was easier with the latter construct; however the low compliance and oblong shape of these balloons meant that this technique was only amenable to wide-necked sidewall aneurysms as they were unable to effectively maintain the patency of the parent vessel or branching arteries when used for the management of more complicated bifurcation lesions. In an attempt to address such aneurysms with the balloon remodeling technique, interventionalists employed round high-compliance latex balloons that were glued to the tip of a flow-guided microcatheter. While temporary occlusion of the neck and maintaining the patency of the parent and branching vessels were feasible with this construct, the use of the flow-dependent microcatheter made stabilization of the balloon during the procedure challenging.

The development of high-compliant over-the-wire balloons such as the HyperForm (Medtronic/Covidien/Ev3), Ascent (Codman Neurovascular), and Scepter (Microvention) allowed for successful coil embolization of complex bifurcation aneurysms using the balloon remodeling technique while maintaining vessel patency. The high compliance of these balloons allows them to change their shape on inflation in order to conform to the neck of the aneurysm and the adjacent branching vessels. Additionally the use of a guidewire as opposed to a flow-dependent microcatheter enables stable positioning of the balloon throughout the procedure [9].

Modifications of the balloon remodeling technique may be employed to treat more challenging cerebral aneurysms. The double-balloon remodeling technique described by Arat and Cil may be used to treat bifurcation aneurysms with necks greater than the length of the balloon catheter [10]. Two compliant balloon catheters are placed in the parent and branching vessels in a Y configuration, while a third catheter is used to deploy the coils into the fundus of the aneurysm. However such techniques require a dual femoral approach; additionally the presence of multiple microcatheters and balloon inflations increases the risk for thromboembolism and vascular injury secondary to overinflation.

Based on most published series, BRT provides comparable or superior anatomic results than standard coiling. The ATENA and CLARITY prospective trials looked at outcomes for unruptured and ruptured aneurysms that underwent endovascular management. In the ATENA series, immediate complete aneurysm occlusion was seen in 59.8% of both the standard coiling and BRT groups [11]. In the CLARITY series, immediate complete aneurysm occlusion was seen in the 46.9% of aneurysms subject to standard coiling and 50.0% of aneurysms treated by BRT [12]. The meta-analyses performed by Shaprio et al. demonstrated that BRT was superior to standard coiling with 73% of aneurysms treated by the former method achieving complete occlusion immediately after intervention as opposed to 49% in the standard coiling group [13]. Similar rates of occlusion were seen at follow-up.

Stent-Assisted Endovascular Occlusion

The impetus for the development of stent-assisted coiling of intracranial aneurysms was twofold. First, while the advent of the balloon remodeling technique increased the armamentarium of the neurointerventionalist, the approach was considered by many to be technically demanding and lacked an effective plan if coils prolapsed into the parent artery. Furthermore a large percentage of wide-necked intracranial aneurysms still remained unsuitable for coiling, as their morphology would not permit the retention of coils within the fundus.

Endovascular stents have been used in the clinical setting since the 1960s in attempt to address and prevent the propagation of dissection after angioplasty, to force asymmetric plaques into a cylindrical shape in the vessel lumen, and to prevent vessel collapse. However it wasn't until 1997 when Higashida et al. reported the use of a balloon-mounted coronary stent in combination with Guglielmi detachable coils for the management of a fusiform vertebrobasilar junction aneurysm [14]. Following this there were several case reports describing the use of balloon-expandable coronary stents to address cerebral aneurysms, intracranial atherosclerosis, and coil prolapse after the embolization of cerebral aneurysms [15–19].

Intracranial stents promote changes in the vascular endothelium and blood flow at the aneurysm parent vessel interface that facilitate embolization of the aneurysm fundus. Following deployment the stent reduces blood flow into the aneurysm and in turn decreases the peak pulsatile velocity and maximum shear strength on the wall of the fundus [20, 21]. The reduced regional blood flow and shear stress in

addition to the scaffold provided by the stent allow for endothelialization of the device within the parent vessel and, most importantly, across the neck of the aneurysm [22]. This will ultimately allow for endoluminal reconstruction of the parent vessel.

Currently there are two types of stents available—balloon-expandable coronary stents (BECS) and self-expanding intracranial stents (SEIS). Balloon-expandable coronary stents (BECS) were the first type of stent utilized in the endovascular treatment of intracranial aneurysms. Initially designed for the revascularization of coronary vessels in the setting of coronary artery disease, their rigid structure made them resistant to intraprocedural damage or migration. However this feature also made them unsuitable for navigating tortuous cerebral vasculature. Furthermore their deployment requires inflation of a high-pressure balloon increasing the risk of vessel rupture. These characteristics ultimately precluded the widespread use of BECS for the management of intracranial aneurysms.

Self-expandable intracranial stents (SEIS) became commercially available in 2001 after the Food and Drug Administration (FDA) authorized the Neuroform microstent (Boston Scientific/Stryker) use for the treatment of intracranial aneurysms via a humanitarian device exemption. These stents were made from nitinol and far more flexible than their balloon-mounted predecessors, thus enabling navigation for a wider variety of landing zones within the cerebral vasculature. Its open-cell design allowed each segment to act as a separate fixation point, thus accounting for its superior vessel wall apposition in comparison to closed-cell designed stents (Fig. 25.1).

Despite this some technical difficulties with deployment still remained with the first iteration of the Neuroform. The stent was preloaded onto a delivery microcatheter making navigation to the landing zone difficult. Interventionalists have circumvented this problem by using a standard microcatheter and microwire to access the site of interest. The microcatheter is then removed over a 300 cm exchange microwire positioned distal to the target site; finally the Neuroform stent delivery microcatheter system is navigated over the exchange microwire [23]. This final maneuver was still technically difficult as the guidewire was prone to distal migration thus placing the involved vessels at risk for perforation. The more recent iterations of the Neuroform stent—the Neuroform EZ stent system—may be delivered via a standard microcatheter removing the need for the exchange maneuver.

The Enterprise (Cordis Neurovascular/Johnson and Johnson) system was the second commercially available SEIS, and unlike the Neuroform, it has a closed-cell design which allows it to be partially delivered, resheathed, and repositioned prior to its final delivery. Additionally navigation and deployment of the Enterprise stent are less technically challenging than the initial Neuroform stent. The collapsed device is premounted on a microwire which is loaded into a delivery catheter after the target zone has been reached, thus removing the need for an exchange microwire and thus reducing the risk of distal vessel perforation during the exchange process [24]. The major disadvantage of the Enterprise system is that its closed-cell design also reduces its ability to conform to tortuous vessels and the resultant reduced wall apposition may decrease the ability of the stent to protect the parent vessel.

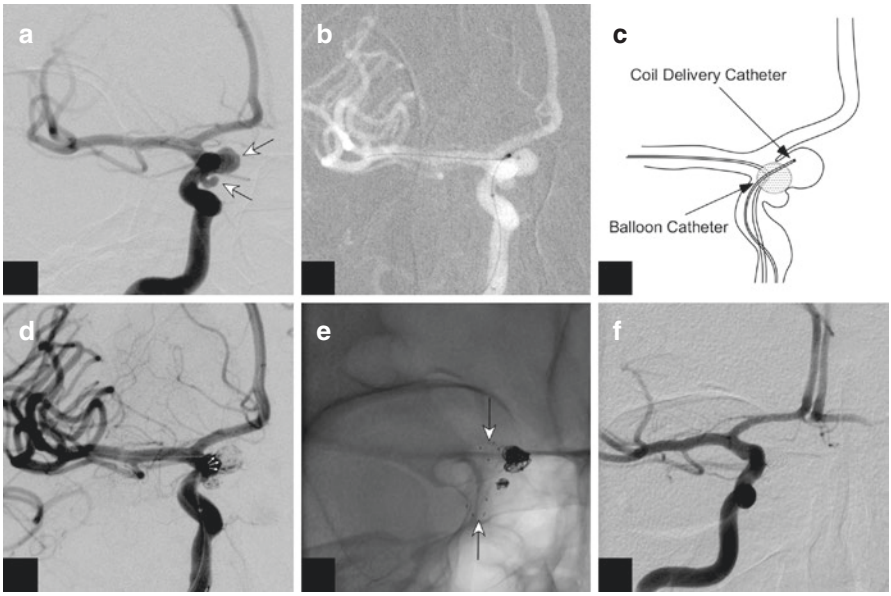

Fig. 25.1 (**a–f**) A 70-year-old woman with neck pain, right internal carotid aneurysm incidentally found on cervical MRI scan. (**a**) Right internal carotid angiogram in frontal projection shows tandem aneurysms (*arrows*), with distal aneurysm projecting into subarachnoid space. (**b**) Digital road map image of the right internal carotid artery following placement of treatment catheters across aneurysms. (**c**) Diagram depicting placement of balloon catheter across the neck, or face, of aneurysm while coil delivery catheter projects into aneurysm fundus. (**d**) Right internal carotid angiogram in the same frontal projection demonstrates placement of multiple detachable platinum coils into each aneurysm using balloon neck remodeling technique. Note that the coils conform to the balloon margin during inflation (not shown) and the wall of the artery (*small arrows*). (**e**) Fluororadiograph obtained during angiography shows subsequent placement of self-expanding nitinol stent into the right internal carotid artery across both aneurysms (*white tip arrows*). (**f**) Surveillance angiography 6 months later shows complete occlusion of both aneurysms and patency of the right internal carotid artery without stenosis

There are several operative strategies that may be employed when pursuing stent-assisted coil embolization of intracranial aneurysms. In the trans-stent technique, the stent may be deployed first, and the microcatheter may be placed inside the fundus through the struts of the stent. It is not uncommon for interventionalists to perform this procedure 1–2 months after the stent has been deployed. This delay allows for endothelialization of the stent which should make it more stable and less prone to migration during trans-stent coiling. Alternatively in the jailed-catheter technique, the microcatheter responsible for coil deployment is positioned inside the fundus of the aneurysm; the stent is then deployed across the neck of the aneurysm prior to coiling. This method is somewhat less susceptible to kickback of the microcatheter during coiling than the trans-cell technique. In the stent-jack technique, a coil delivery microcatheter is placed in the fundus, and an undeployed stent is placed across the neck of the aneurysm. The first coil is then delivered into the

fundus and allowed to take the shape of the aneurysm, and subsequently the stent is deployed. Finally stents may be used as a rescue device in the setting of herniation of a coil mass into the parent vessel in order to maintain vessel patency and decrease embolic risk.

Unlike sidewall aneurysms, wide-necked bifurcation aneurysms are not always adequately addressed with a single stent. In these cases a single stent may not be able to provide adequate parent or branching artery protection from the coil mass. In this setting two stents may be placed in a "Y" configuration, with the one stent deployed through the interstices of the first. This allows for reconstruction of the parent and branching vessels while preventing herniation of the coil mass. This technique has been successfully applied to basilar tip, anterior communicating, and middle cerebral artery bifurcation aneurysms [25–27].

Endovascular stents require dual antiplatelet therapy (DAPT) to prevent thrombosis in the hyperacute, acute, and chronic periods following stent deployment. Aspirin a cyclooxygenase-1 inhibitor which blocks the production of thromboxane 2 and clopidogrel a thienopyridine derivative which prevents platelet activation by irreversibly inhibiting the P2Y12 ADP receptors are usually used for this purpose. Patients are typically given loading doses of aspirin and clopidogrel 3–5 days prior to the procedure, followed by 6 weeks of DAPT and maintained on ASA 81 thereafter. Alternatively a single loading dose of clopidogrel can be given 1 day prior to the procedure. In the setting of unplanned stent deployment in order to achieve adequate embolization or to maintain parent artery patency following prolapse, the glycoprotein IIb/IIIa inhibitor abciximab can be used to achieve rapid platelet inhibition. Following stent deployment and satisfactory positioning, a 0.25 mg/kg bolus is administered followed by a 12 h infusion. Alternatively, instead of a 12 h infusion, the patient may be given loading doses of aspirin and clopidogrel following administration of the loading dose of abciximab [28]. Given the need for DAPT), patients with ruptured cerebral aneurysms are not generally a candidate for stent-assisted coiling; additionally the need for potential adjuvant surgical and invasive procedures including external ventricular drain, shunt placement, lumbar puncture, central line, tracheostomy, percutaneous endoscopic gastrostomy, or angioplasty for cerebral vasospasm often precludes the need for long-term antiplatelet therapy.

Complication Avoidance and Management

The most common complications of the BRT are thromboembolism and intraprocedural rupture.

The risk of thromboembolic events when employing the balloon remodeling technique theoretically increases due to the presence of multiple catheters within the arteries and temporary occlusion of parent and or branching vessels, with repeated inflation and deflation of the balloon [29]. These events are not always symptomatic and may only be detected after follow-up diffusion imaging [30]. However meta-analysis performed by Shaprio et al. has shown that there is no statistically significantly increased risk of thromboembolism associated with BRT in

comparison to the unassisted deployment of Guglielmi detachable coils [13]. Furthermore several single center series and randomized trials have shown that the rate of thromboembolism in BRT is no different than that encountered with standard coiling [31–34].

BRT also carries a theoretical increased risk of aneurysmal rupture as the microcatheter may impinge against the wall of the aneurysm with inflation which may itself result in rupture of the aneurysm or the subsequent deployment of coils while the microcatheter is impinged against the wall may result in rupture. Reported intraprocedural rupture rates associated with BRT range from 1.7 to 4%, and depending on the series, this rate exceeded, was comparable to, or was less than the intraprocedural rupture rate associated with standard coiling [13, 35].

In the event of an intraprocedural aneurysm rupture, protamine should be administered in order to normalize the activated clotting time (ACT), the balloon is temporarily inflated within the parent vessel in order to achieve hemostasis, and the anesthesiologist is immediately informed of the situation and asked to keep the systolic blood pressure less than 140 mm Hg. The fundus of the aneurysm is then rapidly packed with coils. At the end of the procedure, a CT scan is obtained to evaluate for hydrocephalus, and an external ventricular drain may be necessary depending on the patient's neurological exam after the procedure.

Herniation of the coil mass may precipitate thrombus formation or cause parent vessel occlusion. This problem is usually seen with wide-necked aneurysms and typically occurs at the end of the procedure, whereby excessive embolization, or the over-deployment of coils into the aneurysm, fundus promotes their subsequent prolapse. This can be avoided by using shorter and softer coils toward the end of coil embolization and careful removal of the microcatheter following coil detachment. The use of a longer and stiffer coil at the start of the procedure to form a stable initial basket also prevents subsequent displacement by other coils.

Various approaches can be used to address herniated and or migrated coils. A stent or balloon may be deployed across the neck of the aneurysm to trap the prolapsed coils within the fundus of the aneurysm. Stent retrievers, Merci devices, or alligator clips may also be employed to retrieve the prolapsed or migrated coil [36]. The displaced coils may precipitate local thrombus formation which should be addressed with a local low-dose intra-arterial glycoprotein IIb/IIIa receptor inhibitor [28, 37].

The most common complications seen with stenting are thromboembolic and include in-stent thrombosis, delayed parent vessel, or stent occlusion. These complications may result in an ischemic stroke, or they can be asymptomatic and discovered on routine follow-up imaging. Such complications are often due to incomplete platelet inhibition which may in turn be the result of patient noncompliance or poor patient response to the administered antiplatelet regimen. In this setting the patient should undergo platelet function testing to determine patient responsiveness and the need for alternative antiplatelet regimens. Intraprocedural thrombus formation may be treated with a local low-dose intra-arterial glycoprotein IIb/IIIa receptor inhibitor.

Unlike their balloon-mounted predecessors, self-expandable intracranial stents are more prone to misplacement and migration as they exert lower levels of outward

radial force on the involved vessel. Trans-stent manipulation of microcatheters, guidewires, and additional stents may also cause stent migration. Should this occur during the procedure, the interventionalist may elect to proceed with coiling should the functional neck width preclude herniation of the coil mass. If neck coverage is determined to be insufficient for further treatment a second stent may be placed to enhance coverage.

Shapiro et al. published meta-analyses in 2012 which investigated the complications and clinical and angiographic outcomes of stent-assisted coiling of intracranial aneurysms. They reported a 61% rate of complete aneurysm occlusion at variable time points. Twenty-three percent of these aneurysms were judged to have been incompletely treated but progressed to complete occlusion on follow-up imaging. They found an overall complication incidence of 19%; of these thromboembolic complications were the most prevalent (9.6%) followed by stent-related technical complications (9.3%) including failed delivery and stent migration. Hemorrhagic complications were seen in 2.2% of cases but accounted for 43% of the periprocedural mortality observed. It is somewhat difficult to interpret these results given the heterogeneity of the data utilized in the analyses; comparatively single center series often report lower complication rates and a higher incidence of aneurysm occlusion [38].

Few studies have been published comparing outcomes in balloon remodeling and stent-assisted coiling of intracranial aneurysms. However the single center analysis done by Consoli et al. and Chalouhi et al. reached similar conclusions, namely, that stent-assisted coiling achieved higher rates of aneurysm occlusion with similar rates of periprocedural morbidity [39, 40].

Ultimately complication avoidance is the result of meticulous preparation, patient selection and careful selection of the treatment modality to be employed.

Conclusion

Balloon remodeling and stent-assisted coiling have allowed for the endovascular treatment of previously untreatable intracranial aneurysms. Both adjunctive devices and the techniques associated with them are safe and capable of providing durable embolization of aneurysms.

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Aneurysm Treatment with Flow Diverters

26

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Checklist: Aneurysm Treatment with Flow Diverters

Equipment needed	Procedural steps
Radiology technicians • Long sheath (6F–8F) for femoral artery access • Arch selection catheter • Distal access catheter • Microwire • 0.027-in. ID microcatheter for stent delivery • Flow-diverting stent • Heparinized saline drips Nursing • Confirm patient compliance with medications (e.g., aspirin and clopidogrel) • Confirm pre-procedure platelet function testing results; start dual antiplatelet therapy 1 week prior • Confirm negative pregnancy test (if applicable) • Point-of-care assay to target activated clotting time >250 s following arterial access • Document pre-procedure lower extremity pulses • Review serum chemistries for renal impairment, etc. Anesthesia • Procedure done under general anesthesia; routine preoperative medical clearance • Ensure paralysis, especially during critical portion of procedure • Ensure emergency medications are immediately ready for administration upon induction: protamine, abciximab, eptifibatide Neurosurgeon • Review preoperative imaging to estimate stent size needed, need for adjunctive coiling, and aortic arch anatomy	Access • Femoral artery access with long sheath; angiography to confirm entry site appropriate for use of closure device • Placement of triaxial system: guide catheter (cervical carotid artery), distal access catheter (intracranial carotid artery), microcatheter (distal to stent deployment site) Stent deployment • Deployment of stent through microcatheter; initial partial deployment in straight segment of vessel; drag back to ensure coverage across aneurysm neck • Intermittent angiography to confirm blood flow in parent vessel and absence of thrombus formation • Cone beam CT to confirm stent apposition to parent vessel wall • Balloon remodeling as needed Management • Intraprocedural thrombus: management with glycoprotein IIb/IIIa inhibitor • All patients receive dual antiplatelet agents for 6 months or longer • Aspirin therapy for life

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Thromboembolism	Vessel wall injury by stent	Aspirin and clopidogrel preoperatively for at least a week	Continue aspirin and clopidogrel for 6 months then transition to aspirin monotherapy for life
	Alteration of blood flow by stent		
	Stent serves as nidus for platelet aggregation		Functional preoperative platelet reactivity assay to assess level of residual platelet reactivity after a week of treatment with aspirin and clopidogrel
Branch (perforator) vessel occlusion	Occlusion of vessel that arises from parent artery due to redirected flow from stent covering its origin	Coverage of named branches of the anterior circulation and posterior inferior cerebellar artery rarely result in occlusion	Perforating (unnamed) vessels of the M1 segment of the middle cerebral artery, A1 segment of the anterior cerebral artery, and basilar artery have higher incidences of occlusion; oversizing of stent in these areas can increase porosity
Hemorrhagic/ ischemic events	Target aneurysm rupture via thrombus-associated autolysis of aneurysm wall	Mitigate risk by coil packing aneurysm dome as adjunctive technique	Aneurysms greater than 1 cm may benefit from adjunctive coil embolization
	Distal parenchymal hemorrhage possibly due to foreign body embolic material or ischemia	Limit possibility of iatrogenic foreign body emboli; ensure adequate antiplatelet functionality	Limit endothelial injury from catheter; preoperative platelet function testing; monitor for catheter-induced vasospasm

Introduction

Flow diversion is a novel treatment for brain aneurysms that works by redirecting blood flow away from the aneurysm. By placing a stent in the parent vessel that covers more of the opening to the aneurysm with mesh than traditional stents, blood flow is redirected away from entering the aneurysm. The blood within the aneurysm then stagnates and undergoes thrombosis. Over time, a new endothelium develops across the neck, thereby reconstructing the parent vessel and curing the aneurysm. There are several known rare complications associated with this treatment modality and a growing understanding of how to avoid them. For one, ischemic events can occur and are related to either thromboembolism or perforator vessel occlusion. Also, hemorrhagic events can occur unpredictably at distant sites, or even from the target aneurysm. Finally, aneurysm persistence following treatment is an infrequent event but can occur and place patients at risk for future aneurysm rupture. Flow

diversion is an effective method to treat many types of brain aneurysms, and a focus on complication avoidance is necessary to make it an even safer option for patients.

Procedural Overview

Flow diversion is a treatment technique used for large or giant wide-necked intracranial aneurysms of the proximal internal carotid artery. It is currently also used "off-label" for the treatment of other aneurysms, including small aneurysms and aneurysms of the posterior circulation. The general procedural workflow is as follows: Patients begin dual antiplatelet therapy a week before the procedure. The patients are placed under general anesthesia. Femoral artery access is obtained, and then a triaxial catheter system is placed using standard techniques. Using a proximal carotid artery aneurysm as an example, the microcatheter is placed in a straight segment of the middle cerebral artery, ensuring it isn't immediately at a bifurcation point. The flow-diverting stent is then brought up through the microcatheter and partially deployed. The entire microcatheter/stent system is pulled back to the intended landing zone just distal to the aneurysm neck. The remainder of the stent is deployed via a combination of pushing the delivery wire and unsheathing of the microcatheter. The delivery wire can be recaptured with the microcatheter to maintain distal parent vessel access within the stent. Post-deployment inspection ensures that the stent is apposed to the parent vessel wall without kinking. Cone beam CT can be used as an ancillary test. Balloon remodeling of the stent is performed as needed. Final angiography confirms parent vessel patency and the absence of thromboembolic complications (Fig 26.1).

Complication Avoidance and Management

Ischemic Events

Prevention of Thromboembolism

In recent years, blood flow diversion has emerged as a popular treatment option for many types of brain aneurysms that would be otherwise difficult to treat with conventional modalities of surgical clipping or coiling [1–7]. It has also expanded to become a preferred treatment modality for smaller aneurysms of the proximal carotid artery given the favorable risk profile and the high rate of cure [8]. The procedural aspects of stent deployment are methodical and sequential, but the optimal management of one of the main risks of treatment, thromboembolism, is more controversial.

By placing a metal device (the flow-diverting stent) into the vessel lumen, there is an inherent risk of thrombus formation. Two arms of Virchow's triad of vascular thrombosis, namely, vessel wall injury and alteration in blood flow, are directly affected, and the metal surface itself also serves as a nidus for platelet aggregation. In stent thrombosis and distal embolism can have devastating complications, particularly in the intracranial circulation. To combat this, antiplatelet aggregation agents have historically been used for intracranial stents [9–11]. For flow-diverting stents, the typical regimen for periprocedural treatment is dual antiplatelet agents (aspirin and

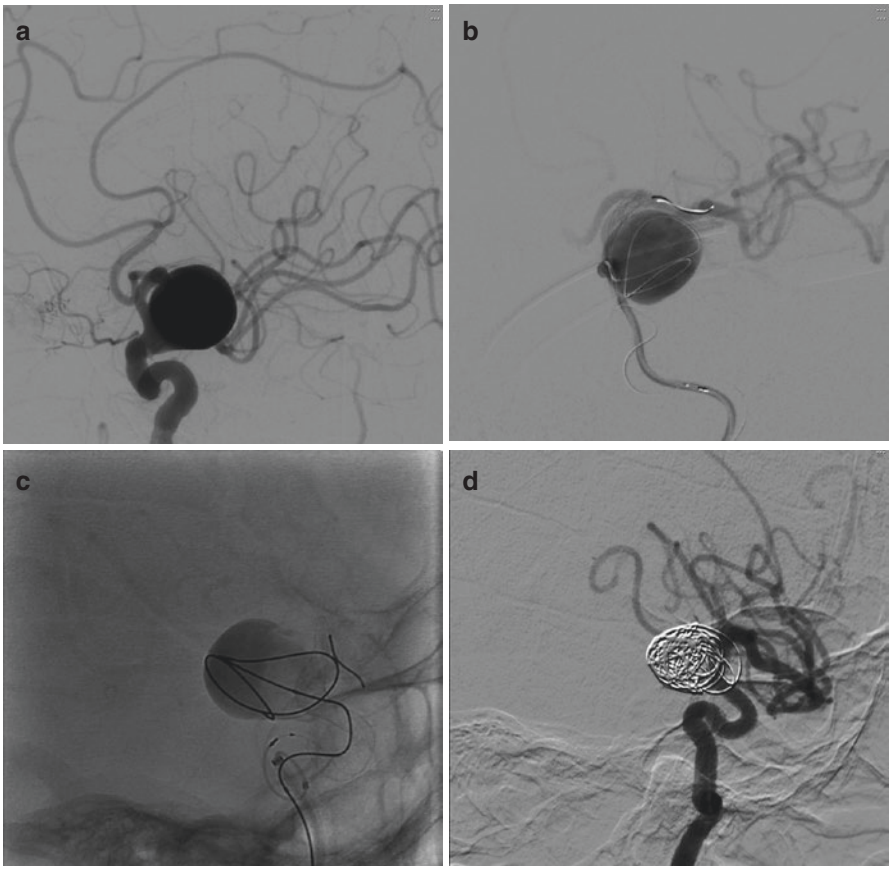

Fig. 26.1 Flow diversion for treatment of a giant unruptured brain aneurysm. (**a**) A middle-aged patient presented with a giant unruptured brain aneurysm arising from the left supraclinoid carotid artery. Treatment with flow diversion and adjunctive coil embolization was undertaken. First, the microcatheter delivering the flow diverting stent was positioned in the distal M1 segment of the middle cerebral artery (not shown). For giant aneurysms, it is important to ensure this distal positioning of the microcatheter in order avoid prolapse into the aneurysm when the stent is loaded and advanced across the aneurysm neck. Next, a separate microcatheter is positioned within the aneurysm dome for adjunctive coil delivery. (**b**) Then, a small segment of the distal stent is advanced out of the microcatheter to allow it to open and it is dragged back to the final deployment zone. After wards, a few coil loops are delivered into the aneurysm. (**c**) The remainder of the flow diverting stent is then deployed completely across the aneurysm neck, there by "jailing" the coiling microcatheter. Coils are then delivered into the aneurysm to mitigate the risk of target aneurysm rupture, a practice that is typically followed for aneurysms >1.5 cm in diameter. Unlike primary coil embolization, the coils are packed relatively loosely without the intention of immediate aneurysm cure. (**d**) Follow-up angiography at six months demonstrates complete exclusion of the aneurysm and reconstruction of the parent artery with the flow diverting stent

clopidogrel) preoperatively for at least a week, which is then continued for 6 months postoperatively. At 6 months, patients are then transitioned to aspirin monotherapy, a medication that extends for life. Even with the use of antiplatelet agents, flow-diverting stents can result in silent ischemia detected by surveillance magnetic resonance imaging in up to 62% of patients [12–14]. This highlights the need for better optimization of thromboembolic prophylaxis. Currently, there exists no randomized trials to direct the optimal agent, dosing, or schedule of administration for placement of any intracranial stent, and practice is dictated by anecdotal and retrospective experience.

It is possible that thromboembolic complications may be related to genetic diversity in individual patient responses to drug response to platelet inhibition [15]. For example, even if a patient is treated with both aspirin and clopidogrel, so-called nonresponders to clopidogrel may be in effect only experiencing the response to aspirin and be therefore undertreated. For this reason, many practitioners utilize a functional preoperative platelet reactivity assay (P2Y12 receptor activation with ADP) to gauge the level of residual platelet reactivity after a week of treatment with aspirin and clopidogrel. Dosage of medications can then be changed, or even switched, in order to achieve an adequate assay result. Paradoxically, a retrospective review of the largest registry of flow-diverting stents suggests that patients undergoing platelet testing may be associated with higher rates of neurologic morbidity [16]. Mechanisms for this finding are not clear, but the results generate a hypothesis that overly aggressive measures to achieve what is perceived as an adequate assay response could be detrimental. It is estimated that genetic diversity in *ABCB1* and *CYP2C19* could contribute to increased risk of major adverse events in almost half of the entire population due to impaired platelet inhibition while on standard doses of clopidogrel, based on genotyping of patients undergoing percutaneous coronary intervention [15]. Unlike clopidogrel, prasugrel is effective in most individuals. Further study with both functional assays and genotyping is necessary to better optimize outcomes for patients with flow-diverting stents.

While aspirin and clopidogrel are the most common antiplatelet aggregation agents in clinical use for intracranial stents, other agents have been studied in randomized trials in the cardiac population. In TRITON-TIMI 38, a trial comparing dual therapy with aspirin and either prasugrel or clopidogrel, the aspirin and prasugrel arm demonstrated decreased percentages for the primary endpoint (12.8% vs. 16.5%; cardiovascular death, myocardial infarction, or ischemic infarction), without an increase in hemorrhagic complications [11]. However, other cardiac trials reported increased hemorrhagic complication risk with prasugrel, despite significantly fewer cardiac ischemic events [17]. The effectiveness profile of various antiplatelet agents in patients undergoing intracranial intervention may be different given the unique risks of intracranial hemorrhage and requires further study.

Branch (Perforator) Vessel Occlusion

In addition to thromboembolism related to platelet aggregation at the site of the flow-diverting stent and/or the target aneurysm undergoing thrombosis, another potential source of ischemia is branch vessel occlusion. This refers specifically to occlusion of a vessel(s) that arises from the parent artery because of redirected blood flow from the stent covering its origin. In theory, flow-diverting stents have an optimal metal coverage across the aneurysm neck resulting in thrombosis within

Table 26.1 Named branch vessel patency and stroke after coverage with flow-diverting stent

Vessel	Aneurysms	Occlusion	Stroke	Publication
Ophthalmic	20	4	0	Puffer et al. [20]
Ophthalmic	69	6	0	Griessenauer et al. [21]
Anterior choroidal	29	1	0	Raz et al. [22]
Posterior inferior cerebellar artery	13	0	0	Levitt et al. [23]
Anterior circulation (ACA, PComm, AChoA, ophthalmic)	127	13	0	Rangel-Castilla et al. [24]
Ophthalmic	95	6	1	Chalouhi et al. [25]
Anterior choroidal	15	1	0	Brinjikji et al. [26]
Posterior communicating	13	3	0	Brinjikji et al. [27]
Anterior circulation (PComm, AChoA, ophthalmic)	74	3	0	Vedantam et al. [28]
Ophthalmic	19	0[a]	0	Durst et al. [29]
Posterior communicating	30	16	0	Daou et al. [30]

ACA anterior cerebral artery, *PComm* posterior communicating artery, *AChoA* anterior choroidal artery

[a]Five were noted to have sluggish but persistent blood flow

the aneurysm, without interfering with normal arteries. This has been studied in animal models, with in vivo experiments supporting this hypothesis [18]. However, there remains concern about the unpredictable nature of vessel occlusion that has been observed in the human intracranial circulation. Small branch vessel occlusion supplying the brainstem can have devastating effects and was initially seen during treatment of vertebrobasilar aneurysms with first-generation flow-diverting stents [19]. With greater experience, vessels in other locations were also noted to undergo spontaneous occlusion following flow-diverting stent placement, but the majority of these occlusions were without clinical sequelae (Table 26.1).

A leading hypothesis is that a low pressure gradient across a blood vessel, from its origin to its termination, is a risk factor for vessel occlusion. Simply stated, if there is collateral supply to a blood vessel (e.g., extracranial-to-intracranial supply of the ophthalmic artery), it is at greater risk for thrombosis. These individualized collateral blood flow patterns, both across the circle of Willis and from the extracranial-to-intracranial circulation, can be appreciated on preoperative angiography and are the subject of ongoing investigation [31]. In summary, coverage of named branches of the anterior circulation and the posterior inferior cerebellar artery rarely result in occlusion and even more uncommonly result in stroke. Still, trepidation exists with covering perforating (unnamed) vessels of the M1 segment of the middle cerebral artery, the A1 segment of the anterior cerebral artery, and the basilar artery [32–34].

Hemorrhagic Events

Target Aneurysm Rupture

Aneurysm cure is not immediately achieved or expected with placement of a flow-diverting stent. Following deployment of the stent, it is common for blood to continue to fill into the aneurysm, albeit with stasis and angiographic signs of a reduced

inflow jet. Only over time does the aneurysm fully undergo thrombosis and an endothelial lining is developed across the aneurysm neck. Related to this, rare early bleeding events from the aneurysm have been reported [3, 35]. The pathophysiology of these early bleeding events is not well understood, but a leading theory is that as the flow-diverting stent induces thrombosis within the aneurysm, thrombus-associated autolysis of the aneurysm wall occurs, further weakening its structure. This, combined with a delayed drop in intra-aneurysmal pressure, may result in aneurysm rupture [36–39]. To mitigate this risk, coil packing of the aneurysm dome has been used as an adjunctive technique at the time of flow diversion [40]. Filling the aneurysm dome with coils can eliminate blood flow into the aneurysm dome and provide protection from hemorrhage nearly immediately, while the flow-diverting stent allows for a new endothelium to grow across the aneurysm neck over time. The adjunctive coiling technique, particularly with larger aneurysms with expected large intra-aneurysmal thrombus volumes, warrants further study, as it may be useful in avoiding this potentially devastating complication.

Distal Parenchymal Hemorrhage

Compared to the rare occurrence of hemorrhage from the treated aneurysm following flow diversion, the etiology for remote and delayed hemorrhage in other parts of the brain is even more difficult to explain [41]. Even though a flow-diverting stent results in hemodynamic and arterial compliance changes in the vessel, it is difficult to hypothesize how this can be expected to result in downstream hemorrhagic events. Histopathologic analysis in a few cases has suggested that foreign body embolic material from the device or a delivery catheter may be a contributing factor [42]. Also, since patients are maintained on dual antiplatelet aggregation agents to prevent thromboembolic complications for several months after treatment, they are also at a slightly higher risk for brain hemorrhage in general. It is possible that iatrogenic embolic events, endothelial injury, or catheter-induced vasospasm at the time of the procedure can result in ischemic stroke, with the potential for hemorrhagic conversion. Further investigation into these rare events is needed (Table 26.2), as they are unpredictable and often devastating.

Aneurysm Persistence Following Treatment

Aneurysm persistence is a measure of treatment failure following flow diversion, with rates of about 10–30% [3, 43–45]. In the original study that propelled the FDA approval of the pipeline embolization device in the USA (PUFS study), Becske et al. evaluated 107 patients with a mean aneurysm size of 18.2 mm, 20.4% of which were larger than 25 mm in maximum dimension. Most of these aneurysms involved the cavernous or paraophthalmic segments of the ICA. Of the 97 patients (93.3%) who underwent follow-up angiography at 180 days, 86.8% showed complete occlusion without major stenosis or use of adjunctive coils [46]. A subsequent meta-analysis of 29 studies with 1654 aneurysms evaluated at 6 months reported a complete occlusion rate of 76% (95% CI of 70–81%). The effect did not significantly differ with aneurysms size, as complete occlusion was noted in 80% of small aneurysms (<10 mm),

Table 26.2 Hemorrhagic and ischemic complications after flow-diverting stents

	Distant parenchymal hemorrhage	Ischemic stroke	Target aneurysm rupture/post-procedural subarachnoid hemorrhage	Neurological morbidity and mortality
Becske et al. [1] (2013, *n* = 107)	1.9	2.8	0.9	5.6
Kallmes et al. [2](2015, *n* = 793)	2.4	4.7	0.6	8.4
Petr et al. [3] (2016, *n* = 122)	0.8	1.6	0.8	2.5 morbidity/1.6 mortality
Brinjikji et al. [4](2013, *n* = 1451)	3.0	6.0	4.0	5.0 morbidity/4.0 mortality
Wakhloo et al. [5] (2015, *n* = 165)	2.5	3.7	2.5	6.0 morbidity/2.7 mortality
Kallmes et al. [6] (2016, *n* = 191)	3.7	4.7	1.6	6.8 morbidity/1.6 mortality

Values presented expressed as % (year of publication, *n* = number patients)

74% of large aneurysms (10–25 mm), and 76% of giant aneurysms (>25 mm) [3]. In a recent multicenter trial evaluating 119 aneurysms of various sizes and locations, overall occlusion rates increased from 81.6%, to 84.1%, to 93.2% in the 6-month, 1-year, and 2+-year time periods, respectively [44]. Various factors, such as anatomical complexity, inadequate coverage of the aneurysm, and the existence of preexisting stents play a role in determining the extent and duration of aneurysm occlusion.

Factors Influencing Aneurysm Persistence

Shapiro et al. reported a 21% (19/92) incidence of aneurysm persistence in their cohort of large and giant ICA aneurysms at 1-year follow-up [45]. In this retrospective review, preexisting stents, along with increasing aneurysm complexity as reflected by saccular lesions with lower dome-to-neck ratios and fusiform morphologies, were found to be significantly associated with treatment failure. Certain radiographic features were common in failed cases as well, including inadequate aneurysm coverage by the stent, presence of branch vessels in the aneurysm fundus, and evolving endoleaks, arising as a consequence of primary maldeployment of the stent.

Treatment failure related to inadequate coverage of the aneurysm usually manifests as broad areas of persistent exchange across the braids of the stent with filling of the aneurysm on angiography. These usually proceed through submillimeter holes in multistent constructs, typically located along curvature convexities where the stent is maximally stretched. As previously mentioned, the presence of previous stents may be problematic as well, particularly when implanted along an acute vessel curve. Laser-cut stents often do not fully appose the parent artery wall, and deploying flow diverters within these stents further limits the apposition of the target vessels. This

not only unmasks the preexisting malapposition of the indwelling stent, but it potentially leads to inadequate intimal overgrowth of the newly deployed flow diverter. Extending the stent landing zone proximally and distally to allow better purchase may maximize efficacy and reduce the incidence of aneurysm persistence.

Anatomic Factors Associated with Flow-Diverting Stent Treatment Failure

Branch vessels of target aneurysms can potentially contribute to aneurysm persistence by allowing persistent filling across the flow diverter through similar physiological principles responsible for preserving jailed branch vessels and perforators. When a significant branch vessel remains a part of the aneurysm wall, flow gradient from the parent artery to the branch vessel overcomes the stagnation and thrombosis from developing within the aneurysm sac. This may prevent the formation of a new endothelial wall on the surface of the flow diverter, which is necessary for aneurysm obliteration. For example, posterior communicating artery (PCOM) aneurysms with fetal posterior cerebral artery (PCA) present a unique challenge to either clipping or coiling due to the inherent necessity to maintain the patency through the PCOM artery, which is the only source of flow to the distal PCA. Traditionally, clipping these aneurysms has been the preferred modality, especially if an optimal dome-to-neck ratio did not exist. However, the advent of flow-diverting stents has expanded the therapeutic target of endovascular therapy to include those aneurysms with enlarged necks.

Unfortunately, endovascular treatment of PCOM aneurysms with fetal PCA is still a challenge. Zanaty et al. reported three cases of flow-diverting stents for these aneurysms and highlighted important limitations [47]. Each of the cases had recurrence at 6-month follow-up angiography and had to undergo microsurgical clipping for definitive treatment. The authors proposed that the treatment failed since the flow through the fetal PCA and the aneurysms sac remains high even after stent placement due to physiologic demand. Kan et al. also reported on their experience of flow-diverting stents for fetal PCOM aneurysms. Four patients were included in their series, each with various presenting symptoms [48]. Three of the four patients received coil embolization prior to flow diversion, and each had persistent aneurysmal filling at their respective follow-up, which varied from 18 to 36 months. They contributed the lack of treatment effect to the continued demand and pressure gradient in a fetal PCA following flow diversion.

The paraophthalmic region is another anatomic site with significant branch vessels that may portend a higher rate of aneurysm persistence following treatment with flow diversion. Through a retrospective multicenter series, Griessenauer et al. evaluated the efficacy of flow diversion in treating small ($\leq$7 mm) paraophthalmic artery aneurysms with three distinct anatomic characteristics: (1) ophthalmic artery (OA) origin that is separate from the aneurysm, (2) OA from the aneurysm neck, and (3) OA that arises from the aneurysm dome [21]. Type 3 OA origin (OA arising from aneurysm dome) was associated with a higher rate of persistence, supporting the hypothesis that continued demand through incorporated vessels can lead to aneurysm persistence following treatment.

Conclusion

Thousands of patients have been successfully treated with flow-diverting stents with low rates of morbidity and mortality. Complication avoidance is centered on the optimization of thromboembolism prophylaxis with antiplatelet aggregation drugs. Other areas of focus include patient-specific computational flow modeling in order to better understand the rare occurrence of target aneurysm rupture and delayed distal hemorrhage after treatment. A growing understanding of how individualized variations in angioarchitecture affect intra-aneurysmal flow dynamics may also be helpful in predicting which aneurysms are more likely to persist following treatment.

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Aneurysm Treatment with Liquid Embolics

27

Andrew J. Ringer and Ralph Rahme

Checklist: Aneurysm Treatment with Liquid Embolics

Equipment needed	Procedural steps
Patient selection • Include those not good candidates for flow diversion because of recurrent stent-embolized aneurysms or nickel allergy • Exclude patients with ruptured aneurysms Preoperative • Dual antiplatelet therapy (aspirin 325 mg/day, clopidogrel 75 mg/day) minimum 4 days	Identify on imaging • Absence of vital perforators near aneurysm neck • Satisfactory balloon seal before Onyx injection • Best for sidewall aneurysms of paraclinoid and proximal supraclinoid ICA Access • Access femoral artery with 1% lidocaine local • Maintain ACT values between 250 and 300 s throughout procedure • Advance 90-cm 6 French Shuttle Select guiding sheath over a 125-cm 5.5 French Slip or 5 French Penumbra Select selective catheter into the distal cervical portion of affected vessel (ICA or vertebral artery) • Obtain standard and 3D rotational angiography, and select working projections

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Radiology technicians
- Balloon (4-mm diameter × 15–20 mm in length)
- Additional (or dual channel) RHV and tubing
- 3D angiography protocol
- Femoral access kit (1% lidocaine)
- Timer display visible on monitors in room

Nursing
- Heparin
- Protamine
- Additional heparinized saline bag
- Short-acting sedatives (for conscious sedation cases)
- Staff pager numbers
  - Neurosurgery
  - Anesthesia attending

Anesthesia
- Light sedation and anesthesia (midazolam 1 mg, fentanyl 50 μg)
  - Target level of sedation should permit clinical evaluation during balloon inflation
- Cardiorespiratory monitoring
- General anesthesia during Onyx embolization using cycles of balloon inflation/deflation

NeuroInterventionalist
- Choice of DMSO-compatible microcatheter
- Choice of compliant or extra-compliant balloon catheter
- Choice of guiding catheter/long sheath with minimum ID 0.070″

Advance to aneurysm
- Use roadmap guidance
- Through guiding sheath, advance Hyperglide balloon catheter over a 0.010″ X Pedion microwire or advance Scepter C over a 0.014″ Traxcess into the aneurysm-bearing segment of the vessel. Position balloon markers across the aneurysm neck
- Advance DMSO-compatible microcatheter through the guiding sheath over a 0.014″ microwire into aneurysmal sac
- Use a Cadence Precision Injector syringe to inflate the balloon to nominal pressure and gently inject contrast
- Perform angiographic seal test. If leak occurs, overinflate balloon slightly and repeat test. If leak persists, abort Onyx injection and consider coils

Onyx injection
- If no contrast leaks, deflate balloon and prime the microcatheter with DMSO using at least 1.5× dead space of the catheter. Slowly inject Onyx with Quick-Stop delivery syringe, about 0.15–0.2 mL to fill most of the dead space
- Inflate the balloon again to nominal pressure. Continue Onyx injection under blank roadmap guidance
- Before embolization, confirm clinical tolerance of continuous balloon occlusion by nuclear medicine perfusion testing. Or during embolization, use continuous neurologic evaluatio
- Obtain baseline neurological assessment (i.e., level of consciousness, verbal fluency/comprehension, cranial nerve function, visual fields, motor/sensory exam in all four extremities). Repeat the assessment every 10–15 min until embolization is complete and the balloon is permanently deflated.
- Continue intermittent Onyx injection until aneurysm volume is completely filled. Ideal result will include a small volume of Onyx leakage into parent artery around the neck, confined to the length of the balloon or less
- Confirm full casting of the aneurysm with neck coverage using 3D angiography

Troubleshooting during onyx embolization
- If the patient develops any clinical signs of cerebral ischemia (e.g., worsening level of consciousness, aphasia, focal neurological deficit), quickly reassess the balloon's position. Reposition if needed to avoid occlusion of collateral flow
- Change momentum and direction of Onyx migration by intermittently pausing for 30–120 s during Onyx injection. Best when most of the aneurysm dome has been filled and Onyx starts to migrate into the neck and laminate around the inflated balloon in the parent artery
- When patient movement causes significant artifact, simply reset and repeat roadmap images; this usually resolves the problem

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
DMSO toxicity	Vasospasm, vessel wall damage, SAH, or infarction	• Stop injecting DMSO immediately • Assess hemodynamics and neurologic exam (if awake procedure) • Perform angiogram via guide catheter to assess nature and extent of vascular damage • Manage accordingly (e.g., verapamil for vasospasm, thrombectomy for intraluminal thrombus, temporary balloon occlusion for active extravasation)	Limit DMSO and Onyx injection rate to 0.1 mL/min
Extra-aneurysmal leakage or embolization of Onyx		• Stop injecting Onyx, assess hemodynamic status, and perform neurologic exam (if awake procedure) • Perform angiogram via guide catheter to assess location and extent of Onyx embolization • Consider mechanical reperfusion depending on clinical and angiographic picture	• Never attempt Onyx embolization if seal test fails (particularly if nearby perforators) • Stop Onyx injection if roadmap images blurred by motion or subtraction artifact. Reset blank roadmap before resuming injection • Periodically confirm balloon catheter position to ensure no migration from its initial position; minimize risk with continuous balloon occlusion in awake or electrophysiologically monitored patient • Keep balloon inflated for 3 min after Onyx injection to allow solidification of the Onyx cast • Always pull microcatheter out under negative pressure (manual syringe aspiration) after embolization is complete. Quickly withdraw from patient's body

(continued)

Complication	Cause	Remedy	Avoidance
Onyx cast instability	Tendency to migrate back into parent vessel when balloon deflated	• Reinflate balloon catheter to push Onyx cast back into aneurysm • Bring up a second microcatheter and deploy stent across aneurysmal neck to stabilize Onyx cast and maintain parent vessel patency	• Consider stent-assisted Onyx embolization if aneurysm is very wide-necked and shallow • Always reinflate balloon to give mechanical support for the intra-aneurysmal Onyx cast before pulling microcatheter out at end of procedure
Cerebral ischemia secondary to balloon occlusion		• If neurologic or neurophysiologic changes occur, immediately stop Onyx injection. Allow 1–2 min of Onyx cast solidification, and then slowly deflate balloon to allow cerebral reperfusion • Reassess position of balloon catheter and reposition if migrated	• Consider awake procedure to allow continuous neurologic monitoring; other options are intraoperative neurophysiologic monitoring, preoperative balloon test occlusion • For general anesthesia, never keep balloon inflated for >5 min. Allow 2 min of cerebral reperfusion after each balloon inflation cycle • Periodically confirm that balloon catheter position is not blocking collateral flow (e.g., carotid terminus, posterior communicating artery origin)
Onyx migrates in undesired direction	Flows into neck rather than dome or tracks along balloon catheter rather than filling	• Pause Onyx injection for 30 s to 2 min, and then reset roadmap and restart injection. Note: About 30 s pauses tend to provide small changes in momentum NOTE: 2-min pauses provide more drastic changes in direction	• Always inject Onyx very slowly under blank roadmap guidance to ensure it follows the path of least resistance and moves in desired direction
Significant ectopic Onyx cast in parent vessel	Much more than desired "hat-brim" configuration	• Reinflate balloon over fresh ectopic Onyx cast to plaster it against vessel wall • Consider stent placement if balloon remodeling unsuccessful	• Always inject Onyx very slowly under blank roadmap guidance for maximum control of its movement • Frequently reset blank roadmap to eliminate motion/subtraction artifact

Complication	Cause	Remedy	Avoidance
Significant resistance to Onyx injection	Onyx solidification inside microcatheter	• Stop injection, and do not force Onyx through the microcatheter. Microcatheter rupture causing Onyx leakage into intracranial circulation can be catastrophic • After 3 min of Onyx cast solidification, withdraw microcatheter • Consider reaccessing aneurysm with new microcatheter versus aborting procedure (depending on angiographic result)	• Always prime microcatheter with DMSO • Never inject DMSO immediately after contrast agent. Always flush contrast medium with heparinized saline before priming with DMSO • Avoid pausing Onyx injection for more than 2 min

Introduction

During the past decade, Onyx® HD-500 (Medtronic Neurovascular, USA), a high-viscosity liquid embolic agent, has been used extensively to treat intracranial aneurysms. Preliminary experience using this relatively novel agent was rewarding in terms of high-occlusion rates and low-recanalization rates of large and wide-necked aneurysms [1, 2]. Use of Onyx HD-500 has since decreased dramatically with the increasing popularity of flow diverters as first-line treatment for complex intracranial aneurysms. Nevertheless, it remains a useful endovascular tool for select patients who are not good candidates for flow diversion because of recurrent stent-embolized aneurysms or nickel allergy.

Some of the serious complications (e.g., aneurysm rupture, parent artery dissection, thromboembolic events) that develop are common to all endovascular aneurysm treatments (discussed in other chapters), whereas others are unique to Onyx HD-500. This chapter focuses on aneurysm growth or delayed rupture from incomplete occlusion, parent vessel compromise or occlusion from leakage or embolization of liquid embolics, and role of postoperative angiograms in detecting the pattern of Onyx deposition near the aneurysmal neck, the most important determinant of treatment.

Procedural Overview

Patient Selection

We routinely assess unruptured aneurysms for possible Onyx embolization, irrespective of their size and neck diameter, considering two major factors. First is the absence of vital perforators arising close to the aneurysmal neck, which could be

easily compromised by Onyx leakage [1, 3]. Second is whether satisfactory balloon sealing of the neck (i.e., positive seal test) can be achieved before Onyx injection. We typically attempt Onyx embolization only when both conditions are met. Considering location and growth pattern, the best candidates for this procedure are usually sidewall aneurysms of the paraclinoid and proximal supraclinoid internal carotid artery (ICA). We seldom use Onyx in ruptured aneurysms given the risk of hemorrhagic complications associated with dual antiplatelet therapy in patients with subarachnoid hemorrhage (SAH). Moreover, the risk of Onyx-related parent artery compromise could be detrimental to patients who later develop vasospasm.

Technique

Preoperatively, patients are maintained on dual antiplatelet therapy (aspirin 325 mg/day and clopidogrel 75 mg/day) for at least 4 days. Embolization is performed under intravenous conscious sedation, and cardiorespiratory monitoring is continuous. Give small doses of midazolam and fentanyl (typically 1 mg and 50 μg, respectively) initially, and repeat as needed during the procedure to maintain light sedation and analgesia. Avoid excessive sedation so that reliable neurological assessments can be regularly performed.

Femoral arterial access is obtained with local anesthesia (e.g., 1% lidocaine). Full heparinization should maintain ACT values between 250 and 300 s throughout the procedure. A 90 cm 6 French Shuttle Select guiding sheath (Cook Medical, Bloomington, IN, USA) is advanced coaxially over a 125 cm 5.5 French Slip Cath H1 selective catheter (Cook Medical) and a 0.035″ Glidewire (Terumo, Somerset, NJ, USA) into the distal cervical portion of the involved vessel (ICA or vertebral artery). Standard and three-dimensional (3D) rotational angiography is performed, and working projections are selected. Under roadmap guidance, an appropriately sized Hyperglide balloon catheter (ev3 Neurovascular, Covidien), or Scepter C (MicroVention, Tustin, CA), is advanced through the guiding sheath over a 0.010″ X-Pedion microwire (ev3 Neurovascular, Plymouth, MN) for the Hyperglide or 0.014″ Traxcess (MicroVention) for Scepter C into the aneurysm-bearing segment of the vessel and positioned across the aneurysm neck. Next, a dimethyl sulfoxide (DMSO)-compatible microcatheter (e.g., Echelon, ev3 Neurovascular; Headway 17, MicroVention) is advanced through the guiding sheath over a 0.014″ microwire (e.g., Transcend EX, Boston Scientific, Natick, MA; Traxcess, MicroVention) into the aneurysmal sac.

Using a Cadence Precision Injector syringe (Medtronic Neurovascular), inflate the balloon to nominal pressure, and gently inject contrast through the microcatheter into the aneurysm. If no leakage into the parent artery or side branches is seen on the angiographic seal test, embolization is pursued. After balloon deflation, prime the microcatheter with DMSO, and slowly inject Onyx (Quick-Stop Onyx delivery syringe, Medtronic Neurovascular). Once 0.15–0.2 mL of Onyx is injected into the microcatheter to fill most of the dead space, inflate the balloon again to nominal pressure. Continue Onyx injection under blank roadmap guidance.

During conventional Onyx embolization, the patient under general anesthesia undergoes cycles of balloon inflation and deflation [3, 4]. During injection, balloon inflation

in the parent artery protects it against embolic leakage, while intermittent deflation allows cerebral reperfusion. Limiting balloon occlusion of the parent artery to 5 min at a time will help to reduce the risk of cerebral ischemia. Intermittent balloon deflation not only prolongs the procedure but risks balloon migration between cycles, thus increasing risk of intimal injury or Onyx leakage in the parent artery.

Pearl: Conscious Sedation, Neurological Assessment, and Cyclic Balloon Technique

During the past 8 years, the senior author (AJR) modified the cyclic technique to one of uninterrupted Onyx injection and continuous balloon occlusion under conscious sedation. This modification addressed the problems of cyclic inflation-deflation and allowed continuous neurological monitoring throughout the procedure.

During Onyx injection, continuous balloon occlusion requires confirmation of its clinical tolerance. One option is formal test occlusion including nuclear medicine perfusion testing before embolization, and a second is continuous neurologic evaluation during embolization. A baseline neurological assessment can determine the patient's level of consciousness, verbal fluency and comprehension, cranial nerve function, visual fields, and motor and sensory exam in all four extremities. Repeat the assessment every 10–15 min until embolization is complete and the balloon is permanently deflated. If the patient develops any clinical signs of cerebral ischemia (e.g., worsening level of consciousness, aphasia, focal neurological deficit), quickly reassess the balloon's position and reposition if needed. If the balloon has migrated to impede collateral flow (e.g., carotid terminus), then it is partially deflated; therefore, reposition it proximally across the aneurysm neck and reinflate to nominal pressure.

If the patient remains symptomatic even with a properly positioned balloon and patent collateral pathways, continue the procedure using the balloon inflation-deflation cycle. If inflation is clinically tolerated, keep the balloon inflated and pursue Onyx embolization under blank roadmap guidance. Because patients are awake during the procedure, some movement is inevitable, thus significant artifact can result. When this occurs, simply resetting and repeating the images usually resolves the problem.

Intermittent pauses of 30–120 s during Onyx injection are sometimes used to change the momentum and direction of the material's migration. This strategy is particularly important when most of the aneurysm dome has been filled, and Onyx starts to migrate into the neck and laminate around the inflated balloon in the parent artery.

Pearl: Refining Onyx Lamination

We aim for complete filling of the aneurysm's dome and neck and mild "hat-brim" lamination around the balloon in the parent vessel. In our patients, this pattern led to the lowest rates of aneurysm recurrence and minimized the risk of

parent artery compromise. In contrast, too little Onyx in the parent artery sometimes failed to provide adequate neck protection, which increased the likelihood of aneurysm recurrence, but too much Onyx outside the aneurysm (i.e., *ectopic*) seemed to promote delayed stenosis and occlusion of the parent vessel.

When injection is complete, keep the balloon inflated for 3 more minutes to permit solidification of the Onyx cast, and then deflate it for 10 min to allow complete diffusion of DMSO for further hardening. Reinflate the balloon. Finally, pull the microcatheter out of the Onyx cast under negative pressure (syringe aspiration) and quickly withdraw it from the patient's body. Final angiograms obtained through the guide catheter document complete aneurysm obliteration and absence of local or distal thromboembolic complications. With removal of the guiding sheath, close the arteriotomy site in standard fashion.

Postoperative

Postoperatively, patients are maintained on a 12 h intravenous infusion of heparin, and dual antiplatelet therapy for 4–6 weeks, after which clopidogrel is stopped and aspirin continued indefinitely.

Complication Avoidance: Predicting Results

Adjunct Devices

Adjunct devices can sometimes increase the safety of the intervention. For instance, placement of a stent can prevent Onyx cast instability in small and shallow aneurysms. In perforator-rich locations, deployment of a few coils in the aneurysm can create a solid frame that reduces the risk of extra-aneurysmal Onyx leakage.

Pearl: Onyx Grading Scheme

Preliminary results have been promising, with high rates of complete occlusion and low rates of late recanalization [2, 5, 6], even in large and wide-necked aneurysms [7–9]. However, little information exists as to what constitutes an optimal immediate angiographic result after embolization or what leads to delayed complications. Observing that some Onyx lamination in the parent vessel around the aneurysmal neck was useful in preventing recurrence and that extent of its extra-aneurysmal leakage seemed to directly affect delayed parent vessel occlusion, we devised a simple grading scheme for the immediate post-embolization angiographic result (Fig. 27.1).

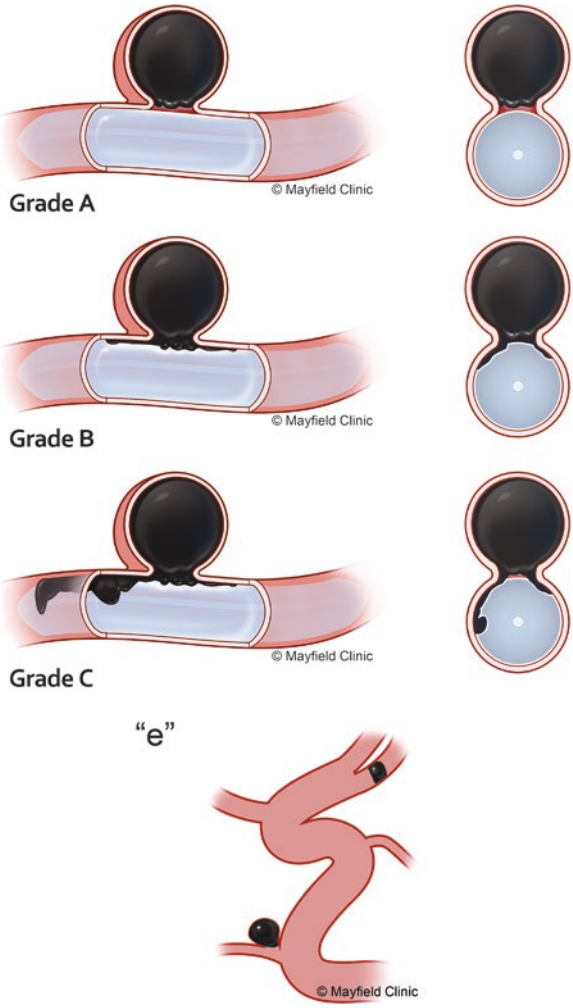

Fig. 27.1 Pattern of Onyx lamination. *Left and right panels*. Grade A, no Onyx outside aneurysm. Grade B, mild "hat-brim" Onyx lamination around balloon in parent vessel. Grade C, "ectopic" Onyx appears as a globular cast in the parent vessel, possibly the result of either its deposition around a suboptimally positioned and/or inflated balloon or from its leakage beyond the balloon's length. Grade C was further subdivided into grades C1 (i.e., non-flow-limiting ectopic Onyx) and C2 (i.e., flow-limiting ectopic Onyx) according to the quality of anterograde flow through the parent vessel. Any change in flow pattern that resulted from ectopic Onyx, whether conspicuous (e.g., slowing of anterograde flow) or occult (e.g., increased contrast streaming through distal collaterals), was deemed a grade C2 result. Suffix "e" was added to the grade (i.e., Ae, Be, or Ce) if distal Onyx embolization occurred (e.g., in middle cerebral artery branches) (Printed with permission by Mayfield Clinic)

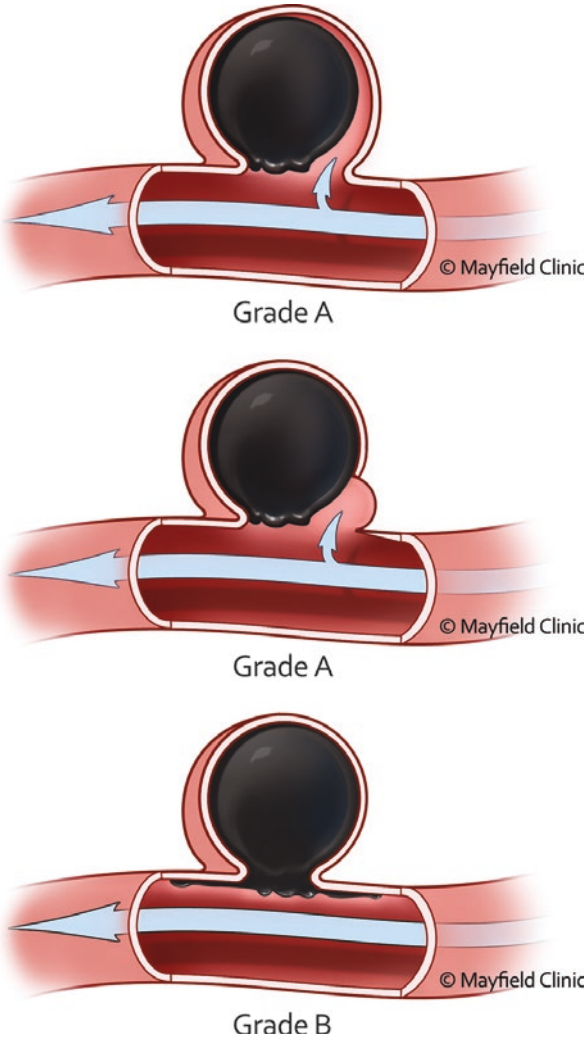

Fig. 27.2 Mechanisms of angiographic recurrence after Onyx embolization. Grade A lesions more commonly recurred, especially with growth at the aneurysm neck than Grade B or higher lesions

Pearl: Defining an Ideal Angiographic Result

In testing our grading scheme for predicting long-term angiographic results, we found that angiographic grade strongly predicted both aneurysm recurrence and parent vessel compromise. Specifically, angiographic recurrence affected more grade A aneurysms (Fig. 27.2) but none of the grade B or C aneurysms ($p = 0.006$). In contrast, severe (>90%) parent vessel compromise occurred in grade C2

aneurysms but none of the grade A, B, or C1 aneurysms ($p = 0.014$). No angiographic recurrence or parent vessel compromise developed for any grade B aneurysms [9].

With these findings, we believe that grade B or grade C1 is the ideal angiographic result, that is, mild extra-aneurysmal Onyx leakage that results in hat-brim lamination on the adjacent parent arterial wall. Coverage of this recurrence-prone area appears to be key in determining long-term angiographic stability. However, a thin line exists between hat-brim lamination and substantial Onyx leakage into the parent artery that could compromise patency. Conversely, if Onyx deposition is confined to the aneurysmal sac and does not cover the perianeurysmal parent arterial wall, risk of angiographic recurrence may be significant. This phenomenon may be due to two mechanisms. First, owing to its nonadhesive properties, blood flow may dissect between the Onyx cast and the aneurysm wall if inflow is not protected by the hat-brimming effect. Second, the intense inflammation that occurs adjacent to Onyx may be a double-edged sword. While it may help occlude the inflow zone with appropriate hat-brimming, as in grade B and C1 results, excessive amounts in the parent artery may lead to intimal hyperplasia and parent artery stenosis or occlusion, as in grade C2 results.

Complication Avoidance and Management

Pearl: Ensuring Aneurysm Occlusion

Pursuit of complete aneurysm filling with a small hat-brim effect is paramount before ending the procedure. Finding that standard 2D angiography was sometimes insufficient, we used two other primary indicators to ensure complete filling. The first indicator is the fluoroscopic density of the Onyx cast; it changes from a nonhomogenous appearance (like Swiss cheese) during filling to become uniformly radiopaque when completely filled. The second indicator is that visualization of filling is best on 3D rotational angiography. In fact, the raw 3D rotational images or 2D reconstructions were often more revealing than 3D reconstructions.

Preventing Onyx Leakage

Onyx-500 is a 20% ethylene vinyl alcohol copolymer dissolved in dimethyl sulfoxide, with micronized suspended tantalum powder to make it radiopaque for easy visualization. Despite this, leakage out of the aneurysm can sometimes go undetected even with adequate balloon inflation. Three strategies are useful to avoid this problem.

First, achieve an effective seal at the aneurysm neck by use of a compliant balloon; it can herniate slightly into the aneurysm neck, a phenomenon visible on fluoroscopy (described above). The authors prefer the Scepter C or Scepter XC balloons (MicroVention).

Second, visualize the liquid embolic as it approaches the aneurysm neck. Problems with visualization of this agent at the aneurysm neck-parent artery interface are sometimes due to bony landmarks within the field or contrast within the balloon. Reducing the concentration of contrast in the balloon can enhance visualization of this liquid agent as it approaches the neck and begins to laminate the balloon surface. The authors typically use a mixture of contrast-saline mixture (2:1) for most balloon-assisted endovascular procedures and a 1:1 (or even 1:2 mixture) for Onyx HD-500 procedures. Of note, the less radiopaque mixture is more easily discerned from the more dense liquid embolic.

Third, minimize the risk of compromising the artery lumen when leakage does occur (usually proximal to the aneurysm when a microcatheter is trapped within the aneurysm). Leakage often occurs in the space between the balloon and parent artery wall created by the microcatheter. For this reason, the authors use balloons much longer than necessary to cover the aneurysm neck alone and center it eccentrically across the aneurysm neck (1/3 of the balloon distal, 2/3 proximal to the aneurysm neck).

Pearl: Managing Onyx Leakage

If leakage occurs beyond the desirable *hat-brim* effect, it is important to avoid compromise of the artery lumen and distal embolus. Onyx that appears stable on continuous fluoroscopy is unlikely to migrate and eventually endothelializes against the artery wall. If a volume of Onyx is visualized in the parent artery after deflation, the authors will reinflate the balloon for several minutes to ensure Onyx hardening and compression against the artery wall. With simple lamination in the artery, Onyx poses no more risk and, in fact, constitutes less foreign material than a stent. As such, the authors do not alter their perioperative management: 12 h of intravenous heparin drip after the procedure and 30 days of dual antiplatelet therapy.

In a rare case of a distal embolus from a fragment of Onyx fractured from the cast during balloon repositioning, the senior author used rotational angiography to reveal lamination of the embolic cast around the wall of the M2 branch of the middle cerebral artery. In one case, we extended routine postoperative heparin drip from 12 to 24 h and hospital stay from 1 to 3 overnights; the patient remained asymptomatic, and the artery remained patent during more than 2 years of angiographic surveillance. If the embolus had not formed a laminated configuration, we would have performed a low-pressure angioplasty in the artery toward that aim.

Conclusion

Conventional techniques for Onyx embolization of intracranial aneurysms have undergone ongoing refinements that lower the risks of aneurysm growth or delayed rupture from incomplete occlusion and parent vessel compromise or occlusion from leakage or embolization of liquid embolics. Complication avoid-

ance and management has improved with subtle refinements in patient selection, use of this novel liquid embolic, roadmap imaging, and repetitive cycles of balloon inflation-deflation during Onyx injection. Fine tuning the amount and position of the Onyx deposition achieved with a postoperative angiographic grading scale gives a realistic prediction of its durability.

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Treatment of Arteriovenous Malformations with Cyanoacrylate

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Checklist: AVM Embolization with Acrylates (AVM rupture)

Equipment needed	Procedural steps
Radiology technicians • n-BCA • 1 and 3 mL syringes • D5W • Detachable coils • Flat Panel CT protocol • EVD kit in the room Nursing • Protamine • Mannitol • Anticonvulsant • Antiemetic • Staff pager numbers – Neurosurgery – Anesthesia attending Anesthesia • Protamine • Mannitol • Anticonvulsant • Antiemetic • Paralysis NeuroInterventionalist • Choice of embolic – n-BCA – Coils Neurosurgery • EVD kit in the room • Number to operating room	Identification • Recognized extravasation on imaging • Signs of increased intracranial pressure – Sudden hypertension – Patient movement Initiate and Engage • Alert ENTIRE team • DO NOT remove microcatheter • Anesthesia: vital signs • Anesthesia: additional assistance • Nursing and Technologists to page for additional assistance • Technicians to prepare n-BCA or coils as directed • Nursing to obtain and prepare protamine, mannitol, anticonvulsant, antiemetic Repair • n–BCA – Confirm catheter position – Clear catheter with D5W – Embolize • Coils – Position microcatheter at perforation site if not already extraluminal • Coil from extraluminal to intraluminal using single coil • Add additional coils until control Assess • Flat panel CT • EVD as needed • Transfer to operating room or IC

Checklist: Nontarget Embolization

Equipment needed	Procedural steps
Radiology technicians • Stent retriever Nursing • Vasopressors • Heparin • Aspirin • Glycoprotein IIb/IIIa inhibitor • Staff pager numbers – Neurology – Anesthesia attending – Neurocritical care Anesthesia • Vasopressors • Heparin • Aspirin • Glycoprotein IIb/IIIa inhibitor NeuroInterventionalist • None Neurology • None	Identification • Recognize filling defect or branch occlusion • Assess collateral circulation Initiate and engage • Permissive or therapeutic hypertension – Consider if further embolization needed for safety prior to hypertension • Evaluate occlusion—thrombus versus acrylate • Repeat imaging to evaluate propagation • Confirm adequate heparinization with ACT • Consider aspirin for thrombosis • Considered glycoprotein IIb/III inhibitor for platelet aggregation • Nursing and technologists to page stroke neurology Repair • Consider aspirin for thrombosis • Considered glycoprotein IIb/III inhibitor for platelet aggregation • Consider mechanical thrombectomy if clot – Acrylates are adherent and should not be manipulated Assess • Neurological examination, NIHSS when feasible

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Rupture	Wire/catheter manipulation	Embolize rupture site—n-BCA versus coil	Frequent roadmaps, proximal position
	Over-injection of contrast	Embolize rupture site—n-BCA versus coil	Crescendo injection with gentle pressure
Nontarget n-BCA embolization	Poor embolic control	None	Meticulous planning injections, blank roadmap
Thromboembolism	Insufficient anticoagulation	Additional heparin, IIb/IIa inhibitor, thrombectomy	Adequate heparinization
Infection	Contamination	Broad spectrum antibiotics, abscess evacuation	Sterile technique

Introduction

Embolization of arteriovenous malformations (AVMs) with acrylates can play an important role in treating these complex lesions. Embolization can be performed with an acceptable safety profile when utilizing proper planning and technique. Heterogeneity among these lesions and treatment decisions and techniques vary dramatically between treating physicians and medical centers. Reported general complication rates vary from 1 to 16%, with permanent morbidity rates of 0.4–12.5% and mortality rates of 0.4–11% [1–21]. Within these reports, rates of ischemic complications range from 0.7 to12.5% [2, 7, 20, 22]. Reported hemorrhage rates range from 2 to 15% [2, 7, 14, 20, 22, 23]. These publications reflect large case series employing different embolic agents, including acrylates, and they reflect a mix of modern and discontinued techniques with higher rates of complication compared to current methods [3].

Procedural Overview

Safe and effective embolization of AVMs requires preparation and planning involving neurointerventionalists, neurosurgeons, radiation oncologists, neurologists, and anesthesiologists. An optimal multimodality treatment plan should be established prior to embolization in order to best tailor endovascular therapy. Included in any treatment plan should be the option for conservative management. While data make the best treatment more evident in extreme cases, conflicting results of large analyses make the optimal treatment unclear for many lesions [24–27]. This is particularly true for unruptured lesions. The plan should then be revisited after each step of treatment. Proper preparation will often involve cross-sectional imaging and dedicated diagnostic catheter digital subtraction angiography (DSA) and subsequent multidisciplinary evaluation and treatment planning. In cases in which liquid embolic agents may be used, it is important to know if the patient has a congenital or acquired cardiac condition that may result in even transient right to left shunting. That situation can allow an embolic agent that has transited entirely through the AVM to pass from systemic veins to pulmonary veins and then be pumped out to the systemic arteries, resulting in nontarget systemic embolization. Similarly, patients with known pulmonary arteriovenous malformations or known or suspected hereditary hemorrhagic telangiectasia syndrome (HHT) should be screened with saline bubble-enhanced echocardiography to assess the potential for right to left shunting. If such shunting is demonstrated, either no liquid embolic or a quickly polymerizing mixture of liquid embolic should be employed to maximize procedural safety.

Mastery of cerebral vascular anatomy is essential to safe embolization. The neurointerventionalist must know both the angioarchitectural features of each AVM and normal anatomy to understand the implications of involvement of certain vessels, whether feeding arteries or draining veins. As such, endovascular AVM treatment should begin with complete diagnostic cerebral angiography. This involves angiography in multiple projections with high frame rates to assess size, location, and flow

within the AVM nidus and to investigate feeding vessels for shared supply to normal parenchyma. It also requires evaluation of the venous system, assessing the number, location, caliber, and flow of draining veins. An optimal treatment projection should be found such that feeding arteries and nidus are not superimposed on draining veins, so that movement of glue through these structures can be easily differentiated when embolization is performed.

After diagnostic angiography has been performed and embolization deemed suitable, a microcatheter must be positioned within the vessel to be embolized. Advances in device technology have led to multiple choices in equipment and embolic agents. For AVMs, the catheter of choice is most commonly a flow-directed microcatheter when a liquid embolic is anticipated to be used [13, 28–35]. However, catheterization of feeding arteries arising at recurrent angles from a parent artery or those with lower flow may require over-the-wire microcatheters and their more steerable nature. Once positioned in a vessel, contrast should be gently injected under fluoroscopy to confirm position [36]. Microcatheter angiography should then be performed to evaluate flow within the selected pedicle, meticulously looking for supply to normal parenchyma, feeding artery or nidal aneurysms, nidal components fed by that vessel, and venous outflow [36]. After angiographic interrogation, small test injections of contrast should be performed using blank roadmap technique to plan for the volume and rate of embolic agent injection as well as the concentration of n-BCA that will be best for embolization [36].

Prior to embolization, communication with the anesthesia provider should confirm general anesthesia and paralysis for the treatment portion of the procedure. If systemic heparinization is administered (some practitioners forgo heparinization in high-flow AVMs), then the emergency dose of protamine should also be reviewed [36]. Blood pressure, heart rate, and—if an external ventricular drain is in place—intracranial pressure should be assessed as baselines against which any changes can be measured. Tight blood pressure control is often important, with some physicians advocating therapeutic hypotension prior to embolization [37].

n-BCA should then be prepared using meticulous technique, diluting the acrylate with Ethiodol to achieve the desired concentration. Very high concentrations of n-BCA mixed with tantalum have largely fallen out of favor, except in extraordinarily high-flow situations, as fluoroscopic technology has improved and now allows better visualization. If, however, needed, a small volume of Ethiodol/lipiodol should be mixed with tantalum powder into a paste that then may be added to the pure n-BCA. Acrylates polymerize upon contact with ions, so preparation should only be performed after changing to clean gloves, and equipment must be kept in a sequestered area of the sterile table that is free of blood or saline. After mixing of n-BCA, the syringe containing it should be examined under fluoroscopy outside the patient to confirm that it is radiopaque, thus avoiding injection of non-radiopaque n-BCA. The microcatheter should then be cleared with 5% dextrose in sterile water (D5W), and a separate syringe of D5W should be kept on the sterile table in case further injection is needed after injecting the entire contents of the prepared diluted n-BCA syringe. Injection is performed under blank roadmap visualization and should be carried out until reflux to the catheter tip occurs or n-BCA fills the distal

feeding artery and penetrates into the nidus but not into the outflow veins. Note, as the resistance to flow within the arterial pedicle increases, as is to be expected as the AV shunt is diminished, the rapidity of n-BCA reflux often exceeds its heretofore anterograde movement. This change in flow pattern is important to anticipate because of the increased risk of reflux back to an arterial branch providing physiological supply should these changes not be anticipated. Conversely, this phenomenon may be harnessed to enable embolization of serial AVM feeding vessels from the most distal of the pedicles as well. In either setting, the operator must appreciate that a constant syringe delivery pressure will have varying rates of n-BCA flow depending on the impedance of the vascular circuit. Immediately upon completion of injection, the microcatheter and guide catheter must be swiftly removed from the patient's body while applying gentle aspiration on the microcatheter to prevent leakage of glue and consequent nontarget embolization. Once outside the patient, the guide catheter should be thoroughly cleared with heparinized saline immediately if intended for further use, and the microcatheter should be discarded. Diagnostic angiography should then be repeated to assess the embolization and plan for any further embolization. In the absence of apparent contraindications, heparinization (when used) typically should not be reversed in order to prevent thrombosis of venous outflow and secondary nidus rupture [38–41]. Venous patency should also be encouraged with liberal intravenous fluids through the posttreatment period, and therapeutic hypotension is often warranted [37, 42–46].

Posttreatment care should occur in a neurologic intensive care unit to perform frequent evaluation of neurological status and maintain tight control on blood pressure and intracranial pressure, if needed [36, 44]. Communication is then important for all parties participating in patient care in order to optimize posttreatment management and confirm or adapt next steps in treatment.

Complication Avoidance

Complications during and after endovascular treatments of intracranial vessels can be generally divided into those that are technical in nature and those that result from the pathophysiology of the lesion itself. This heuristic applies to AVM embolization with n-BCA. While the most common and deleterious complications likely result from hemodynamics of the lesion itself, the number of potential technical complications is far greater. Prior to assessing the lesion itself, general knowledge of the patient's medical history, baseline neurological examination, and status of the normal brain and ventricular system provides context for any complication that may arise. The risks of complications of all types can be reduced by knowledge of lesion angioarchitecture and hemodynamics, which in turn informs technical decision-making and patient management. It is important to know that AVMs with prior hemorrhage, associated aneurysms, infratentorial location, deep venous drainage, fewer draining veins, and venous outflow restriction are more prone to rupture [22, 24–26, 33, 47–80]. Such traits should be characterized during the diagnostic portion of an embolization procedure since perturbing the lesion by altering its

hemodynamics can accentuate the risks inherent in each factor. Additionally, when examining angioarchitectural features that lead to hemorrhage after embolization, additional variables have been implicated, some of which are counter to those associated with rupture in natural history investigations. These include supratentorial location, presence of steal phenomenon, increased number of feeding arteries, lobar location, venous ectasia, and venous stenosis [14].

Multiple complications can result from improper technique. Even before acrylate is prepared, opportunities for technical complication abound. Blank roadmap test injections allow for evaluation of the microvasculature, planning for volume and injection rate of embolic, and confirmation that the catheter tip is not folded on itself, which can lead to disastrous results [36].

Premature polymerization can result from contact with ionic material that may result from inadequate syringe and catheter preparation. Additionally, stagnant blood in the catheter tip can initiate polymerization of n-BCA, so the embolic material must be advanced through the dead space of the catheter promptly. This is a technical nuance that must be emphasized for practitioners who are more experienced with ethylene vinyl copolymer (EVOH) liquid embolization and accustomed to slowly advancing that agent through the catheter to limit potential DMSO toxicity. In the event that the acrylate will no longer advance through the catheter and there is high or increasing resistance to manual pressure on the syringe, it is imperative that the n-BCA injection be halted and the microcatheter removed while aspirating. Forcing injection against polymerized acrylate can cause catheter rupture along any point of the catheter or explosive, poorly controlled embolization beyond the tip of the catheter if acrylate becomes dislodged, and forward flow regained within the catheter. The financial costs of a new microcatheter and prolonged angiography suite procedure are inconsequential compared to the human costs of nontarget embolization.

At the completion of injection, swift removal of the microcatheter is needed to prevent a retained microcatheter [81–84]. The need for more rapid removal of the catheter is commensurate with the n-BCA concentration. The higher the concentration of glue, the more likely the microcatheter may be fixed in position. It is seldom that at concentrations less than 30% n-BCA, microcatheters will be glued into position even with prolonged intervals on the order of 60 s with the catheter tip, or approximately 5 mm, embedded within the cast. For this reason, most concentrations utilized in our practice are 25–30% strength unless there are indications for higher concentration. Microcatheter retention has arguably become less common with advances in technology, although it is still of concern. Additionally, detachable tip microcatheters have recently received FDA approval in the United States following years of successful use outside the United States [85, 86]. As the catheter is removed, aspiration on the microcatheter can prevent nontarget embolic embolization, and removal of the guide catheter in concert with the microcatheter can prevent dislodgement of small amounts of acrylate adherent to the microcatheter tip that could lead to nontarget embolization.

Nontarget embolization can occur in additional ways and lead to ischemia of normal brain parenchyma [2, 8, 18, 87, 88]. A thorough search for small branches arising from a selected vessel should be conducted prior to proceeding with embolization.

En passage supply to potentially eloquent normal parenchyma should be considered a contraindication to treatment with liquid embolics. After excluding supply to the normal brain, microcatheter position should be achieved deep enough in the target vessel to prevent reflux into unintended branches [2, 8, 18, 87, 88]. During injection of acrylate, blank roadmap technique allows the best visualization of the embolic so that injection can be halted at the first sign of reflux [2, 8, 18, 87, 88].

Control of injection is best achieved with the safest distal position possible and the optimal concentration [89–94]. If possible, wedged position just proximal to the nidus allows for the best control of injection [93–95]. Higher concentrations of n-BCA polymerize more quickly and will not penetrate as deeply, whereas dilute concentrations will penetrate further into the lesion and require more volume and time to achieve vessel occlusion. Higher concentrations of acrylate increase the likelihood of the microcatheter adhering to the embolic material and being retained in the lesion, but they can be beneficial in lesions for which close proximity to venous outflow is too dangerous for lower concentrations of n-BCA. In addition to distal position, column technique with continuous injection of n-BCA is preferable to the older technique of using a D5W bolus to advance a small plug of high concentration of n-BCA [93, 94].

Technical complications can also lead to hemorrhage, which may be the most common and is arguably the most dangerous adverse event that can occur during AVM embolization with acrylates. It is possible for wires and catheters to perforate vessels, so knowledge of anatomy is important, and good visualization is necessary. Abnormal feeding arteries, particularly those harboring flow-related aneurysms, are more prone to rupture during instrumentation and should be treated delicately [36]. Use of softer flow-directed catheters may be safer than those requiring over-the-wire technique when accessing these abnormal vessels. Additionally, the force exerted on dysplastic vessel walls while pulling a microcatheter can tear the vessel. Prompt removal at the earliest feasible moment is key to limit adherence of the microcatheter in embolic agent that immediately adheres to the vessel wall.

At any new position achieved in a vessel, test injection must be performed to confirm intraluminal position within the desired vessel. While catheterizing a small perforating artery or crossing through the vessel wall with the microcatheter is to be avoided, it is much better to realize such positions prior to more forcefully injecting contrast for an angiographic run. When adequate position is confirmed, a crescendo injection starting with gentle hand injection is safest. This is particularly important when injecting arteries that supply distal nidal aneurysms, as these may frequently be pseudoaneurysms that are not lined by all layers of the vessel wall and, thus, can be exquisitely fragile (Fig. 28.1).

During the embolization procedure itself, efforts must be made to preserve venous outflow. Most importantly, this means halting embolization well before venous penetration occurs [2, 96, 97]. As mentioned above, venous patency can also be promoted with liberal intravenous hydration and heparinization without reversal at the completion of the procedure, while lower blood pressures can reduce hemodynamic stress on the nidus that has been recently perturbed during embolization [37, 42–46].

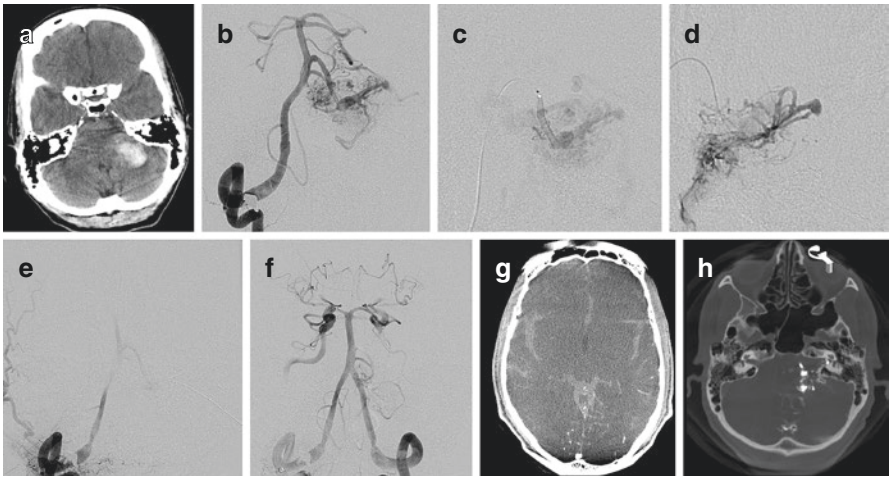

Fig. 28.1 A middle-aged man presented with headache and was found to have intraparenchymal hemorrhage in the left cerebellar hemisphere on noncontrast CT (**a**). LAO Waters projection angiogram (**b**) during injection of the right vertebral artery demonstrates an AVM fed predominantly by duplicated left anterior inferior cerebellar arteries (AICAs) (**b**). The larger superior AICA demonstrated an irregular dysplastic segment distally suspicious for a pseudoaneurysm and the site of rupture. Selective microcatheter injection of the superior AICA again demonstrates the lesion and pseudoaneurysm (**c**). After sudden, severe increase in blood pressure and patient movement under deep anesthesia, repeat injection of the microcatheter demonstrated extravasation of the contrast inferomedially (**d**). During preparation of n-BCA for embolization, injection of the right vertebral artery (**e**) demonstrated minimal opacification of intracranial circulation with outflow predominantly across the occipital knot and into occipital artery branches. Following embolization of the superior AICA branch, selective injection of the right vertebral artery (**f**) demonstrates no residual filling of the embolized branch or arteriovenous shunting. There is somewhat improved opacification of intracranial vessels, although most contrast crosses bilateral posterior communicating arteries and flows inferiorly down the internal carotid arteries. Flat-panel CT with blood window (**g**) demonstrates widespread hemorrhage in the subarachnoid space. Denser contrast is noted in peripheral posterior cerebral artery branches where it persists due to poor venous outflow due to increased intracranial pressure. Bone window through the posterior fossa (**h**) demonstrates denser n-BCA in the AVM nidus, including the pseudoaneurysm, as well as peripheral AICA branches in the internal auditory canal. Dense contrast is also noted in the compressed fourth ventricle

Efforts must also be made to avoid hemorrhage in the posttreatment window. Such hemorrhage is directly related to each lesion's hemodynamics, which can be assessed by angioarchitectural features. Most important among these features is venous flow and characteristics that affect it. With the exception of ruptured associated aneurysms, it is widely believed that AVMs typically rupture from fragile veins, and venous hemorrhage is more likely to occur when there is impaired outflow (Fig. 28.2) [54, 60, 66, 67, 69, 98–103]. To evaluate the status of venous outflow, one must remember the increased risk of hemorrhage seen with fewer draining vessels, deep venous drainage, and venous outflow restriction [22, 24–26, 33, 47, 48, 50–78, 80, 104]. Additionally, the presence of stenoses or varices can be informative. While there have been conflicting results in studies assessing their role in

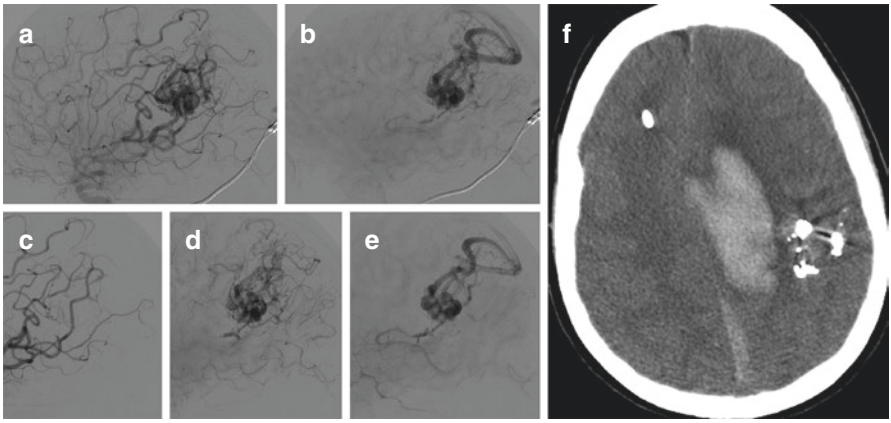

Fig. 28.2 A middle-aged woman presented with headache and was found to have intraventricular hemorrhage (not pictured), for which a right frontal external ventricular drain was placed. Lateral projection during injection of the left internal carotid artery (**a**) in the early arterial phase demonstrates an AVM nidus and arteriovenous shunting. Venous phase image (**b**) shows venous drainage via two superficial veins that empty into the superior sagittal sinus as well as drainage through the basal vein of Rosenthal. Following embolization of an MCA branch, early arterial (**c**) and early venous (**d**) images demonstrate reduced shunting through the nidus. Late venous image (**e**) demonstrates restriction of flow in one of the superficial draining veins. Noncontrast CT (**f**) obtained due to sudden deterioration in neurological status several hours after embolization demonstrated large intraparenchymal hemorrhage and subdural hematoma along the falx

hemorrhagic risk, their presence or absence can be instructive in the overall context of venous outflow from a lesion, particularly when venous reflux is present [22, 50, 60, 61, 63, 64, 67–69, 71, 77, 104–108]. Such assessment is important because hemodynamic changes can lead to rupture. Various theories exist regarding the true source of hemorrhage: mural necrosis from embolization, normal perfusion pressure breakthrough syndrome, and occlusive hyperemia leading to hemorrhage from small arteries with impaired autoregulation or progressive thrombosis with subsequent rupture from dysplastic vessels due to increased pressures from the arterial pressure head, respectively [38–44, 46, 109–115].

Embolization should be performed to target arterial pedicles without impairing venous outflow. Arterial embolization should seek to reduce flow of high-flow lesions to limit blood loss in the event of rupture in the operating room, preferably targeting areas that are most difficult to access surgically and target any aneurysms that may exist [13, 49, 98, 107, 116–119]. When managing lesions with multiple feeders, it is important to stage treatment, spacing out treatment by days, weeks, or months to allow the lesion to achieve a new hemodynamic equilibrium before proceeding with further treatment [7, 120–122]. Overly aggressive reduction in nidal flow in one session is more likely to lead to hemorrhage [7, 120–122].

Efforts to prevent hemorrhage must continue after the patient leaves the angiography suite. Most posttreatment hemorrhages occur early, typically within the first 48 h after treatment [2, 13, 14, 16, 88]. Vigilant monitoring under the care of

neurointensivists is important to closely monitor neurological status, manage hemodynamics, and screen for signs of hemorrhage or increased intracranial pressure that could necessitate emergent neurosurgical management.

Another potential technical complication to note is infection. While exceedingly rare, infections are possible and tend to present in the form of cerebral abscess [123, 124]. Prevention is key: strict adherence to sterile technique minimizes the risk for infection. No data exist to suggest benefit from prophylactic antibiotics.

Complication Management

Despite meticulous technique, even the most skilled and experienced interventionalists will experience complications. Knowing the patient's medical history, physiology, and lesion characteristics lays invaluable groundwork for mitigating the effects of a complication. Having anticipated questions about the patient and lesion that will arise in the event of a complication and preemptively gathering answers expedite definitive management of the complication. Having communicated with colleagues prior to the intervention, vital minutes can be saved as the team carries out the plan to rectify the malady. As the leader of the procedure room, the interventionalist must remain calm and focused. When a complication occurs, all participants in the case must remain in the room unless following direct orders that send them elsewhere. It can be helpful to clear out nonessential personnel from the angiographic suite and into the control room in order to improve efficiency. Whenever orders or requests are made, it is important to communicate clearly with one individual after establishing eye contact. Calling out commands to the room may achieve no response or a response from all people in the room who then scatter to complete that task and leave no one behind.

Besides hemorrhage, most technical complications encountered during AVM embolization do not require immediate amelioration. This is particularly true in the case of retained catheters. When this happens, it may be helpful to obtain more imaging, either angiographic or with flat-panel CT, to assess the situation. If the catheter is intact, the best course is often applying gentle traction on the catheter and cutting it at the femoral insertion site. Upon release of the tension, it will often retract so that its proximal tip will lie within the femoral or iliac artery and no longer through the arteriotomy [82, 83]. In such cases, patients should be treated with aspirin to prevent thrombotic complications from the device. Endothelialization will occur, and the catheter will incorporate into the vessel wall. If surgery is planned in the short term, it is sometimes possible to remove the catheter antegrade through the artery in the brain into which the distal tip is glued after surgical exposure of the lesion [81, 125]. If a catheter is left in place after cutting at the groin site, serial clinical and sonographic follow-up is important because delayed femoral artery pseudoaneurysms can occur [126]. If the microcatheter fractures, it is important to identify the position of both ends. If the distal end is retained but is no longer adherent to the acrylate, endovascular retrieval with a snare can be attempted [84]. If the tip remains embedded in glue, it is important to leave the fractured end in the safest

position possible. This may involve manipulating the free end with a microcatheter to tuck it into an external carotid artery branch or retrieving the free end from an intracranial branch to pull it into the descending aorta.

In the rare case of infection, broad-spectrum antibiotics should be initiated immediately. Contrast-enhanced MRI can confirm embolized parenchyma as the site of infection and demonstrate degree of involvement. If infection proceeds to abscess, surgical management becomes necessary [123, 124]. If a retained catheter is the nidus of infection, removal of the retained microcatheter should only be attempted if safe. Endothelialization of the proximal microcatheter after weeks in situ could lead to significant vascular injury if attempts at removal are made after a delay.

In the setting of nontarget embolization, if safe, hypertension should be induced to perfusion from adjacent vessels [37, 127, 128]. This must be weighed against risks of hemorrhage from the lesion, as described above. If occlusion is due to thrombus rather than acrylate, mechanical thrombectomy or thrombolysis can be considered. However, high magnification views should be obtained in multiple projections as well as spot films to confirm that no acrylate is present at the site of occlusion. Presence of embolic material at the occlusion should be considered an absolute contraindication for mechanical thrombectomy since acrylate will be adherent to the vessel wall and can lead to tearing if pulled upon. A report exists, however, of over-penetration of n-BCA into the venous system treated with mechanical thrombectomy from a transvenous approach in order to prevent venous restriction and resultant hemorrhage [97]. Aspirin should be given after nontarget embolization by n-BCA. This can prevent stump emboli when there is complete occlusion of a vessel and can prevent thrombus formation and progression in the event of nonocclusive acrylate within a vessel. Repeat angiography should be performed in 5–10 min to evaluate for development or progression of thrombus. If platelet aggregation is noted, a glycopyrrolate IIb/IIIa inhibitor may prove beneficial. Posttreatment care should involve induced hypertension to perfuse around the occluded or stenotic vessel if safe. Further treatment plans for the AVM may need to be modified.

While the above-described complications warrant a few moments to pause and consider the best approach to management, the same is not true for intra-procedural rupture. The urgency of intracranial vascular rupture warrants a rapid, calm, efficient approach in order to maximize the chances of a good outcome. Efficiency will be aided by preparation and conversations that occurred prior to the treatment portion of the procedure. Heparin should be reversed immediately [36]. Ten mg protamine sulfate should be administered for every 1000 units of heparin expected to be active in the circulation. As a rule of thumb, 50 mg protamine sulfate is safe to give and should be the standard emergency dose administered in adults. Overdosing of protamine sulfate can lead to paradoxical anticoagulation, so a more precise dose is warranted in children, when small doses of heparin have been administered or when the active amount of circulating heparin is thought to be well below 5000 units, calculated based on a half-life of 60 min. Protamine sulfate should be given quickly, which contravenes conventional anesthesia training to give it slowly over 5 min to

avoid hypotension or anaphylaxis [36]. The benefits of heparin reversal outweigh the small risk of a reaction, and this should be communicated to anesthesia colleagues during the discussion prior to treatment. Additional efficiency gains can be appreciated by simultaneously having colleagues prepare for placement of an external ventricular drain and ready an operating room for decompressive craniectomy. Hemorrhage can lead to both vomiting and seizures, so antiemetics and antiepileptics should be considered [36]. These can prevent harmful patient movement and spikes in intracranial pressure during definitive management of the complication. If increased pressures are present or suspected, a mannitol bolus can be administered intravenously.

In the case of wire perforations, the first instinct is often to pull the wire back. However, this should be avoided. The wire will often be occluding the perforation site [36]. If an over-the-wire catheter is being used that is compatible with coils, attempts should be made to advance the catheter to the site of occlusion and deploy coils at that site [36]. If the catheter has crossed through the vessel wall, a coil should be deployed partially into the subarachnoid space, the catheter then withdrawn into the vessel near the perforation, and the coiling completed [36]. This approach is standard for cerebral aneurysms and is likely most applicable to AVMs with associated aneurysms that are the site of perforation. Perforations that occur in normal arteries are more likely to heal than abnormal vessels within an AVM nidus, so the latter may require denser coil packing to achieve hemostasis compared to the former [36]. In the case of perforations while using flow-directed microcatheters, a similar approach is needed, although fine control of the catheter near the perforation site is less likely to be feasible. Prompt embolization with n-BCA should be undertaken. Previously performed diagnostic runs can guide the embolization, although more extensive embolization may be warranted to ensure the site of perforation is adequately sealed (Fig. 28.1).

As soon as safe, flat-panel CT should be performed in the angiography suite to assess the hemorrhagic burden (Fig. 28.1). This can assess the site of hemorrhage and ventricular status. Knowing the pretreatment appearance of imaging and lesion features aids formulation of next steps in management. Emergent craniectomy is often needed, although this is not always the case. For instance, supratentorial lesions in patients with volume loss may not experience mass effect that requires management beyond external ventricular drainage. The degree of lesion resection, if any, should also be considered in conjunction with decompression. The decision for such management should be made with colleagues participating in management of the patient and should be informed by initial strategies for treatment prior to the complication.

In the setting of postsurgical hemorrhage, management decisions are much the same except for the possibility of immediate endovascular treatment. Definitive surgical management is most commonly best, although ruptured lesions without significant mass effect may be amenable to emergent embolization.

Finally—after a complication has been managed and explained to the patient, patient's family, and other members of the care team—the interventionalist must come to terms with the complication. Most interventionalists are excellent at

reviewing the technical and anatomic details that led to the complication. Many interventionalists, however, are not as skilled at examining their own personal emotional response to complications [129]. The emotional weight of the complication on the interventionalist must be admitted, and progression through the phases of grieving—denial, undoing actions, acceptance, and sublimation—must be acknowledged as a personal and professional goal in order to ensure the long-term mental health of the interventionalist. If more patients are to be helped, the interventionalist must learn from complications including how to cope with them emotionally.

Conclusion

Embolization with acrylates is beneficial in the multidisciplinary management of AVMs and can be performed with an acceptable safety profile. Pretreatment planning and appropriate communication with colleagues during treatment can prevent complications and improve outcomes by optimizing management when they occur. Prompt diagnosis and appropriate definitive management can be achieved best with optimal preparation.

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29

Endovascular Treatment of Arteriovenous Malformations Using Ethylene Vinyl Alcohol Copolymer

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Abbreviations

ACA	Anterior cerebral artery
AVM	Arteriovenous malformation
CE	Conformité Européenne
DMSO	Dimethyl sulfoxide
EVOH	Ethylene vinyl alcohol copolymer
FDA	US Food and Drug Administration
LES	Liquid embolic system
MCA	Middle cerebral artery
NBCA	*N*-butyl cyanoacrylate
PCA	Posterior cerebral artery

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Checklist: Endovascular Treatment of Arteriovenous Malformations Using Ethylene Vinyl Alcohol Copolymer (One of Two—AVM Rupture)

Equipment needed	Procedural steps
Radiology technicians • Onyx 18, onyx 34 • NBCA • Additional rotating hemostatic valve and tubing • Additional lines and sheath for bilateral transfemoral access • DynaCT protocol • EVD kit in the room • Balloon test occlusion catheters Nursing • Mannitol • Protamine • Additional heparinized saline bag • Anticonvulsant • Staff pager numbers Anesthesia • Pressure monitoring equipment for ICP • Strict blood pressure control • Protamine available in the room Neurointerventionalist • Coaxial versus triaxial system (intermediate catheter) • Choice of microcatheter (e.g., detachable tip, flow-guided vs. over-the-wire) • Choice of embolysate (Onyx 18 vs. Onyx 34) • Plug-and-push technique Neurosurgery • EVD kit in the room • Number to operating room	Identification • Recognized extravasation on imaging • Recognized shift in microcatheter position • Recognized hemodynamic changes (e.g., hypertension, bradycardia) • Recognized distal migration of Onyx beyond AVM nidus • Recognized early venous outflow obstruction due to distal Onyx migration Initiate and engage • Alert *entire* team • Perform immediate heparin reversal • *Do not* remove microcatheter • Determine if balloon or additional access is needed • Anesthesia: obtain vital signs • Anesthesia: seek additional assistance • Ask nursing staff and technologists to page for additional assistance • Technicians to open additional embolysate, as requested Repair • Rapid parent vessel or nidus occlusion with Onyx (consider NBCA) • Temporary balloon occlusion • Microcatheter run to check for continuous contrast extravasation • Intraoperative CT to evaluate ICH size • Additional imaging, as needed • EVD, as needed

AVM Arteriovenous malformation; *EVD* External ventricular drain; *ICP* Intracranial pressure; *ICH* Intracerebral hemorrhage; *NBCA* *n*-butyl cyanoacrylate

Checklist: Endovascular Treatment of Arteriovenous Malformations Using Ethylene Vinyl Alcohol Copolymer (Two of Two—Retained Microcatheter)

Equipment needed	Procedural steps
Radiology Technicians • Onyx 18 • Onyx 34 • Contralateral transfemoral access kit ready • DynaCT protocol • EVD kit in the room Nursing • Mannitol • Protamine • Additional heparinized saline bag • Anticonvulsant • Staff pager numbers Anesthesia • Pressure monitoring equipment for ICP • Strict blood pressure control • Protamine available in room Neurointerventionalist • Coaxial versus triaxial system (intermediate catheter) • Choice of microcatheter (e.g., detachable tip, flow-guided vs. over-the-wire) • Choice of embolysate (Onyx 18 vs. Onyx 34) • Plug-and-push technique • Continuous surveillance of degree of Onyx reflux Neurosurgery • EVD kit in the room • Number to operating room	Identification • Onyx reflux past proximal marker • Transmitted tension to Onyx cast with microcatheter pull • Hemodynamic changes with prolonged microcatheter pull • Stable microcatheter position despite continuous, sustained, prolonged countertension Initiate and engage • Alert *entire* team • *Do not* pull microcatheter • Control angiography to confirm no intraoperative rupture or contrast extravasation. • Anesthesia: vital signs • Consider small volume of DMSO through microcatheter before repeat attempt to withdraw catheter from Onyx cast Repair • If no hemorrhage, do not reverse systemic heparinization • Obtain contralateral femoral access for diagnostic angiography • Cut microcatheter hub and withdraw coaxial system, leaving microcatheter in place • Cut microcatheter flush with the skin and bury proximal segment • Consider stenting of microcatheter segments at hypermobile segments (ICA, CCA, CFA) • Initiate antiplatelet therapy

CCA Common carotid artery; *CFA* Common femoral artery; *DMSO* Dimethyl sulfoxide; *EVD* External ventricular drain; *ICA* Internal carotid artery; *ICP* Intracranial pressure

Complication Avoidance Flowchart

Complication	Cause	Management	Avoidance
Inability to access AVM	Inadequate coaxial support		• Adequate preoperative selection of endovascular equipment • Liberal use of long femoral sheaths (45–65 cm) • Triaxial system (guide, intermediate, microcatheter)
Intracranial hemorrhage	Vessel perforation	• Heparinization reversal with protamine • Do not remove microcatheter from perforation site • Onyx embolization of perforation site or parent vessel • Temporary occlusion with balloon occlusion catheter (e.g., HyperForm or HyperGlide [Covidien], Scepter XC [MicroVention])	• Biplane navigation at all times • Careful selection of microcatheter or microwire combination • Over-the-wire vs. flow-guided navigation • Four-hand technique for microcatheter navigation
	AVM rupture (postoperative)	• Heparinization reversal with protamine • Intubation, if indicated • Avoid hypotension • External ventricular drain placement (intracranial pressure monitoring) • CT of the head • Close observation with repeat imaging (if neurological examination is stable) • Emergent surgical evacuation ± AVM resection	• Limit percentage of AVM nidus volume reduction per session (<50%) • Avoid distal Onyx migration into draining vein • Avoid embolization through several different arterial pedicles in the same session (AVM hemodynamics interference) • Strict blood pressure control (frequently, systolic blood pressure < 100–110 mmHg)

Complication	Cause	Management	Avoidance
Ischemic infarct	Equipment-related thromboembolism	• Systemic anticoagulation • Pharmacological thrombolysis (IA) • Endovascular mechanical thrombectomy (aspiration ± stent retriever)	• Meticulous continuous heparinized saline irrigation of all catheters • Systemic heparinization • Double-flush technique (guide, diagnostic, intermediate catheters)
	Embolization-related	• Permissive hypertension • Reposition microcatheter • Catheterize different arterial feeder (if embolization is continued)	• Preoperative functional MRI of brain (for lesions in eloquent area) • Adequate microcatheter positioning • Do not embolize through en passage arterial feeders • Intraoperative neurophysiologic monitoring (intubated, asleep patient) • Sodium amobarbital microcatheter provocative testing prior to embolization • Avoid significant Onyx reflux over the microcatheter • Thorough knowledge and continuous monitoring of the normal parenchymal feeders located proximal to the AVM

(continued)

Complication	Cause	Management	Avoidance
Retained microcatheter	Microcatheter entrapment at the Onyx cast	• Negative Onyx syringe aspiration during microcatheter removal • Gentle but continuous microcatheter traction over several minutes • Push-pull-push technique • Trim microcatheter at the transfemoral access site • Antiplatelet therapy	• Adequate plug-and-push technique • Pressure-cooker technique • Negative Onyx syringe aspiration during microcatheter removal • Gentle but continuous microcatheter traction over several minutes • Avoid significant Onyx reflux over the microcatheter • Use of detachable-tip microcatheters

AVM Arteriovenous malformation; *IA* Intra-arterial

Introduction

During the past 20 years, endovascular embolization has become a fundamental part of a frequently multidisciplinary approach for the treatment of intracranial arteriovenous malformations (AVMs). The introduction of liquid embolic agents represented a substantial advancement in the endovascular treatment of AVMs. Liquid embolic agents are designed to solidify intravascularly and therefore can be delivered through small microcatheters [1]. Two of these liquid embolic agents—*n*-butyl cyanoacrylate (NBCA) and ethylene vinyl alcohol copolymer (EVOH)—have revolutionized the endovascular management of intracranial AVMs. The indications and technical nuances for the use of NBCA to treat AVMs are described in Chap. 28. The goal of this chapter is to describe the pertinent properties, endovascular techniques, and pitfalls of the use of EVOH for the endovascular management of intracranial AVMs.

Historical Background

The use of EVOH for embolization of AVMs was first described in 1990 by Taki and colleagues [2] at Kyoto University, Japan. The product was developed to overcome some of the disadvantages encountered with the use of isobutyl 2-cyanoacrylate and NBCA for the embolization of AVMs—namely, their rapid polymerization, steep operator learning curve, and unpredictable embolization pattern—and the frequent occurrence of microcatheter entrapment or the need for intraprocedural microcatheter exchange. Severe angiotoxicity was initially attributed to the EVOH solvent (dimethyl sulfoxide [DMSO]). Murayama et al. [3] showed that contact time with the arterial wall and the volume of DMSO were the two most important factors that influenced DMSO vascular toxicity. Since then, the DMSO toxicity phenomenon had been infrequent.

Onyx liquid embolic system (LES) (Covidien/Medtronic, plc, Dublin, Ireland) is commercially available as a nonadhesive embolic system in three formulations: Onyx 18, Onyx 20 (not yet approved for use in the United States as of this writing), and Onyx 34. It has been Conformité Européenne (CE)-mark approved for the treatment of AVMs in Europe since 1999. Onyx 18 and Onyx 34 have been approved in the United States by the US Food and Drug Administration (FDA) since 2005. The main change made to the product since the original description by Taki et al. [2] was the replacement of metrizamide with micronized tantalum as the radiopaque contrast agent.

Onyx Properties

Onyx LES consists of three components:

- EVOH, the actual embolic material
- DMSO, the solvent for liquid delivery of EVOH
- Micronized tantalum powder for radiographic visualization

EVOH is formed of 48 mol/L ethylene and 52 mol/L vinyl alcohol. The polymer is dissolved in DMSO and is prepared in three commercially available concentrations:

- Onyx 6% (6% copolymer, 94% DMSO)
- Onyx 6.5% (6.5% copolymer, 93.5% DMSO)
- Onyx 8% (8% copolymer, 92% DMSO)

Onyx LES is supplied as a kit in ready-to-use vials. Each kit contains one 1.5-mL vial of Onyx 18 or Onyx 34, one 1.5-mL vial of DMSO, and three 1-mL delivery syringes (two whites for Onyx, one yellow for DMSO). Micronized tantalum powder is added to the Onyx for radiopacity. Onyx must therefore be shaken for at least 20 min before injection to achieve homogeneous radiopacity of the mixture, and the vials must be kept on the shaker until the time of injection [4, 5]. When Onyx comes into contact with aqueous solutions, such as blood, precipitation of the copolymer is initiated by diffusion of DMSO [5, 6].

Procedural Overview

Procedure and Embolic Systems

At Barrow Neurological Institute, all neurointerventional procedures are performed with the patient under general endotracheal anesthesia, with neurophysiologic monitoring (somatosensory evoked potentials and electroencephalography for supratentorial AVMs, with additional brainstem auditory evoked responses for infratentorial AVMs). Systemic heparinization is used in all patients but judiciously in patients with hemorrhagic AVMs. Hypertension should be strictly avoided. Unless there is a clear contraindication, transfemoral endovascular access is achieved using standard Seldinger and coaxial techniques. Long reinforced sheaths (45–65 cm) are frequently used for adequate proximal system stability in elderly patients or patients with

Table 29.1 DMSO-compatible microcatheters

Manufacturer	Microcatheter
Balt Extrusion	SONIC[a]
Boston Scientific Corp.	Renegade HI-FLO Fathom
	Direxion
	Direxion HI-FLO
ev3/Covidien/Medtronic, plc	Apollo[a]
	Marathon
	UltraFlow
	Echelon
	Rebar
MicroVention, Inc.	Headway Duo
Stryker Neurovascular	Excelsior XT-17

DMSO Dimethyl sulfoxide
[a]Detachable-tip microcatheter

tortuous aortoiliac anatomy. All procedures are initiated in anticipation of using a triaxial support system that includes a 6F or 8F sheath (the latter in patients for whom a larger intermediate catheter is more suitable), a guide catheter (typically navigated into the distal cervical internal carotid artery or the V2–3 junction of the vertebral artery), and an intermediate catheter (navigated to the A1, M1, and P1–2 junctions or to the distal V4, as needed, for embolization of the pedicles). A triaxial system allows for expedient access when multiple pedicle embolizations are anticipated and during rare complications, such as vessel rupture, which requires prompt recatheterization and management. This system also allows for expedient acquisitions of angiographic images after pedicle embolization. Our recent report of our experience showed a mean of 3.2 pedicles embolized per session, over a mean of 1.2 sessions [7].

Various flow-related and over-the-wire DMSO-compatible microcatheters are commercially available (Table 29.1). Of these, the detachable-tip microcatheters have made a dramatic impact on the endovascular embolization of AVMs. Their use was first reported in 2008 [8]. The SONIC microcatheter (Balt Extrusion, Montmorency, France) is available in two different diameters (1.2F and 1.5F), and it has three different detachable-tip lengths (15 mm, 25 mm, and 35 mm). It can be used as a flow-directed catheter or it can be directed with a guidewire, and it is compatible with both Onyx and NBCA. The microcatheter has three radiopaque markers (from distal to proximal): (1) the distal tip, (2) the detachment point, and (3) the maximum reflux marker [9].

In May 2014, the Apollo (Covidien/Medtronic, plc) became the first detachable-tip microcatheter to gain FDA approval for use in endovascular embolization of AVMs using Onyx. Since then, few reports have been published on its use [10–13], and a post-market safety study—sponsored by the US National Institutes of Health—is ongoing as of this writing (ClinicalTrials.gov NCT02378883). The Apollo microcatheter has a stainless-steel proximal coil for structural support and nitinol distal braiding for high kink resistance. It is available with distal tip lengths of 15 and 30 mm. The catheter has a typical proximal diameter of 2.7F, a distal outer diameter of 1.5F, an inner diameter of 0.33 mm, and a total length of 165 cm. The microcatheter has two radiopaque markers: a distal one at the microcatheter tip and a proximal one at the level of the detachment zone.

Preprocedural Superselective Angiography

Before embolization, microcatheter angiography is used to evaluate the opacification of pial and/or en passage vessels and to quantify the rate of arteriovenous shunting. Angiographic views should ideally have minimal overlap of the microcatheter tip and the AVM nidus, and they should allow the endovascular neurosurgeon to discern AVM nidus penetration and embolysate reflux. The location of draining veins is meticulously scrutinized to identify the maximal point of desired embolysate penetration. In cases with high-flow shunting and/or close proximity to the AVM nidus, the neurosurgeon may use NBCA rather than Onyx 34. In AVMs with very high-flow shunting, balloon microcatheters may be used with the balloon inflated at the time of embolization; alternatively, if the pedicle is adequately capacious, coils may be deposited before the glue.

Microcatheter Preparation

After the microcatheter tip is navigated to the desired intranidal or perinidal location, a superselective angiogram is performed to confirm the distal tip position, nidal angioarchitecture, and draining vein pattern. The Onyx vial is retrieved from the shaker immediately before injection. The microcatheter preparation then follows a standard protocol: (1) The microcatheter is flushed with 5–10 mL normal saline with no heparin. (2) The microcatheter dead space is filled with DMSO. (3) Onyx is aspirated into a 1-mL syringe, and a meniscus-to-meniscus connection is fashioned. The syringe should preferably be held vertically, with the tip pointing downward on connection, after which it should immediately be turned 180° so that its tip is pointing upward, and the injection should be started directly. Doing so will ensure a sharp interface that distinctly divides the DMSO from the Onyx inside the microcatheter. (4) Onyx is then injected slowly over 90–120 s to displace the DMSO from the microcatheter dead space; the final seconds of this step are performed under fluoroscopy to reliably visualize the beginning of the embolization.

Plug-and-Push Technique

The first step of the initial Onyx injection consists of producing an "Onyx plug" around the catheter. This plug creates a pressure gradient within the AVM nidus, which is subsequently supported by "pushing" the Onyx carefully into a more distal position in the nidus. With this so-called plug-and-push technique, the embolic agent is released under free-flow conditions and fills the nidus in an antegrade direction. The Onyx subsequently refluxes into the feeding artery just proximal to the microcatheter tip (first penetration) [6]. The procedure is interrupted for 30–120 s to allow the Onyx cast to form. The Onyx application continues at intervals of injection and pauses; these breaks should not exceed 2–3 min because of the high risk of unintentional catheter tip occlusion secondary to Onyx solidification.

After multiple rounds of injection, reflux, and waiting, a reflux as long as 1.0–1.5 cm is formed at the tip of the microcatheter [14]. The Onyx cast reflux should not exceed 1.5–2.0 cm from the microcatheter tip (to avoid difficulty with

microcatheter retrieval) and should not reach within 1 cm of any sizable branch of the catheterized arterial pedicle. The embolization should be stopped if (1) the maximum safe distance for reflux is exceeded, (2) increasing resistance to Onyx injection is met with no appreciable forward Onyx flow, or (3) angiographic opacification of a draining vein is noted (Figs. 29.1 and 29.2).

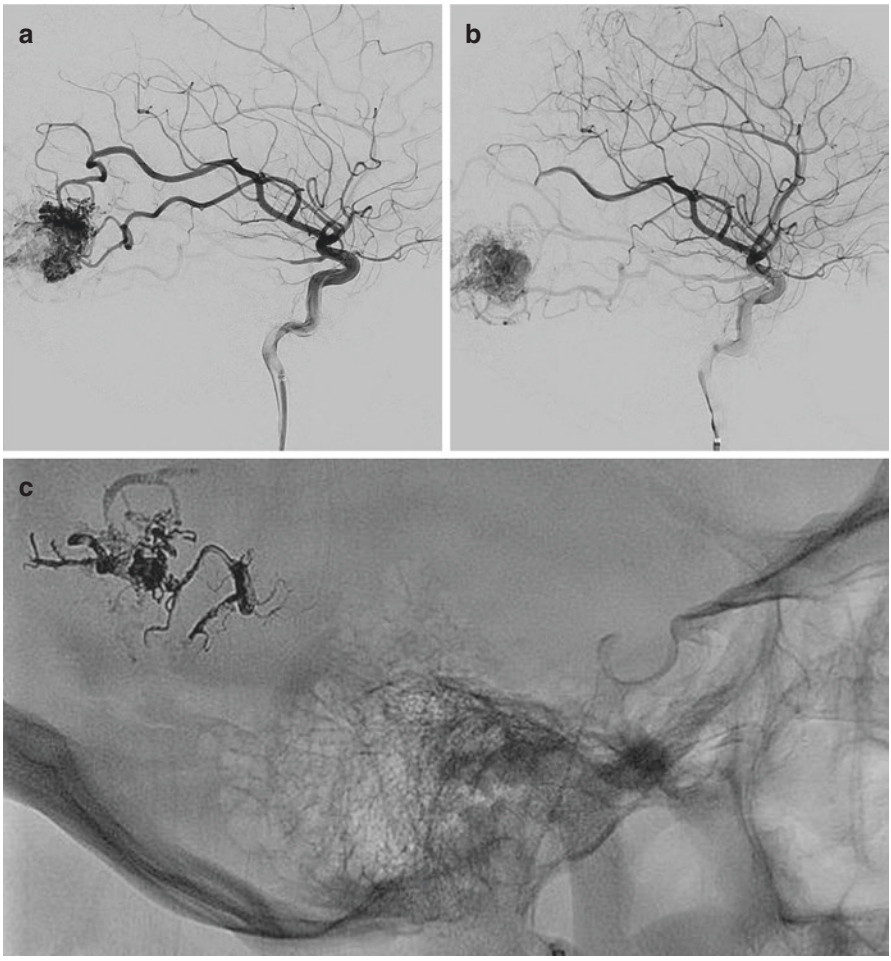

Fig. 29.1 Stage I endovascular Onyx embolization of an unruptured temporo-occipital arteriovenous malformation (AVM) diagnosed on work-up for headaches and vision changes. (**a**) Selective internal carotid artery cerebral angiogram (lateral view) shows the AVM with a compact nidus and arterial supply from two branches of the inferior division of the middle cerebral artery (MCA). (**b**) Approximately 50% volume reduction was achieved after superselective catheterization of the MCA feeders and Onyx embolization over a single session. Note the now more conspicuous arterial supply from the posterior cerebral artery shown by contrast opacification of the ipsilateral posterior communicating artery. (**c**) Unsubtracted magnified lateral view shows the extent of the Onyx cast after completion of Stage I embolization (*Used with permission from Barrow Neurological Institute, Phoenix, Arizona*)

At the conclusion of the injection, the syringe is aspirated as it is withdrawn under traction. Although a greater amount of Onyx reflux may correlate with difficulty in microcatheter withdrawal, reflux along a relatively straight segment is generally well tolerated, whereas reflux around a vessel curve may be more difficult and risky.

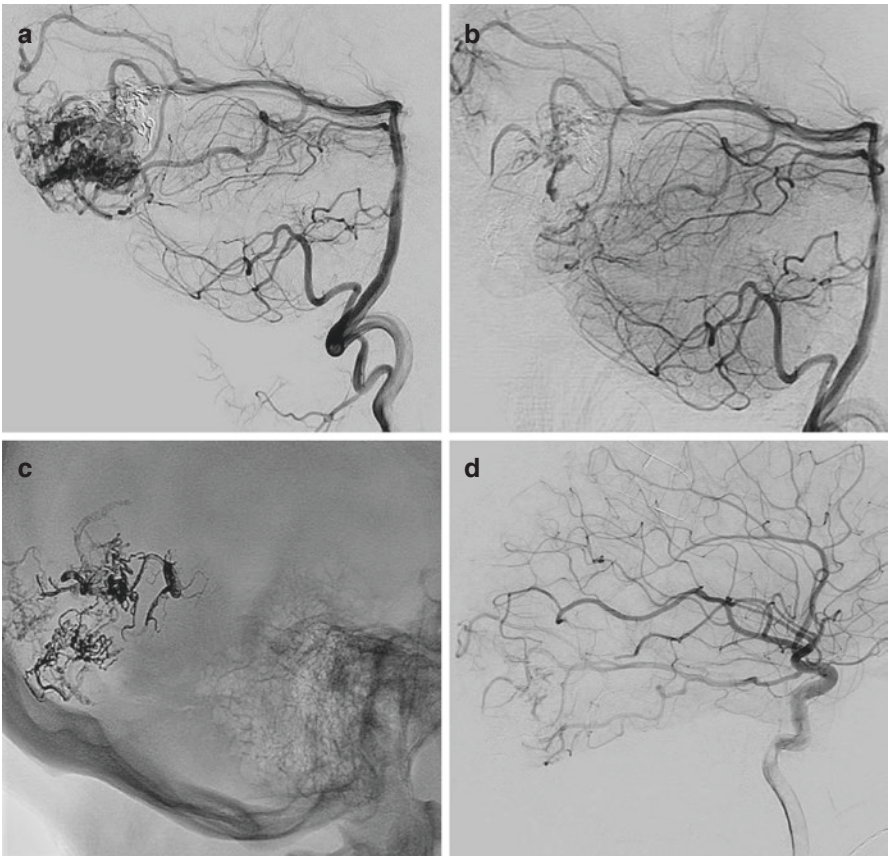

Fig. 29.2 Stage II endovascular Onyx embolization of an unruptured temporo-occipital arteriovenous malformation (AVM) diagnosed on work-up for headaches and vision changes. (**a**) Selective vertebral artery cerebral angiogram (lateral view) shows residual AVM nidus filling, with main arterial supply through distal branches of the posterior cerebral artery (PCA). (**b**) More than 95% nidus obliteration was achieved with a single Onyx treatment after superselective catheterization of three distal PCA branches, with minimal residual filling from the middle division of the distal P4 segment. (**c**) Unsubtracted magnified lateral view shows the Onyx cast. (**d**) The patient subsequently underwent gross total resection of the AVM the following morning (*Used with permission from Barrow Neurological Institute, Phoenix, Arizona*)

Pressure-Cooker Technique

Reflux can be avoided, and Onyx penetration can be augmented by using the pressure-cooker technique [15]. This technique consists of using NBCA to create a proximal plug between the microcatheter tip and the detachment zone of a previously placed DMSO-compatible detachable-tip microcatheter. The main advantage of this technique is that it enables continuous injection of Onyx while avoiding reflux. Two microcatheters, one a detachable-tip microcatheter, are used to catheterize the feeding pedicle. The second microcatheter is used to intentionally glue in the detachable tip of the microcatheter with NBCA. The glued-in microcatheter is then used to inject Onyx. The pressure-cooker technique is analogous to the plug-and-push technique, but it allows for swift early penetration of Onyx and better control of reflux with the cyanoacrylate plug.

Double-Arterial Catheterization Technique

To increase Onyx penetration into the nidus, Lopes et al. [16] used a double-arterial catheterization technique. After bilateral transfemoral catheterizations, two Marathon (Covidien/Medtronic, plc) microcatheters were advanced into either different vascular territories or different pedicles on the same arterial distribution. As soon as Onyx refluxed into one of the pedicles, the injection was paused and initiated through the second microcatheter. To prevent catheter occlusion with Onyx, Lopes et al. avoided pauses longer than 2 min without injecting in a catheter. No procedural complications were described.

Postembolization Hospital Care and Follow-Up

At our institution, most patients with AVMs undergo one or two sessions of embolization, followed by surgical resection the next day. Close neurological monitoring is performed until surgery, and strict normotension (systolic blood pressure 100–120 mm Hg) is maintained in the immediate postprocedure period while the patient is in the intensive care unit.

Complication Avoidance and Management

The complications from the Onyx embolization of AVMs can be grossly classified as preoperative, intraoperative, and postoperative complications.

Preoperative Complications

Adequate preoperative understanding of the AVM anatomy is paramount for a safe endovascular procedure. The goals of the AVM embolization should be specifically defined preoperatively. Adequate selection of a coaxial system preoperatively can minimize the chances of unnecessary intraoperative frustration on the part of the neurointerventionalist, can reduce radiation exposure, and can maximize the chances of an effective nidus obliteration. As mentioned previously, triaxial systems with an intermediate catheter should be considered whenever the AVM is distally located in the intracranial circulation.

Embolization for cure is rarely attempted at our institution. As part of a multidisciplinary approach to AVMs, Onyx embolization is frequently used as a preoperative adjuvant tool for microsurgical resection. Thus, we try to limit the degree of AVM nidus volume reduction—especially on lesions with higher Spetzler-Martin grades—to less than 50% for each planned endovascular session (Figs. 29.3, 29.4 and 29.5).

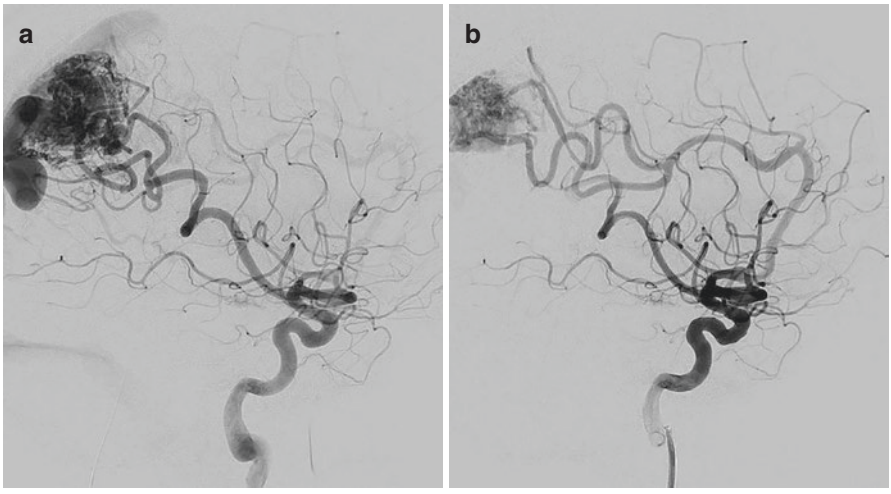

Fig. 29.3 Stage I endovascular embolization of an unruptured posterior parietal arteriovenous malformation (AVM) diagnosed on work-up for vision symptoms. (**a**) Preoperative selective internal carotid artery cerebral angiogram (lateral view). Note the three distinct terminal middle cerebral artery (MCA) arterial feeders and the superficial venous drainage to the posterior superior sagittal sinus through a single enlarged draining vein. (**b**) Approximately 30% overall nidus volume reduction was achieved after Onyx plus *n*-butyl cyanoacrylate embolization through MCA feeders over a single session. Note that the medial arterial supply through a distal, dilated anterior cerebral artery is now visualized (*Used with permission from Barrow Neurological Institute, Phoenix, Arizona*)

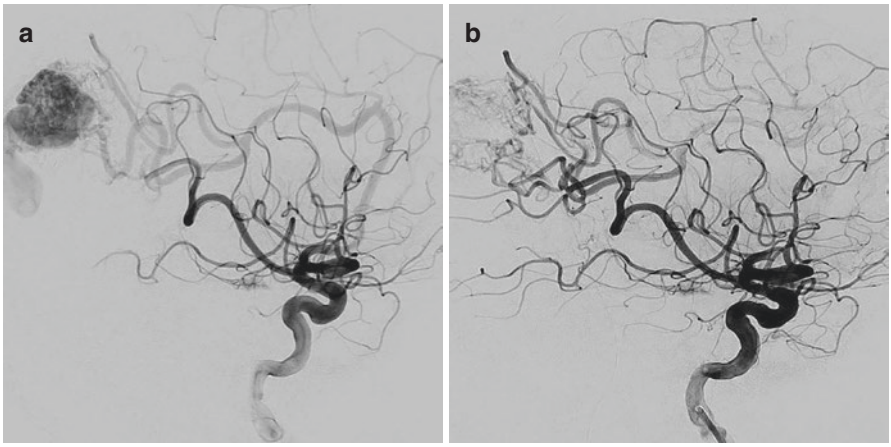

Fig. 29.4 Stage II endovascular embolization of an unruptured posterior parietal arteriovenous malformation (AVM) diagnosed on work-up for vision symptoms. (**a**) Preoperative selective internal carotid artery cerebral angiogram (lateral view) shows unchanged nidus-filling pattern compared to postembolization angiogram obtained after Stage I. (**b**) Approximately 60% overall nidus volume reduction is noted after Onyx plus *N*-butyl cyanoacrylate embolization over two separate anterior cerebral artery (ACA) pedicles. Note the persistent nidus filling through the superior pedicle from the ACA (*Used with permission from Barrow Neurological Institute, Phoenix, Arizona*)

Vessel Injuries

Intraoperative complications can usually be classified as hemorrhagic or ischemic. Catheter-related vessel injuries are rare. They are most commonly seen during intracranial microcatheter or microwire manipulation, more specifically during microcatheterization of the frequently tortuous and friable AVM distal arterial feeders. Careful selection of the endovascular equipment is an important step to minimize this risk. However, some of these cases are caused by actual technical errors. Biplane intraoperative navigation under road map guidance is mandatory. A J-shaped microcatheter can provide for a less traumatic navigation at the proximal intracranial vasculature, but it is often inadequate for catheterization of perinidal feeders. Some microcatheters (e.g., Marathon, Magic [Balt Extrusion], SONIC, Apollo) can be navigated using either over-the-wire or flow-guided techniques, and they are especially useful for final microcatheter positioning at the pedicle-nidus interface. At our institution, every step of the intracranial microcatheterization is performed by two neurointerventionalists. The lead surgeon is responsible for the microwire navigation. The assistant surgeon is responsible for maintaining the stability of the coaxial construct and for advancing the microcatheter after adequate distal access has been achieved with the microwire.

Vessel perforation is suspected when unexplained changes occur in the intracranial microcatheter position on road map fluoroscopic navigation, when abrupt changes occur in hemodynamic parameters, and when active contrast extravasation is observed through microcatheter or guide catheter injections. Systemic heparinization should be immediately reversed with intravenous protamine sulfate. The microcatheter should

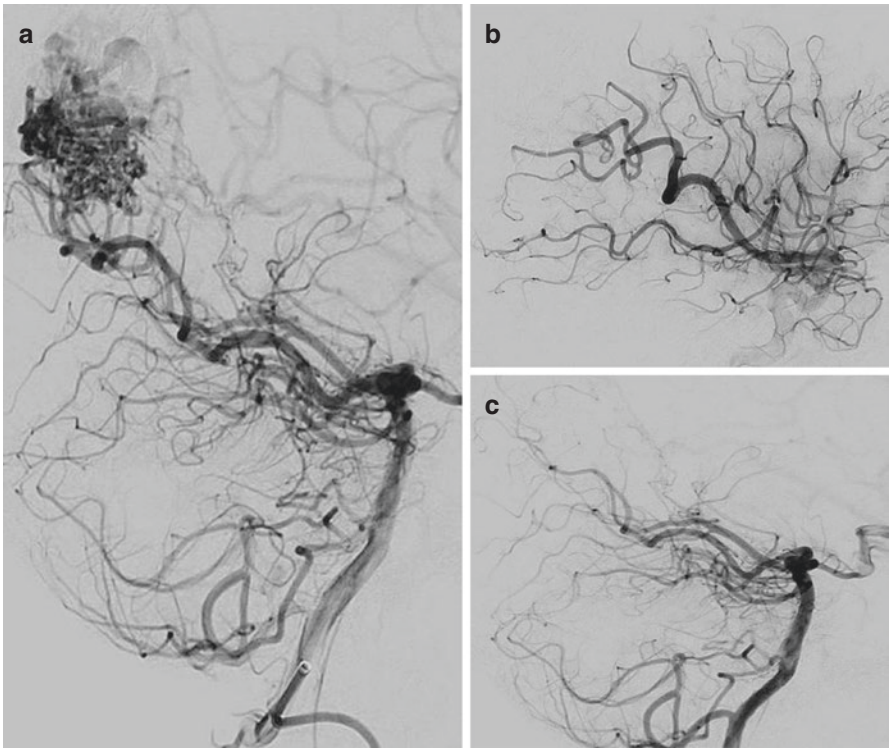

Fig. 29.5 Stage III endovascular embolization of an unruptured posterior parietal arteriovenous malformation (AVM) diagnosed on work-up for vision symptoms. (**a**) Preoperative selective vertebral artery cerebral angiogram (lateral view) shows a residual nidus arterial supply through the distal terminal posterior cerebral artery (PCA). Superselective catheterization and Onyx embolization of three PCA pedicles and one last anterior cerebral artery pedicle achieved approximately 70% overall nidus volume reduction of the AVM. The patient subsequently underwent surgical intervention and gross total resection the next morning without complications ((**b**) internal carotid artery and (**c**) vertebral artery cerebral angiograms) (*Used with permission from Barrow Neurological Institute, Phoenix, Arizona*)

not be pulled back. In fact, it should be used to deliver a small amount of Onyx as the microcatheter is withdrawn, with the goal being to occlude either the perforation site or the parent vessel itself. If resultant extravasation is minimal, arterial feeder is well sealed, and hemodynamic parameters are stable, the embolization may continue. Otherwise, the procedure should be aborted immediately.

Arteriovenous Malformation Rupture

Intracranial aneurysms associated with AVMs can be found in 10–20% of patients with AVMs. In those patients who present with hemorrhage, the initial treatment should be directed toward the ruptured lesion first [17]. In patients who present with unruptured

AVMs, the treatment decision-making for AVMs and for aneurysms depends on the location of the aneurysm in relationship to the AVM nidus and the estimated annual hemorrhage risk for each lesion. Microcatheterization of arterial feeders containing proximal or distal flow-related aneurysms should be done with extreme caution, given the potential risk for intraoperative aneurysm rupture due to catheter-related injury. In those cases, considerations should be made to treat the aneurysm before treating the AVM.

Early Onyx migration with incomplete nidus obliteration, but with resultant venous outflow obstruction, is also associated with risk of AVM rupture. The same complication can occur with rapid changes in AVM nidus hemodynamics, secondary to an aggressive nidus obliteration in a single session [18]. Meticulous analysis of the AVM nidus flow pattern and selection of the optimal microcatheter tip position for Onyx embolization may reduce the likelihood of rapid migration of the liquid embolic agent into the draining vein. For the same reason, even in patients for whom angiographic cure is the preoperative endovascular goal, AVM volume reduction by Onyx embolization should be limited to a low percentage of the total AVM nidus volume per session.

Ischemic Infarction

Ischemic complications may result from intraoperative thromboembolism or arterial occlusion caused by the Onyx embolization. The likelihood of thromboembolic complications can be minimized by constantly flushing all catheters with heparinized saline solution. At our institution, systemic heparinization is achieved after transfemoral access is obtained in unruptured lesions and immediately before intracranial microcatheterization of ruptured AVMs. We do not routinely reverse systemic anticoagulation with protamine sulfate unless an intraoperative rupture occurs or unless the concern for AVM postoperative hemorrhage is high.

Retained Microcatheter

Care should be taken at all times to prevent significant Onyx reflux during embolization. The Onyx cast reflux should not exceed 1.5–2.0 cm from the microcatheter tip (to avoid difficulty with microcatheter retrieval), and it should not reach within 1 cm of any sizable branch of the catheterized arterial pedicle. At the end of an Onyx injection, the microcatheter should be withdrawn slowly while aspirating the syringe, which can take several minutes. This step may cause considerable morbidity. If the catheter does not release immediately from the cast, we apply constant pressure for several minutes by clamping the catheter hub to the hemostatic valve using a hemostat. We then incrementally increase the pressure and reapply the hemostat. If the catheter cannot be removed, it is left in place and cut off at the groin insertion site [19]. This residual catheter can often be removed from the groin without difficulty after the vessel cast with Onyx is cut at the time of surgery. As part of the informed consent process before the procedure, the patient should be counseled about the possibility of this complication. Detachable-tip catheters may minimize the likelihood of this complication.

The nonadhesive properties of Onyx have overcome some of the disadvantages of cyanoacrylates. Nonetheless, in 2012 the FDA issued a safety communication alert about the potential risks of catheter entrapment also associated with the use of Onyx. Since 2005, more than 100 cases of catheter breakage or entrapment have been reported to the FDA, including nine deaths [20]. In at least 54 cases, the microcatheter could not be retrieved. Detachable-tip microcatheters were developed to minimize the possibility of catheter entrapment.

Embolization Results

Since the development of EVOH by Taki et al. [2] and the publication of the first large case series in 2001 [4], relatively few publications have described results of endovascular treatment for AVMs. The heterogeneity of embolization goals in those studies (i.e., embolization alone or in combination with microsurgical resection or adjuvant radiosurgery) does not allow for any meaningful conclusions to be drawn on this subject. Embolization for cure of an intracranial AVM is not a common strategy in the United States. Most of the reports in the medical literature on this theme come from European centers [21–25]. Careful interpretation of those results—sometimes indicating angiographic cure rates of 82% or higher [25–27]—is advised, given significant selection bias. Natarajan et al. [6] reported active arteriovenous shunting (confirmed intraoperatively) even for four surgically resected AVMs that were previously considered cured by endovascular means.

In 2010 Loh and Duckwiler [28] published the results of an industry-sponsored, prospective, randomized, controlled trial of Onyx versus NBCA for embolization of AVMs. The primary end point was technical success in achieving a 50% or greater reduction in AVM volume. Secondary end points were operative blood loss and resection time. The use of Onyx led to a 50% or greater reduction in AVM volume in a similar number of cases as NBCA (96% for Onyx, 85% for NBCA); resection times, adverse event rates, and intraoperative blood loss were also similar between the two groups. The data from this Onyx trial demonstrated the noninferiority of Onyx to NBCA in presurgical embolization of intracranial AVMs. Its preliminary results served as the basis for FDA approval of Onyx in 2005.

Analysis of the published series evaluating preoperative or preradiosurgical Onyx embolization of AVMs shows an average postembolization volume reduction of 63–90% [4–6, 27, 29–40]. The morbidity and mortality rates do not appear to be substantially different for multimodality studies (Onyx plus surgery, Onyx plus radiosurgery) and studies with Onyx embolization alone as the primary approach. The reported morbidity and mortality rates in the literature vary from 0% to 23.9% and from 0% to 4.3%, respectively.

The complication rates found with the use of Onyx are similar to those in previous studies examining the use of other embolysates [18, 41]. In our recent institutional review, permanent and transient postprocedural neurological deficits were found in 9.6% and 1.8% of all cases, respectively [7]. Despite the greater number of sessions required and the greater number of arteries embolized for Onyx cases than for NBCA cases, no statistically significant difference was

found in the risk of neurological deficits after cerebral AVM embolization with Onyx and NBCA [7]. Periprocedural hemorrhagic events appear to be more frequent than ischemic events (6.3% and 3.5%, respectively; unpublished meta-analysis [data not shown]). However, when procedure-related hemorrhages that were asymptomatic (identified intraoperatively or on postoperative surveillance computed tomography) are excluded, the incidence of both complications seems equivalent. Mortality rates directly related to the embolization procedure are reported to be less than 4.5%.

Conclusion

The widespread implementation of EVOH has resulted in a positive improvement in the endovascular management of cerebral AVMs. Significant experience has been accumulated with the use of EVOH since the first published clinical study in 2001. Catheters and other technological advancements, such as the introduction of detachable-tip microcatheters, have continued to expand the numerous options for its application in AVM treatment. Judicious use of preoperative and preradiosurgical endovascular embolization of AVMs with EVOH should be considered in every multimodality treatment strategy. For select patients, the endovascular treatment of AVMs using EVOH is associated with angiographic cure, a favorable risk profile, and low rates of long-term recurrence.

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Principles for Complication Avoidance and Management in Thrombectomy for Ischemic Stroke

30

Alexander G. Chartrain, Ahmed J. Awad, and J Mocco

Checklist: Thrombolysis for Ischemic Stroke (One of Two—Intraparenchymal or Subarachnoid Hemorrhage)

Equipment needed	Procedural steps
Radiology technicians • Balloon (4 mm diameter) • Coils of 3 mm and less • Additional RHV and tubing • Dyna-CT protocol • EVD kit in the room	Identification • Recognized extravasation on imaging Initiate and engage • Alert ENTIRE team • DO NOT remove microcatheter • Determine if balloon/additional access needed • Anesthesia: vital signs • Anesthesia: additional assistance • Nursing and technologists to page for additional assistance • Technicians to open additional coils or balloon as requested • Nursing to give protamine and mannitol to anesthesia
Nursing • Mannitol • Protamine • Additional heparinized saline bag • Anticonvulsant • Staff pager numbers – Neurosurgery – Anesthesia attending	Repair • Deploy balloon or coils through additional RHV • Begin introducing coils to vessel proximal to rupture point • Add additional coils until vessel occluded • No interval imaging • ALTERNATE: deploy and inflate balloon proximal to rupture point and determine point of occlusion and place coils sequentially until the vessel is occluded
Anesthesia • Pressure monitoring equipment for ICP • Propofol • ETT (if under MAC)	
Neurointerventionalist • Choice of balloons • Choice of multiple coils (short)	
Neurosurgery • EVD kit in the room • Number to operating room	Additional imaging as needed EVD as needed

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Checklist: Thrombolysis for Ischemic Stroke (Two of Two—Distal Embolization)

Equipment needed	Procedural steps
Radiology technicians • Embolectomy devices of choice • Additional RHV and tubing • Dyna-CT protocol Nursing • Mannitol • rtPA • Intravenous antiplatelet agents • Additional heparinized saline bag • Anticonvulsant • Staff pager numbers – Neurosurgery – Anesthesia attending Anesthesia • Pressure monitoring equipment for ICP • Propofol • ETT (if under MAC) • Pressor medications Neurointerventionalist • Choice of embolectomy devices • Recombinant tPA in 1:10 dilution Neurosurgery • ICP monitor in the room • Number to operating room	Identification • Recognized distal embolization on imaging Initiate and engage • Alert ENTIRE team • Determine location of occlusion • Anesthesia: vital signs • Anesthesia: additional assistance • Nursing and technologists to page for additional assistance • Technicians to open additional embolectomy devices as requested • Nursing to give rtPA to interventional team for dilution and antiplatelet agent to anesthesia as requested Repair • If small caliber occlusion, consider intra-arterial tPA alone • If large caliber (circle of Willis), consider additional embolectomy devices • Interval imaging as required • At conclusion obtain CT scan • Consider intravenous antiplatelet agents as indicated

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Intraparenchymal hemorrhage	– Excess traction on vascular tree – Multiple thrombectomy passes	– Reverse anticoagulation – Treat hypertension – Consider balloon occlusion or vessel sacrifice if severe	– Use second-generation device over first-generation device – Use conscious sedation rather than general anesthesia – Gentle traction when performing thrombus retrieval – Avoid more than 3 thrombectomy passes
	– Postoperative hemorrhagic transformation	– Reverse anti-coagulation – Treat hypertension – ICU care	– Avoid thrombectomy in cases of large infarct size – Hold anti-coagulation for 24 h post-operatively – Treat hypertension aggressively

Complication	Cause	Remedy	Avoidance
Subarachnoid hemorrhage	– Vessel perforation – Excessive wire manipulation – Over-inflation of balloon guide catheter	– Reverse anticoagulation – Treat hypertension – Vigilance for secondary vasospasm	– Careful unsheathing of device into vessel lumen – Careful wire technique – Correct sizing of balloon to target vessel
Vasospasm	– Excessive wire manipulation – Secondary to SAH	– Intra-arterial vasodilation if severe	– Intra-arterial vasodilation agent prior to retrieval attempt
Vessel dissection	– Excessive wire manipulation – Multiple thrombectomy passes	– Observation if mild – Anti-coagulation or anti-platelet therapy – Endovascular stenting if flow occlusion is present	– Careful wire technique – Avoid more than 3 thrombectomy passes
Distal embolization	– Fragmentation of thrombus – Proximal plaque rupture	– Thrombectomy of large emboli – IV thrombolysis of smaller, more distal fragments	– Use balloon guide catheter for flow occlusion during retrieval – Use intermediate catheter for aspiration during retrieval
Stent detachment	– Device fracture	– Leave in place and start anti-coagulation – Endovascular retrieval of detached stent – Surgical removal of detached stent	– Use correct stent sizing to target vessel – Avoid stent retrievers if proximal stents have been previously placed – Re-sheath proximal portion of stent retriever before pulling back – Adhere to device recommendations regarding number of passes per device
Revascularization failure	– Resistant thrombus	– Use a combination of thrombectomy devices – Intra-arterial thrombolysis and anti-platelet therapy – Stenting at the area of occlusion	– Perform first-pass with aspiration device (ADAPT technique) – Use bridging thrombolysis

Introduction

Until recently, anterior circulation acute ischemic stroke (AIS) has been managed solely with intravenous tissue plasminogen activator (tPA), as it has been the only treatment proven to confer benefit to eligible patients with AIS. Although tPA is reasonably effective, with an overall revascularization rate of 46.2% [1], rates drop to 30–32% in proximal MCA occlusion and to 4–6% in cases of carotid-T occlusion [2, 3]. Efforts to achieve higher revascularization rates, particularly in cases of these proximal occlusions, led to the development of the endovascular thrombectomy (EVT) procedure. EVT aims to reperfuse ischemic brain through direct manipulation or aspiration of the clot. Although initial randomized controlled trials (RCTs) examining the technique were discouraging, more recent RCTs have clearly established the superiority of EVT over tPA for a select subset of patients with AIS. As evidence continues to accumulate in support of EVT efficacy, and as it becomes available in an increasing number of medical centers, there will be a growing need to understand the procedure and its benefits, as well as the associated complications. This chapter will review the procedure's most common complications and provide insight on complication avoidance and management.

Endovascular Thrombectomy RCTs

In 2013, an initial set of large RCTs investigating the clinical efficacy of combining EVT with tPA treatment failed to demonstrate superior outcomes compared to medical treatment with tPA alone [4–6]. However, several shortcomings in their design and in the available equipment at the time of their inception called into question their conclusions and their applicability to current clinical practice. Notably, these initial RCTs used first-generation mechanical thrombectomy devices; however, shortly after their conclusion, second-generation thrombectomy devices with superior reperfusion rates became available to endovascular centers.

The availability of a superior class of second-generation thrombectomy devices launched a renewed inquiry into the benefits of combining EVT with tPA to treat AIS. In 2015, five RCTs were published that demonstrated an improved functional outcome in carefully selected patients treated with EVT in addition to tPA [7–11]. Several systematic reviews with meta-analyses of pooled trial data confirmed these conclusions [12–14]. This ultimately led the American Heart Association and American Stoke Association (AHA/ASA) to incorporate EVT into the most recent AIS treatment guidelines [15].

Common Complications

Although the benefits of EVT have now been well defined, the procedure itself is not without its complications. The complications observed with EVT include intracranial hemorrhage (ICH) [16, 17], vasospasm, vessel dissection, embolization to downstream

vascular territories, intravascular stent dislocation, and recanalization failure, in addition to the medical complications associated with AIS and its attendant hospitalization. Together, rates of serious adverse events, including those that accompany hospitalization, have a reported rate of 47.2% in patients with AIS [7]. While there is no statistical difference in mortality between EVT plus tPA and tPA alone (15.3–16.6% vs. 18.2–18.9%), pooled data suggest there is a trend favoring the former [13, 14, 18].

Most complications are inconsistently reported across RCTs, limiting the ability to delineate their statistical significance. However, symptomatic ICH and one of its subsets, intraparenchymal hemorrhage (IPH), were recorded in each of the recent RCTs. This allowed for the analysis of pooled data samples, which has demonstrated a lack of statistical difference between those receiving EVT plus tPA and tPA alone (symptomatic ICH: 4.4–5.3% vs. 4.3–4.8%, IPH: 5.1% vs. 5.3%) [14, 18]. Individually, the recent RCTs reported the following complication rates for the EVT plus tPA treatment group: IPH (5.8–11%) [7, 9–11], arterial perforation (0.6–4.9%) [8, 11], vasospasm (3.9%) [11], arterial dissection (3.9%) [11], and distal embolization (4.9–5.6%) [7, 11]. Although uncommon, and certainly outweighed by the benefits of treatment, when complications do arise, they often result in poor outcomes. An understanding of the techniques to avoid complications and knowledge of the appropriate management when complications do arise is crucial to preserving the therapeutic benefit of EVT. These will be the focus of this chapter.

Procedural Overview

The patient is placed in the supine position and the area is prepared and draped in a sterile fashion. The femoral artery is the preferred access point and is identified with palpation below the inguinal ligament. Once the artery has been located on examination, a radiopaque object is used to mark the intended puncture site, and a plain radiograph is performed to ensure the location lies over the femoral head. This ensures a rigid surface is available behind the puncture site and allows for compression of the artery and prevents hematoma formation. After ensuring all equipment is prepared and primed, and all air is removed from the manifold system, puncture is performed. Once a pulsatile stream of blood returns through the needle, confirming arterial access, a guidewire is inserted and the puncture needle removed. The dilator catheter is then passed over the guidewire to secure access to the femoral artery.

Thrombectomy requires a long 6-F sheath or 8-F guide catheter to be placed in the internal carotid artery (ICA) [19]. To do so, a guidewire is advanced under fluoroscopic guidance, followed closely by the guide catheter. Angiographic confirmation of the presence and location of the large vessel occlusion (LVO) is performed. After LVO has been confirmed, intracranial vessel maneuvering is required to access the affected artery, and a 0.014 in. guidewire is used for this purpose [19].

The procedural details diverge depending on the available equipment. Although second-generation stent retrievers and aspiration catheters have demonstrated superior recanalization rates and are currently more popular, first-generation ET devices are occasionally still used when other options fail. In contrast to the mechanical disruption and coil retriever mechanisms by which first-generation devices achieve

reperfusion, the second-generation stent retriever devices deploy a retrievable stent into which the clot becomes entangled and is subsequently extracted. Aspiration thrombectomy devices perform their function as their name implies, by aspiration of the clot through a catheter attached to a specialized external aspiration pump or to manual aspiration via a large syringe.

First Generation: Coil Retriever Thrombectomy

First-generation mechanical thrombectomy devices are designed to deploy a shape-memory wire beyond the occluding thrombus [20, 21]. First, a guidewire is maneuvered into the intracranial vessels to the area of occlusion and is passed through the entire length of the thrombus. A microcatheter is advanced over the guidewire until its tip is positioned distal to the occlusion. The guidewire is then removed and the coil retriever is advanced within the microcatheter sheath. Once it reaches the orifice of the microcatheter, it is delicately advanced out of the microcatheter, and it immediately reassumes its coil form inside the vessel lumen. The device is then pulled back until its coils are wrapped around the occluding thrombus. The balloon of the guide catheter is inflated to occlude blood flow, and gentle manual aspiration is applied via a syringe. Gentle, deliberate retraction of the device and microcatheter as a unit will dislodge the thrombus and retrieve it into the guide catheter. Following retrieval, vessel patency and reperfusion of the affected vascular tree are confirmed angiographically. The Thrombolysis in Cerebral Infarction (TICI) score is used to grade the extent of reperfusion, and the procedure is repeated until TICI 2b or TICI 3 is achieved.

Second Generation: Stent Retriever Thrombectomy

The guidewire is maneuvered into the affected vessel and passed entirely through and beyond the clot. The microcatheter is passed over the guidewire until it is also situated distal to the clot. The guidewire is removed and the stent retriever device is introduced into the microcatheter. It is advanced until its distal, radiopaque markers are located at the tip of the microcatheter. It is deployed by retraction of the microcatheter and gently unfolds in the vessel lumen. Stent deployment applies a radial force, compressing the thrombus against the vessel wall, and results in immediate, partial reperfusion of the distal vasculature. Adequate deployment and patency of distal vessels are confirmed angiographically. A minimum of 3 min should be allowed after full deployment of the stent to permit maximal integration of the stent struts into the thrombus. With successful deployment, the clot becomes entangled in the stent. The balloon on the guide catheter is inflated and gentle aspiration is applied with a syringe. Careful retraction of the stent and microcatheter as a single unit removes the clot. Patency of the affected vasculature is again confirmed angiographically. The procedure is repeated until TICI 2b or TICI 3 is achieved (Fig. 30.1).

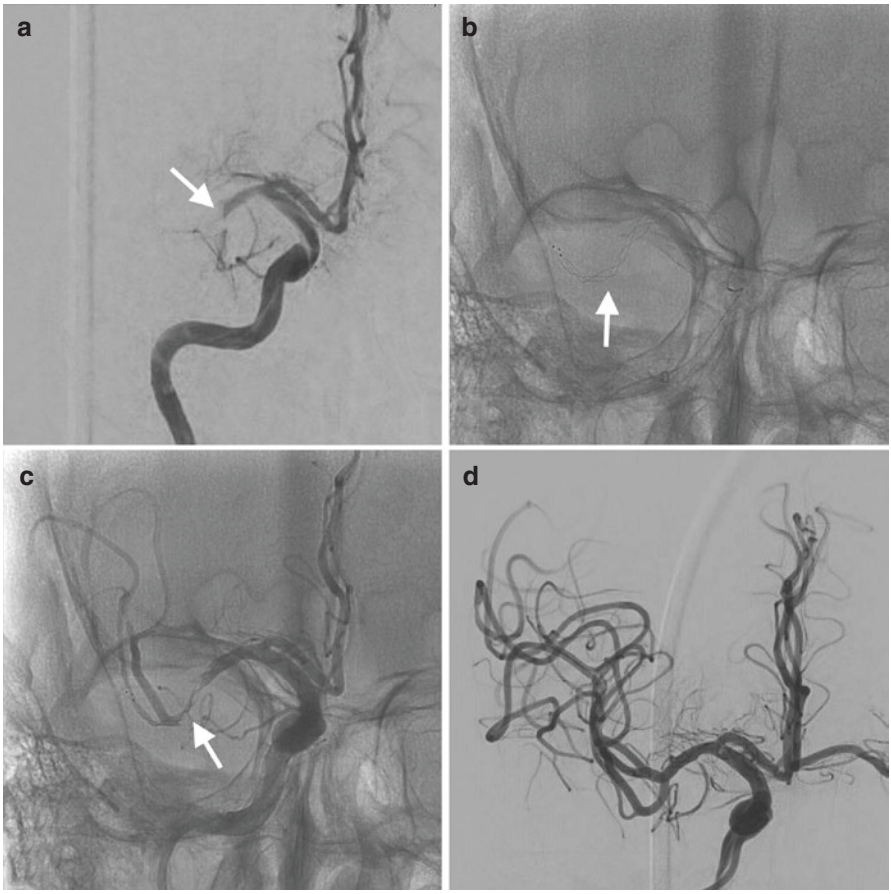

Fig. 30.1 Stent Retriever Thrombectomy. (**a**) An angiogram (AP view) demonstrated an occlusion of the right M1 segment (*arrow*). (**b**) A stent retriever was deployed across the thrombus (*arrow*). (**c**) A contrast injection after stent deployment demonstrated patency through its lumen (*arrow*). (**d**) Following retrieval of the thrombus, a contrast run demonstrated restoration of flow (TICI 3)

Second Generation: Aspiration Thrombectomy

Although stent retrievers are remarkably effective, there are some thrombi and other vessel occlusions that are not amenable to stent retriever therapy. These include hard thrombi, air emboli, and occlusions located in the proximal ICA [19]. When using the aspiration device, the guidewire, followed closely by a microcatheter, is advanced to the proximal portion of the occlusion, without passing through it. The aspiration catheter is advanced over the microcatheter until it is also situated flush with the proximal edge of the occlusion. The guidewire and microcatheter are removed. Aspiration is then applied with a large syringe or with an external aspiration pump. If the clot is difficult to aspirate or if the suction tip becomes clogged, a mechanical disruption

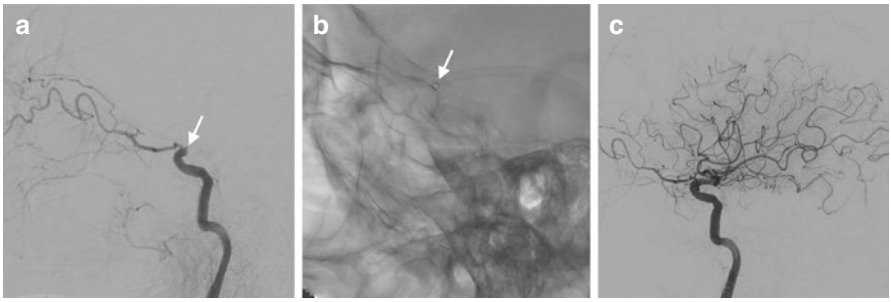

Fig. 30.2 Aspiration Thrombectomy. (**a**) An angiogram (sagittal view) demonstrated an occlusion at the terminus of the right internal carotid artery (*arrow*). (**b**) An aspiration catheter was advanced to the site of the occlusion (*arrow*). (**c**) Following the aspiration attempt, a contrast run demonstrated complete reperfusion of the left MCA territory (other imagining showed ACA filling from the contralateral side, TICI 3)

wire is introduced within the aspiration catheter to separate the clot, while still under aspiration. A bulbous tip on the end of the separator wire prevents accidental vessel perforation. The clot is aspirated, either in full or piecemeal, until the occluded vessel has been cleared completely. After aspiration has been completed, patency of the vasculature is confirmed angiographically, and TICI score is assessed. The procedure is repeated and continued until TICI 2b or TICI 3 is achieved (Fig. 30.2).

Complications: Avoidance and Management

Intracranial Hemorrhage

Intracranial hemorrhage (ICH) is the most feared complication of revascularization with EVT for it is characterized by high rates of morbidity and mortality [22–24]. The term encompasses several clinical entities that include subarachnoid hemorrhage (SAH) and intraparenchymal hemorrhage (IPH). The presence of ICH following EVT is typically categorized clinically as either symptomatic or asymptomatic. Symptomatic ICH (sICH) is defined as the presence of blood anywhere on CT imaging in the setting of clinical deterioration or a four-point drop on the National Institutes of Health Stroke Scale (NIHSS) [25, 26]. In the recent RCTs, sICH was the only consistently reported complication and rates ranged between 0 and 7.7% for those treated with EVT plus tPA and from 1.9 to 6.4% for those treated with tPA alone [7–11]. Meta-analysis of the pooled data from the initial and recent RCTs found no statistical difference between the two treatment groups, indicating that EVT does not confer an increased risk of sICH when compared with tPA alone [13, 14]. Asymptomatic ICH, on the other hand, is typically discovered incidentally on routine imaging after EVT and is not associated with the development of neurologic exam changes or declines in overall neurologic status. One recent RCT reported the rate of asymptomatic ICH at 16.5% in the EVT plus tPA group and 10.7% in the tPA-only group [11]. The two main subsets of ICH, intraparenchymal and subarachnoid, are discussed below.

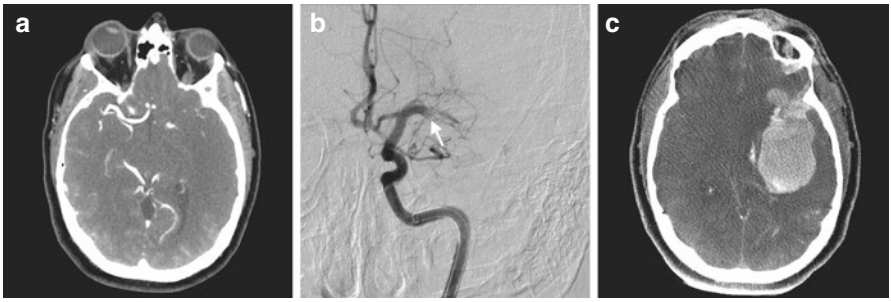

Fig. 30.3 Complication: Intraparenchymal Hemorrhage. CT angiography (axial view) demonstrated lack of filling in the left MCA vessels. (**b**) A subsequent angiogram (AP view) demonstrated an occlusion in the left M1 segment (*arrow*). (**c**) Following multiple thrombectomy attempts, reperfusion was accomplished. Ten minutes postoperatively, the patient was noted to have a dilated, unreactive left pupil. An intraoperative CT in the angiography suite was performed, revealing a large intraparenchymal hemorrhage

Intraparenchymal Hemorrhage

Intraparenchymal hemorrhage (IPH), also called intracerebral hemorrhage, is a hemorrhage into the brain tissue itself (Fig. 30.3). In cases of AIS, IPH tends to occur in the location of the affected vascular territory. Intraoperative injury to the vessel wall leading to arterial perforation during the EVT procedure can result in IPH. Injury of this type can occur as a result of excessive traction on the artery of interest, displacement of the normal vasculature during thrombus removal, or multiple passes to remove tenacious thrombus [27, 28]. The thrombectomy devices themselves, stent retrievers more than aspiration catheters, have a recognized association with intraoperative vessel injury [29, 30]. IPH is also a known complication of reperfusion to ischemic brain, which is unrelated to the EVT procedure itself [31]. Meta-analysis found no significant difference in IPH between EVT and tPA treatment groups suggesting that EVT does not increase the risk in appropriately selected patients [18]. The recent RCTs report rates of IPH that range from 5.8 to 11% for treatment with EVT plus tPA and 5% to 9% for treatment with tPA alone [7, 9–11] .

Avoidance

Appropriate patient selection for EVT is essential to avoiding IPH. Large infarct size at presentation increases the likelihood of hemorrhagic transformation, and these patients should be considered poor candidates for the procedure [32]. The recent RCTs employed various imaging techniques to ensure this appropriate patient selection was made [7–11].

The use of conscious sedation affords the operator significant advantage over general anesthesia, as it allows the operator to recognize the development of intraoperative procedure-related complications, including IPH, and to closely monitor any progression [33].

Careful surgical technique can help avoid vessel injury. First-generation thrombectomy devices involve a technique that requires active extrusion of the device tip out of the delivery microcatheter. This places the affected artery at increased risk for

injury and perforation [20]. Stent retrievers, on the other hand, are designed to be passively unsheathed from the delivery catheter. If the stent retriever is instead extruded from the delivery catheter, risk of injury to the vessel is considerably more likely.

After proper unsheathing of the stent retriever device, gentle traction should be applied when performing thrombus retrieval from the occluded vessel. Excessive traction increases the shear stress on the vessel walls and is more likely to result in injury and perforation. During the retrieval process, manual aspiration via a large syringe is recommended to prevent distal embolization, though care should also be taken to avoid excessive aspiration, which can also increase the shear stress on the vessel walls and risk perforation.

Attentive postoperative care can detect the development of reperfusion IPH resulting from the return of blood flow to previously ischemic brain. Routine and frequent neurologic examinations are required following EVT Systolic blood pressure control is key to averting hemorrhagic transformation and is typically maintained below 130 mmHg. Antiplatelet and anticoagulation therapy should be held for the first 24 h after EVT, as it may help decrease the chance of IPH in the immediate postoperative setting.

Management

IPH generally occurs intraoperatively or within 24 h of reperfusion [34]. If the patient is under conscious sedation, rather than general anesthesia, development of IPH can be detected during the procedure with routine neurologic examination. If suspected, IPH can be confirmed with extravasation of contrast fluid on angiography or, in operative suites with advanced equipment available, an intraoperative CT scan. Once discovered, the initial steps in management are contingent on the patient's hemodynamic stability. When the vessel perforation is deemed minor, conservative management with systolic blood pressure control below 140 mmHg [35] and reversal of anticoagulation are recommended. For patients with severe vessel perforation, a drastic increase in blood pressure and rapid neurologic decline can occur within minutes. In addition to blood pressure control and anti-coagulation reversal aggressive intervention with balloon occlusion or vessel sacrifice can be performed in severe cases. If the hematoma is large and persists, hematoma evacuation can be considered as further therapy. If hematoma is large, expanding, or if surrounding edema threatens to cause herniation, craniotomy and evacuation may be considered.

Subarachnoid Hemorrhage

Subarachnoid hemorrhage occurs when vascular injury disrupts the fragile intracranial vessels and causes blood to accumulate in the subarachnoid space. Iatrogenic SAH after EVT is generally the result of wire and catheter manipulation during the deployment or removal of the thrombectomy device [30]. Intraoperative or postoperative hypertension can precipitate its occurrence [36]. SAH can occur in isolated fashion or can accompany IPH. Isolated SAH with limited extension tends to be

asymptomatic and is frequently clinically insignificant. Extensive SAH, or if accompanied by IPH, tends to portend a poorer prognosis [36]. The recent RCTs report similar rates of SAH for EVT with tPA (0.9–4.9%) and tPA alone (0–4%) [7, 10, 11]. SAH can be compounded by subsequent vasospasm, a secondary complication that requires vigilance and treatment when neurologic function is affected.

Avoidance

Measures for IPH prevention, mentioned above, can also help avoid SAH. Intraoperative blood pressure control is an important consideration [36]. Fewer wire and catheter manipulations, attention to careful surgical technique, and reduction in the number of passes are reasonable steps to avoid procedure-related vessel injury, perforation, and resultant SAH. Balloon guide catheters are routinely used in EVT to occlude blood flow during thrombus retrieval. Balloon-vessel size mismatch can lead to pressure-related vessel wall injury and progress to micro-perforation and SAH. Appropriate balloon size choice and care in avoiding balloon over-inflation may help to prevent vessel injury. Vessel injury and perforation prevention can be maximized with stent retriever deployment into a straight portion of the artery, when possible [37].

Management

Rapid identification and prompt reversal of anticoagulant and antiplatelet medications are crucial steps to appropriate SAH management. Adequate control of blood pressure is recommended and should be monitored closely with the anesthesiology team. After surgery, vasospasm and herniation are additional concerns and should be managed in an intensive care setting.

Vasospasm

Arterial vasospasm following EVT can stem from mechanical irritation to the vessel wall caused by the wires and catheters that are passed during the procedure. It can also result as a consequence of SAH, a complication associated with EVT, discussed above [38]. Vasospasm can occur intraoperatively or postoperatively, depending on its inciting factor. Vasospasm triggered by mechanical irritation of angiography equipment is more likely to take place intraoperatively, whereas vasospasm due to SAH, whether symptomatic or asymptomatic, is more likely to occur in the early postoperative period (2–14 days). In the short term, endovascular procedure-related vasospasm can lead to significant blood flow restriction and recurrent strokes. In the long term, procedure-related vasospasm is associated with intimal hyperplasia and delayed arterial stenosis [39]. Intraoperative vasospasm is common but is rarely severe [39]; treatment is only required if flow restriction of the affected artery is a concern. Vasospasm requiring treatment was only reported in one of the recent RCTs. It was found in 3.9% of patients treated with EVT and 0% of patients treated with tPA alone [11]. Another of the RCTs reported a 4% rate of vasospasm requiring treatment in the EVT group, but did not report the rate for tPA alone [10]. A large prospective case series reported a similar 3% rate of vasospasm requiring treatment after EVT [40].

Avoidance

The use of wires and catheters is a defining feature of endovascular treatment, and their presence within the vessel is unavoidable. Nonetheless, careful surgical technique to minimize vessel manipulation may help reduce the degree of intimal irritation and, thus, the likelihood of vasospasm [39]. Intra-arterial injection of glyceroltrinitrate or other vasodilating agent prior to deployment of a stent retriever or aspiration catheter, and then again before thrombus retrieval, may also assist in avoiding the complication [39]. Postoperative vasospasm secondary to blood in the subarachnoid space may be detected with serial examinations in the intensive care setting and can be treated promptly with endovascular intervention.

Management

Intraoperative vasospasm is common and often clinically insignificant. Intraoperative detection allows the interventional radiologist to assess its severity and provide treatment with vasodilatory agents immediately, if required. Postoperative vasospasm is typically first detected by the presence of a new focal deficit. In these cases, computed tomography angiography (CTA) or angiogram may be performed for confirmatory diagnosis. If significant blood flow restriction is present, intra-arterial vasodilation treatment is generally advised.

Vessel Dissection

Intracranial arterial dissection (IAD) occurs when a tear in the internal elastic lamina allows for the accumulation of blood within the vessel wall that can extend and expand to varying degrees with the potential to result in occlusion of the affected vessel or its branches [41]. IADs can also generate thrombi, which can embolize to downstream vascular territories. IAD is a known iatrogenic complication of EVT that can occur as a result of the intra-arterial manipulation of catheters and wires (Fig. 30.4). IAD can have a range of consequences depending on clinical severity, which ranges from clinically insignificant to severe, causing ischemia. As mentioned above, vessel dissection was only reported in one of the recent randomized controlled trials at a rate of 3.9% [11]. Other large EVT patient cohorts have reported similar rates ranging from 1.5 to 4.5% [40, 42–45]. Diagnostic angiogram, without any treatment interventions, is associated with a lower rate of vessel dissection ranging from 0.14 to 1.2% [21, 22]. Endovascular treatment cases are considered to have an inherently higher risk of dissection due to introduction of catheter systems into the smaller intracranial vessels [46] .

Avoidance

Reasonable steps that may help avoid IAD include minimizing catheter manipulation and the number of passes needed to extract the thrombus [28, 30, 36]. Blood pressure optimization during the procedure is recommended and also has the potential to prevent propagation of a dissection.

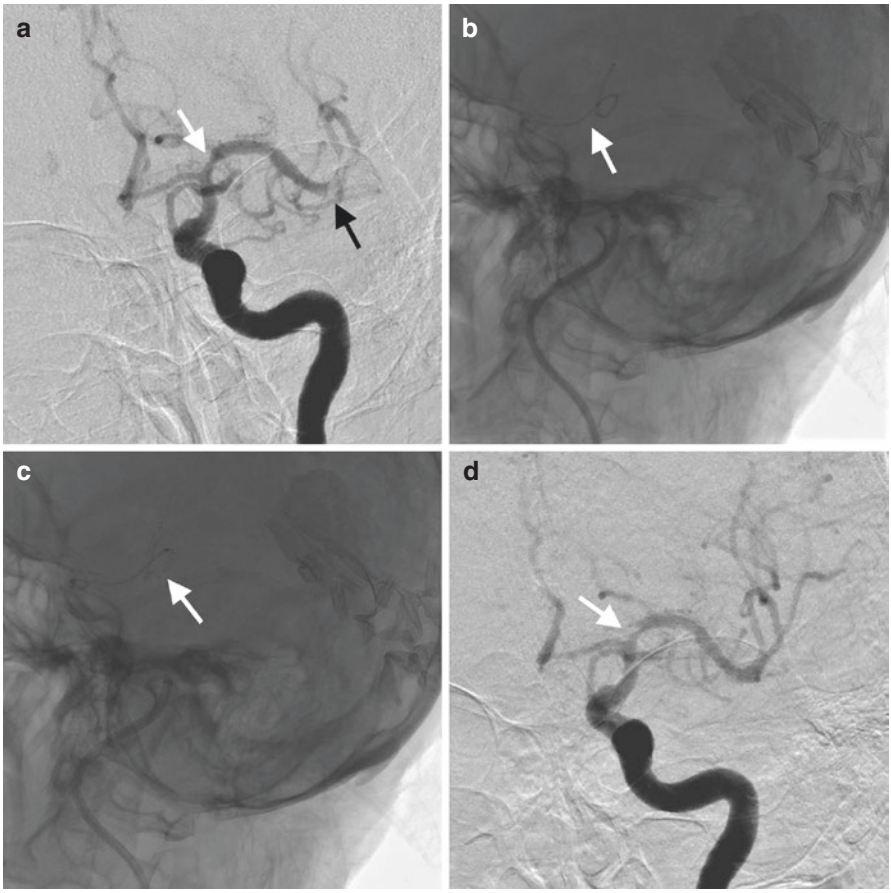

Fig. 30.4 Complication: Intracranial Vessel Dissection. An angiogram (AP view) demonstrates an occlusion of the left M1 (*black arrow*). Stenosis of the proximal M1 is also noted (*white arrow*). (**b**, **c**) A stent retriever (*white arrow*) is deployed across the occlusion (sagittal view). (**d**) Following retrieval of the thrombus, an angiogram demonstrates patency of the left M1. A non-flow-limiting dissection of the proximal M1 is noted (*arrow*)

Management

IAD can present in several ways on imaging, including dilation, stenosis, occlusion, or a combination of these [41]. Depending on the degree of flow restriction through the affected blood vessel, IAD can be managed in one of three ways: (1) observation without treatment, (2) medical treatment with antiplatelet or anticoagulant medication, or (3) endovascular stenting [47, 48]. The natural history and management of iatrogenic dissection are generally uneventful; most patients are able to be managed conservatively with good outcomes [46]. High-grade stenosis, concomitant thromboembolic events, and hemodynamic instability each warrants more aggressive treatment with stenting, which has shown good results with few complications, though it requires antiplatelet or anticoagulant medications be continued after placement [49].

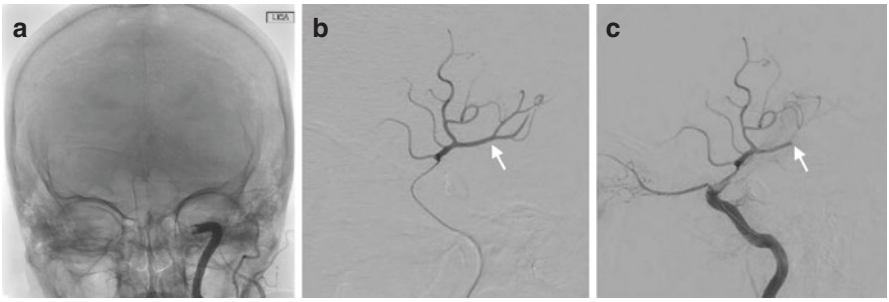

Fig. 30.5 Complication: Distal Embolization. (**a**) An angiogram revealed an occlusion of the horizontal portion of the petrous internal carotid artery (ICA). (**b**) Prior to stent retriever deployment, a microguidewire and microcatheter were advanced past the thrombus and a contrast run was performed. Note that the inferior division M2 is patent (*arrow*). (**c**) Following the initial thrombectomy attempt, a second contrast run revealed persistent occlusion of the ICA. The microguidewire and microcatheter were again advanced beyond the occlusion and a contrast run was performed prior to deploying the stent retriever for a second attempt. On this contrast run, the inferior division M2 was found to be occluded, indicating that a fragment of the thrombus had embolized distally (*arrow*). Following subsequent thrombectomy attempts, the ICA occlusion was successfully retrieved and the M2 occlusion was addressed separately

Distal Embolization

Symptomatic distal embolization as a consequence of EVT can occur in either the same vascular territory as the occluded vessel or in a new vascular territory (Fig. 30.5). Embolization in the same vascular territory typically results from the release of small fragments from the main thrombus during removal. Embolization to new vascular territories can occur by this same mechanism during the clot retrieval stage or by the disruption of preexisting plaques in the proximal vasculature when accessing the intracranial arteries. The rates of distal embolization reported in two recent RCTs ranged from 4.9 to 5.6% [7, 11]. Distal embolization can preclude maximal revascularization to TICI2b or TICI 3 and may relegate patients to poorer outcomes after EVT.

Avoidance

Balloon Guiding Catheter with Aspiration Thrombectomy

When the aspiration thrombectomy technique is used, there are several ways in which the likelihood of distal embolization can be reduced. The first is the use of a guiding catheter with a large-lumen balloon able to arrest blood flow while clot aspiration is performed. During the aspiration procedure, the balloon guide catheter is positioned in the cervical ICA, into which the large-bore distal aspiration catheter is advanced to the site of occlusion. Proximal flow arrest prior to beginning aspiration prevents thrombus fragments from traveling distally [50].

Distal Aspiration-Assisted Stent Retriever Technique

Stent retriever thrombectomy can be performed with a balloon guide catheter and proximal aspiration. Preliminary evidence has demonstrated that combining the stent retriever device with aspiration through a distal intermediate-sized catheter

can also aid in the prevention of distal embolization [50–52]. In this technique, an 8-F guide catheter is positioned in the cervical ICA, and a 5-F intermediate guide catheter is advanced to the origin of the affected artery. The guidewire and microcatheter are advanced through the clot via the intermediate catheter. The stent retriever is introduced and deployed as outlined above. After adequate time has passed to allow integration of the stent into the clot, the microcatheter is removed completely, leaving the stent retriever and the intermediate catheter in place. Aspiration is then applied through the intermediate catheter as it and the stent retriever are retracted as a unit through the guide catheter.

Management

Distal embolization is generally noted intraoperatively and can be confirmed with additional angiographic runs. If embolization has affected a proximal vessel (e.g., ICA, M1–M3, A1–A2), immediate thrombectomy is indicated and can be performed during the same procedure. In particular, stent retrievers are able to access the smaller M3 and A2 branches, while the aspiration catheter thrombectomy devices are generally limited to the M2 and A1 branches. Emboli affecting smaller branches may be difficult to access and may be managed with intravenous thrombolysis postoperatively, if indicated.

Stent Detachment

The Solitaire FR stent retriever (Medtronic/Covidien/ev3, Dublin, Ireland) was originally designed for stent-assisted aneurysm coiling but was found to have potential as a thrombectomy device through off-label use [53]. The stent is designed to expand into the vessel lumen and includes an option for permanent stent release that is driven by an electrolytic mechanism. If permanent release is not desired, or repositioning is necessary, the stent can be re-sheathed. During EVT, the stent is deployed but is not released, thus allowing the stent with entangled clot to be retracted and removed from the vasculature to provide reperfusion.

The Solitaire device is marked with radiopaque bands at its proximal and distal ends. The proximal marker houses the ball and socket joint that allows for flexibility and maneuverability in the intracranial vessels but generates a weak point at which stent detachment can occur [54, 55]. Solitaire stent detachments can be categorized as Type A (before the proximal marker) or Type B (after the proximal marker), based on their relation to this proximal marker [37]. Type A detachments occur between the push wire and the proximal marker, which leaves the detached stent with its proximal struts held together by the radiopaque proximal marker. Type B detachments occur distal to the proximal marker, causing the stent struts to splay apart and unfold against the vessel sidewalls. Type B detachments, since the proximal stent struts are not radiopaque and are therefore invisible under fluoroscopy, are more difficult to manage.

Large thrombus size, hard thrombus consistency, calcified vessels, significant plaque burden, and tortuous anatomy have been described as contributing factors of inadvertent stent retriever detachment and fracture [56]. The incidence of this complication is unknown due to lack of consistent reporting in the literature.

However, recent queries of the device experience databases have revealed an approximate rate less than 1% [53, 56]. One of these studies found that stent detachment accounted for 54% of adverse event reports [53]. Large case series in the literature that have reported the complication cite rates of 0.66–2.3% [32, 37, 53, 57]. Although rare, the potential consequences of unintended stent detachment can be severe and fatal [37].

Avoidance

Correct Stent Sizing

After deployment, retraction of the device to remove the thrombus may produce significant stress at the proximal marker and initiate detachment [53, 56]. Oversized stents in small arteries increase the radial force on the vessel and thus require greater retraction force during retrieval [58]. Accurate estimation of the target vessel caliber to optimize stent sizing may help avert unintended detachment of the thrombectomy device.

Proximal Stents

Preexisting proximal stents are problematic for stent retrieval thrombectomy. Patients with tandem occlusion stroke may require proximal stent placement to access the more distal occlusion. Other patients may have previously had stents placed for treatment of extracranial vessel disease. Irrespective of the indication for previous stent placement, stent retriever thrombectomy devices have been reported to entangle themselves in these previously placed stents during the retrieval process [53]. Entanglement within a proximal stent accounts for approximately 11–24% of the stent detachments reported in the adverse event databases [53]. Stent retrievers are not the preferred devices in these patients, as aspiration thrombectomy can avoid the complication altogether. However, if a stent retriever is used, the complication can be minimized by placing the balloon guide catheter distal to the stent so as not to draw the stent retriever through it.

Proximal Zone Protection with Microcatheter

Solitaire stent deployment into the thrombus is performed by retraction of its overlying microcatheter. The stent retriever expands radially as it unfolds into the vessel lumen. Full deployment of the stent retriever is generally performed, exposing both distal and proximal radiopaque markers, as well as the detachment zone. Exposure of the proximal marker and the detachment zone to the intravascular environment has the potential to activate the electrolytic mechanism [58]. Combined with the mechanical forces that converge at the proximal zone, this may weaken the area and place it at increased risk for fracture [54]. To avoid the potential for this occurrence, the stent retriever can, instead, be just partially deployed by halting microcatheter retraction before the proximal junction is exposed [54, 58]. Partial re-sheathing after full stent retriever deployment may also be performed to protect the proximal zone from mechanical stress prior to attempting thrombus retrieval. This technique is recommended in the Solitaire device Instructions for Use (IFU) manual that is provided by the manufacturer.

Number of Passes with Thrombectomy Device

The Solitaire FR IFU manual recommends a limit of two retrieval attempts per device to avoid inadvertent detachment. Still, 21% of reported cases occurred on the first pass, and caution is advised at every attempt [56].

Management

Management options in the event of stent retriever detachment, depend upon the degree to which the affected vessel is occluded. If the vessel is patent, the stent can be left in place where it detached. In these cases, angioplasty can be performed to ensure that the stent is fully unfolded into the vessel lumen. However, if the stent is left in place, dual antiplatelet therapy is required to prevent stent thrombosis, which may increase the risk for hemorrhagic reperfusion injury postoperatively. Furthermore, if the detached stent is left in place, the integrated thrombus remains in situ and may act as a nidus for thrombus propagation and embolization.

For cases in which retrieval of the detached or fractured stent is necessary, suggested strategies include capture with a snare device [37], partial deployment of a second stent retriever [55, 59], and the microcatheter loop and snare technique [55]. Reports indicate that interventionalists attempt stent retrieval in approximately 25% of detachment cases and are successful around 55% of the time [56].

The benefits and risks inherent in endovascular retrieval of an inadvertently detached stent need to be carefully weighed. Towing a fully deployed stent through the vasculature can denude and injure the endothelial layer of the vessels and has the potential to lead to vessel dissection, perforation, and intracranial hemorrhage. Open surgical removal or vessel bypass may be indicated if all other options fail, but have demonstrated mixed outcomes in the small number of reported instances [32, 60, 61].

Revascularization Failure

The time from stroke onset to angiographic recanalization demonstrates a strong correlation with functional outcomes [62, 63]. Although recanalization rates with combined EVT plus TPA are significantly greater than those with tPA alone (77% vs. 34%) [14], successful revascularization to achieve the TICI2b/3 benchmark is not always possible. In these cases, the approach to recanalization can be modified and combined with other treatment modalities to maximize the probability of success

Avoidance

Bridging Thrombolysis

Thrombolysis with tPA prior to EVT, known as bridging thrombolysis, is a heavily debated topic in the literature [45]. Although no RCTs have yet investigated the topic, several large studies have demonstrated that bridging thrombolysis is

not an independent predictor of favorable functional outcome [45, 64, 65]. However, the utility of bridging thrombolysis prior to EVT, rather than simply performing EVT alone may depend upon the thrombus characteristics, as bridging thrombolysis in cases of large and rigid thrombi may help to reduce the number of passes, reduce EVT procedure times, and maximize the recanalization rate [66]. It may also depend upon the location of the thrombus [65]. Bridging thrombolysis should be considered in cases of distal vessel occlusions or in the event that distal embolization occurs during the EVT procedure itself [65]. Note, however, that bridging thrombolysis may actually increase the occurrence rate of distal embolization and may contribute to a reduced proportion of full (TICI 3) revascularization [65]. As EVT gains even further support in the literature and more treatment centers implement EVT-centered AIS protocols, many patients may proceed directly to endovascular treatment without bridging thrombolysis; such a work flow strategy may, in fact, increase the likelihood of recanalization and favorable outcomes [63, 67].

A Direct Aspiration First-Pass Technique

The direct aspiration first-pass technique (ADAPT) utilizes large-bore aspiration thrombectomy as the primary method for recanalization [68]. The technique places emphasis on complete reperfusion to TICI 3 [68]. To achieve more complete reperfusion, use of the thrombus separator wire that is typically used for aspiration thrombectomy is avoided in order to minimize the risk of distal embolization [68]. The ADAPT technique is effective as a standalone therapy for EVT [68–70]. and, by itself, achieves reperfusion to TICI 2b or TICI 3 in 56–84.4% of cases [68–73]. Compared with stent retrievers as first-line therapy, the ADAPT technique demonstrates improved revascularization rates (82.3% vs. 68.9%). Additional use of a stent retriever when the aspiration-only ADAPT technique does not result in recanalization is recommended and has been called upon as a supplement in 18–45% of front-line ADAPT cases [71, 72, 74]. The combination of aspiration and stent retriever thrombectomy is effective as a rescue therapy and reaches revascularization to TICI 2b/TICI 3 in 84–96% of cases [69–73].

Management

Although the inability to achieve adequate recanalization occurs in only a minority of cases, there remains the need for rescue strategies and alternatives for recalcitrant occlusions. Persistent thrombi, despite several thrombectomy attempts, can be approached in several ways.

Intra-arterial Thrombolysis and Antiplatelet Therapy

Intra-arterial thrombolysis can be easily performed during EVT by direct delivery of thrombolytic agents through the microcatheter at the level of the occlusion. Urokinase or tPA are the first-line thrombolytic agents typically employed. Alternatively, antiplatelet agents, such as glycoprotein IIb/IIIa inhibitors, are

suggested. The success of intra-arterial thrombolysis following EVT failure is uncertain, with studies reporting widely variable recanalization rates ranging between 3.8 and 77.7% [75, 76]. It is of note that delivery of thrombolytic agents through a deployed stent retriever may be more effective than delivery at the proximal side of the thrombus [76].

Stenting

Arterial stenting is an alternative rescue therapy available for patients with thrombus refractory to EVT and intra-arterial thrombolysis. Stenting has been shown to provide good recanalization rates in cases of refractory thrombus, achieving recanalization rates in 83% of patients without an increase in procedure-related adverse events or mortality [75]. In fact, a retrospective case series found that patients who received stenting following EVT failure benefited from decreased rates of cerebral herniation and improved functional outcome at 3 months [75].

Conclusion

Endovascular thrombectomy has amassed resounding support in the literature and rapidly gained popularity among neurointerventionalists for the treatment of select patients with acute ischemic stroke. Here we have presented the common complications and provided the operator with techniques that may help avoid these problems. We have provided an overview of the management practices that are currently available should these complications occur. As the endovascular thrombectomy procedure is continually studied and device improvements are developed, new techniques for complication avoidance and management will undoubtedly lead to improved patient outcomes in the very near future.

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Endovascular Embolization of Head and Neck Tumors

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Checklist: Tumor Embolization Procedure

Equipment needed	Procedural steps
Radiology technicians • Guide catheter • Microcatheter • Balloon microcatheter • Embolic agent (coils, Onyx, NBCA, etc.) • Additional RHV and tubing • 18G or 20G spinal needle for direct puncture Nursing • Decadron • Staff pager numbers – Neurosurgery – Anesthesia attending Anesthesia • Pressure monitoring equipment for ICP if necessary • Propofol • ETT Neuroendovascular surgeon • Choice of guide catheters • Choice of microcatheters/balloons • Choice of embolic agents	Identification • Six-vessel cerebral angiogram to identify supply to tumor Embolization • Place guide catheter in most distal aspect possible of the vessel supplying the tumor • Advance microcatheter/balloon catheter as far distally into vessel directly supplying the tumor • Perform tumor embolization using embolic agent of choice • Perform control angiogram following embolization to ensure no additional vessels supplying the tumor exist as well as no unintended embolization of other vessels • Repeat steps above as necessary if additional vessels supplying the tumor are identified

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Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Inadvertent nontarget embolization	ECA-ICA anastomosis		Knowledge of possible ECA-ICA anastomoses
			Use of blank roadmap
			Careful analysis of six-vessel angiogram prior to embolization
Reflux of embolic material into parent vessel	Reflux of embolic material		Use of blank roadmap
			Use of radiopaque embolic agents
			Use of pressure cooker technique
			Use of balloon microcatheter
Thromboembolism	Insufficient anticoagulation	Additional heparin and consider integrilin	Ensure ACT is two to three times baseline
Tumor swelling	Necrosis from tumor embolization	Decadron or operative resection	Decadron prior to tumor embolization
Tumor hemorrhage	Use of PVA particles less than 150 μm		Avoid using PVA particles less than 150 μm
Transient facial nerve injury or trigeminal neuralgia	Excess traction while withdrawing microcatheter		Limit reflux of liquid embolic agent around microcatheter

Introduction

Preoperative embolization of meningiomas was originally described by Manelfe et al. [1] in 1973. Since that time there have been many reports on the potential advantages and disadvantages of preoperative embolization of hypervascular head, neck, and spinal tumors [2–32]. Preoperative embolization of head, neck, and spinal tumors is often utilized to limit intraoperative blood loss, improve visualization during resection, and facilitate surgical resection. Many agents have been used for embolizing these tumors including polyvinyl alcohol, Gelfoam, *N*-butyl cyanoacrylate (NBCA, Codman Neurovascular, Raynham, MA), coils, and ethyl vinyl alcohol copolymer (Onyx, eV3, Irving, CA).

Embolic Agents

Each of the following agents can be used to reduce the blood supply to tumors of the head, neck, and spine. An understanding of their characteristics as well as their advantages and disadvantages when used for tumor embolization is critical in achieving safe tumor embolization. The basic properties of each of the embolic agents listed below are summarized in Table 31.1.

Table 31.1 Embolic agents and their basic properties

Embolic material	Radiopaque	Permanent occlusion	Tumor bed penetration possible
PVA	No	No	Yes (depending on size used)
Gelfoam	No	No	No
Coils	Yes	Yes	No
NBCA	Yes	Yes	Yes
EVOH	Yes	Yes	Yes

Polyvinyl Alcohol (PVA)—PVA is found in particles of different sizes ranging from 45 to 1180 μm. Particle size is selected based on the intended embolization target with larger particles being used for parent vessel occlusion versus smaller particles being used to penetrate the capillary or tumor bed. These particles are radiolucent and, thus, must be mixed with a contrast agent for visualization. PVA has the advantage of being relatively cheap and easily available. The particles dissolve over time which can be considered advantageous when used in the setting of epistaxis with decreased risk of mucosal necrosis. However, in the setting of tumor embolization, this may be disadvantageous as there is the potential of parent vessel recanalization of the occluded vessel if the tumor is not resected within a few days to weeks. The biggest disadvantage of PVA is the poor visualization of the particulate material. Even when mixed with contrast there is a risk of inadvertent embolization to normal blood vessels and unintended ischemia. There is an increased risk of post-embolization hemorrhage or ischemic stroke, particularly with particles 45–150 μm in size [3, 4].

Gelfoam (Pfizer, New York, NY)—Gelfoam is an embolic agent derived from porcine skin and gelatin. Gelfoam is often used in combination with PVA particles, most commonly as a plug to occlude the parent vessel after more distal particulate embolization with PVA. As with PVA particles, Gelfoam provides only temporary occlusion as it dissolves over time. When applied to bleeding mucosa, Gelfoam dissolves over 2–5 days. Surgical resection should be planned within 5–7 days to reduce the risk of tumor revascularization.

Coils—Coils can also be used to diminish the blood supply to a tumor by occluded the parent vessel. Coils can be safely deployed with a low risk of unintended branch vessel occlusion. However, over time a tumor can recruit new vascular supply from other nearby arteries via neo-angiogenesis as the coils do not penetrate the tumor itself. In addition, the main arterial branches supplying the tumor can become permanently occluded leaving only small branches that are inaccessible via microcatheters if further embolization is required or if a tumor recurs after surgical resection.

N-Butyl Cyanoacrylate (NBCA)—NBCA is a liquid embolic agent that provides permanent occlusion of the parent vessel with good penetration into distal vessels of the tumor bed. The ratio of NBCA to ethiodized oil is variable and can be changed to affect the rate of polymerization as well as viscosity of the liquid embolic agent.

NBCA is adhesive and as such has the potential to adhere to the microcatheter being used to deliver the agent which increases the risk of catheter retention. To prevent NBCA from adhering to the microcatheter and possibly occluding it prior to tumor embolization, NBCA should be mixed with ethiodized oil as per the IFU in a separate container prior to injection through the microcatheter.

Ethyl Vinyl Alcohol Copolymer (EVOH/Onyx)—EVOH is a liquid embolic agent that provides permanent occlusion of vessels as well as good penetration of the tumor vasculature. Unlike NBCA, EVOH is cohesive and polymerizes on contact with blood. Microcatheters must be lined with dimethyl sulfoxide (DMSO) prior to the administration of EVOH to prevent it from polymerizing within the microcatheter. The delivery microcatheter must be DMSO-compatible. Catheters that are not DMSO-compatible may dissolve with the administration of DMSO and subsequently cause nontarget occlusion of a vessel. DMSO must be administered at a rate of 0.1 mL/min in order to minimize the risk of side effects of DMSO administration which can include cardiac arrhythmias. It is felt that EVOH has better visualization and better controlled injection than many of the other agent. In addition, it is possible for onyx to pass through the tumor bed (capillary network) and into the venous drainage of the tumor causing venous infarction of the tumor. This may cause necrosis and softening of the tumor allowing for an easier surgical resection. In many institutions, Onyx has become the preferred agent of choice for tumor embolization.

Vascular Supply

One must be cognizant of the vascular supply of cranial nerves, eloquent areas of the brain, as well as potential anastomoses with these vessels when planning a tumor embolization (see Tables 31.2, 31.3, and 31.4) [36]. Likewise, it is important to be aware of critical vessels supplying the spinal cord when embolizing spinal tumors.

In the anterior cranial fossa, most tumors are supplied by the middle meningeal artery, artery of the falx cerebri, or from branches of the sphenopalatine artery. Careful attention must be paid to anastomoses with the ophthalmic artery (Fig. 31.1). This is particularly true when embolizing a tumor via branches of the internal maxillary

Table 31.2 Dangerous anastomoses that can potentially harm the optic nerve

Artery	Anastomosis
MMA	OA via lacrimal artery, anterior falcine artery, septal arteries, anterior and posterior ethmoidal arteries
Infraorbital artery	OA via inferior branch of lacrimal artery and dorsal nasal artery
Anterior deep temporal artery	OA via inferior branch of lacrimal artery
Frontal branch of STA	OA via supraorbital artery
Angular branch of facial artery	OA via dorsal nasal artery

Table 31.3 Risk of injury to CN VII with embolization of these arteries

Artery	Anastomosis
Petrous branch of MMA	None
Stylomastoid branch of posterior auricular artery	MMA and ascending pharyngeal artery
Stylomastoid branch of occipital artery	Muscular branches of the vertebral artery
Internal auditory branch of AICA (CN VIII also at risk of injury)	None

Table 31.4 Vascular supply of lower cranial nerves and important anastomoses

Artery	Anastomosis	CN at risk
Neuromeningeal branch of ascending pharyngeal artery	None	IX, X, XI, and XII
Superior laryngeal artery	Contralateral thyroid arteries (superior and inferior)	CN X
Musculospinal branch of ascending pharyngeal artery	None	Spinal root of CN XI
Ascending and deep cervical arteries	Vertebral artery (V1 segment)	Spinal root of CN XI
Lingual artery	Contralateral lingual and superior thyroid arteries	CN XII

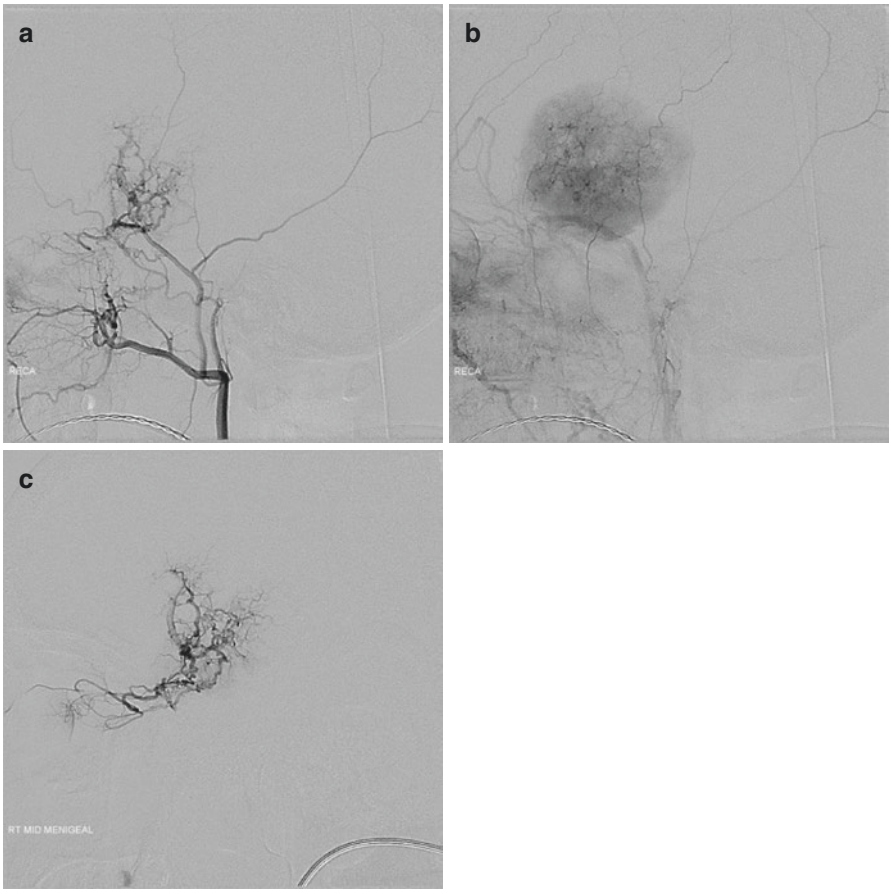

Fig. 31.1 (**a**) Right ECA lateral angiogram showing tumor supply via middle meningeal artery. (**b**) Right ECA lateral angiogram capillary phase showing tumor blush as well as choroidal blush. (**c**) Superselective right middle meningeal artery angiogram demonstrating tumor blush as well as choroidal blush, thus confirming anastomosis between right MMA and right ophthalmic artery

artery such as middle meningeal or ethmoidal arteries. Superselective angiography should be performed after selecting these vessels to ensure the absence of an ophthalmic artery anastomosis and retinal blush. If an anastomosis with the ophthalmic artery does exist, embolization can still be performed safely if the microcatheter is distal to the anastomosis and there is adequate room to allow reflux of the embolic material without compromising the anastomotic channel. It is critical that the central retinal artery (branch of the ophthalmic artery) is not occluded during embolization as this results in ipsilateral blindness. The middle meningeal artery is also rarely the origin of the ophthalmic artery, and the endovascular surgeon must be aware of this possibility when embolizing a tumor supplied by the middle meningeal artery.

There are several important considerations when embolizing tumors of the middle fossa. As with anterior skull base tumors, many of these tumors are supplied by the MMA and the ascending pharyngeal artery. It is important to be cognizant of anastomoses between branches of the external carotid artery and the internal carotid artery. The ascending pharyngeal artery (APA) provides multiple potential anastomotic connections with the internal carotid artery (see Tables 31.3 and 31.4). The APA divides into the neuromeningeal trunk (located posteriorly) and the pharyngeal trunk (located anteriorly). In addition to the dangers of embolic agents reaching the ICA or its branches via anastomoses, the possibility of lower cranial nerve dysfunction is also possible with embolization of tumors that are supplied by the neuromuscular division of the ascending pharyngeal artery.

In addition to the potential anastomotic connections to the ophthalmic artery, the middle meningeal artery as well as the accessory meningeal artery can form an anastomotic connection with the inferolateral trunk of the internal carotid artery leading to deficits of cranial nerves running through the cavernous sinus [36]. Most importantly there is a risk of facial paralysis if the MMA petrosal branch is embolized as it provides blood supply to the facial nerve within the middle ear.

In the posterior fossa, most tumors are supplied by branches of the posterior meningeal artery, branches of the AICA, and potentially the ascending pharyngeal artery. Again, it is critical to maintain the neuromeningeal trunk of the ascending pharyngeal artery as it supplies the lower cranial nerves. If blood supply to a tumor comes from branches of the anterior inferior cerebellar artery (AICA), it is important to maintain the labyrinthine branch of the AICA as this branch travels with the vestibulocochlear nerve and supplies the vestibular apparatus as well as the cochlea. The occipital artery frequently forms an anastomosis with the extracranial segment vertebral artery.

Procedural Overview

Tumor embolizations can be performed either transarterially or through a direct percutaneous method. The procedure is usually performed with general anesthesia and standard arterial access. A diagnostic angiogram is performed to identify

vascular supply to the tumor. Heparin is administered intravenously to maintain an activated clotting time of 2–2.5 times the patient's baseline.

Guide Catheters—Generally, a 6 French guide catheter is placed into the vessel of interest, and control angiograms are performed to document vascular supply to tumor and potential anastomosis. Different guide catheters can be used depending on which vessel is going to be selected for embolization. A stiffer guide catheter such as the Envoy DA or Chaperon can be used to provide support if the external carotid artery is the vessel that will be selected. Guide catheters with softer, more flexible distal ends such as the Sofia or Benchmark can be used if access to the petrous segment of the internal carotid artery or V3 segment of the vertebral artery is required.

Microcatheter—A suitable microcatheter or balloon microcatheter (Scepter Balloon, MicroVention, Destin, CA, USA) to deliver the target embolic agent can then be advanced through the guide catheter into the vessel directly supplying the tumor. Knowledge of the different microcatheters and their properties is critical as not all microcatheters are compatible with all of the embolic agents used. Some microcatheters such as the Magic are incompatible with DMSO, and thus, Onyx cannot be used to embolize tumors using this catheter. In addition, if a significant amount of reflux of a liquid embolic agent is anticipated, a detachable-tip microcatheter such as the Apollo microcatheter can be used. If prevention of reflux is critical, then the use of a dual-lumen balloon microcatheter (Scepter Balloon) should be considered for the embolization procedure. Intermittent control angiograms should be performed to document progress of tumor embolization, parent vessel occlusion, nontarget embolization, and opening of potential collaterals as flow changes.

Direct Puncture Embolization

Percutaneous direct puncture of tumors have been described (references) previously. It is possible to embolize tumors of the head and neck via direct puncture (Fig. 31.2). A full diagnostic angiogram should be performed to first determine if endovascular embolization of the tumor is possible. The skin overlying the puncture site should be prepped and draped in the usual sterile manner. Ultrasound, fluoroscopic road map, or intraoperative DynaCT can be used to localize tumors of the head and neck as well as to guide needle insertion into the tumor. Ideally a 20 or 18 g spinal needle is utilized. Care must be taken to ensure that any tubing used to connect the needle to syringe is DMSO combatable. Aspiration of blood through the needle should be performed after it is inserted into the tumor. This is followed by injection of contrast to ensure the tumor was penetrated. Finally, embolization of the tumor through the needle can then be performed using a liquid embolic agent.

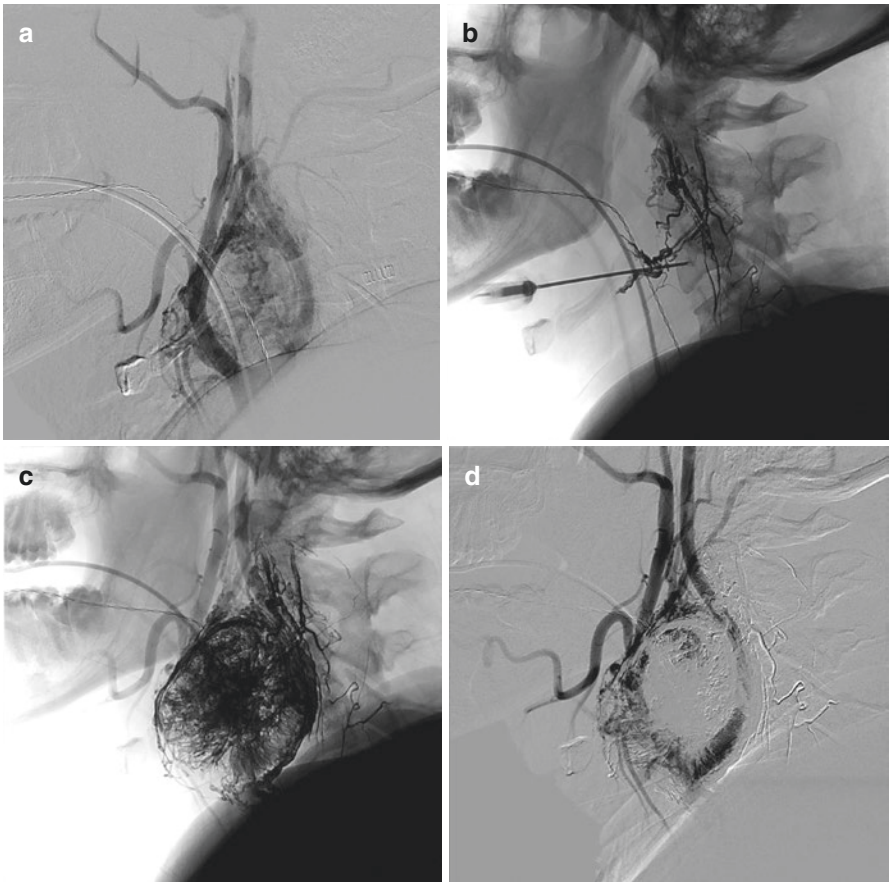

Fig. 31.2 (**a**) Lateral angiography demonstrating left carotid body tumor. (**b**) Partial endovascular embolization of the left carotid body tumor using Onyx and initial placement of the 20G needle for direct puncture of the tumor. (**c**) Native lateral angiography of left carotid body tumor s/p endovascular embolization as well as embolization via direct puncture using Onyx for both. (**d**) Subtracted lateral angiography of left carotid body tumor s/p endovascular embolization as well as embolization via direct puncture using Onyx for both

Hypervascular Neoplasms of the Head and Neck

Meningiomas

Meningiomas are extra-axial or intraventricular tumors that can become symptomatic as they increase in size. Vascular supply to these tumors can come from branches of the external and internal carotid arteries as well as the posterior circulation. A six-vessel diagnostic angiogram should be performed when evaluating these tumors for

possible embolization. The classic appearance of these tumors is that of a sunburst pattern (Fig. 31.3).

Hemangiopericytomas

Hemangiopericytomas, also known as angioblastic meningiomas, originate from spindle cells surrounding capillaries and venules [33]. These tumors represent only 0.4% of intracranial tumors, are almost always attached to the dura, tend to recur locally, and have the ability to metastasize [34].

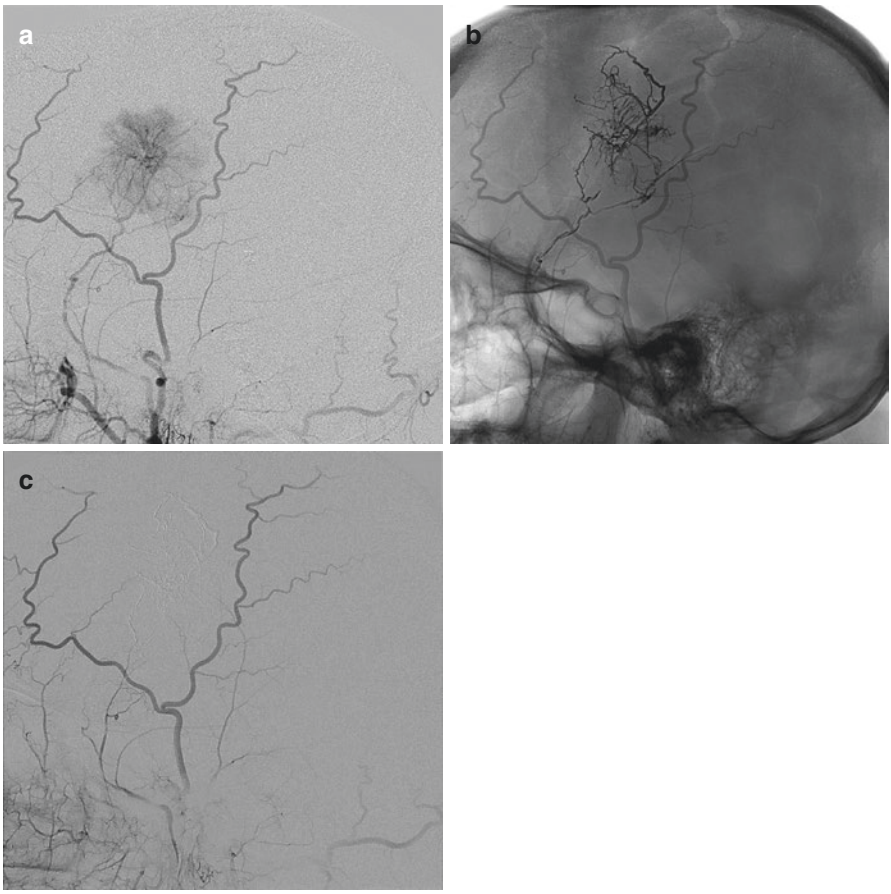

Fig. 31.3 (**a**) Lateral angiography showing supply to a convexity meningioma via the middle meningeal artery with classic sunburst vascular pattern. (**b**) Native lateral angiography showing Onyx cast s/p endovascular embolization of convexity meningioma. (**c**) Subtracted lateral angiography of convexity meningioma showing no further tumor blush s/p Onyx embolization via the middle meningeal artery

Hemangioblastomas

Hemangioblastomas are benign vascular tumors that represent 7–12% of adult posterior fossa tumors [35]. Because of their intra-axial nature, hemangioblastomas located in the cerebellum typically obtain their vascular supply from the anterior inferior cerebellar artery, posterior inferior cerebellar artery, or superior cerebellar artery. These tumors can also be located within the brainstem or spinal cord.

Paragangliomas

Paragangliomas typically arise from the vagus nerve nodose ganglion, carotid body, or temporal bone. The vascular supply of these tumors can be predicted based on tumor location as well as the size of the tumor. It is possible to predict the vascular supply as these tumors have a neural crest origin and arise where neural crest cells are found in the body. These tumors typically obtain their vascular supply from branches of the external carotid artery, predominantly the ascending pharyngeal artery and rarely the thyrocervical trunk and deep cervical artery. These tumors have an impressive blush on angiography (Fig. 31.2). Some paragangliomas are catecholamine-secreting, in which case embolization can precipitate a potentially fatal vasomotor attack. Alpha antagonists should be used to combat this potential complication as beta-blockers are contraindicated in this situation.

Juvenile Nasopharyngeal Angiofibromas

Juvenile nasopharyngeal angiofibromas (JNAs) are benign yet highly aggressive and infiltrating tumors. JNAs typically occur almost exclusively in adolescent males and are commonly fed by branches of the internal maxillary artery, ascending palatine artery, ascending pharyngeal artery, accessory meningeal artery, and internal carotid artery (vidian or palatine branches when present) (Fig. 31.4). These tumors typically exhibit high-flow shunting from the arterial to the venous phase which can make particle embolization challenging. Liquid embolics such as glue or onyx may be a better choice with more controlled delivery of the embolic to the target vessel.

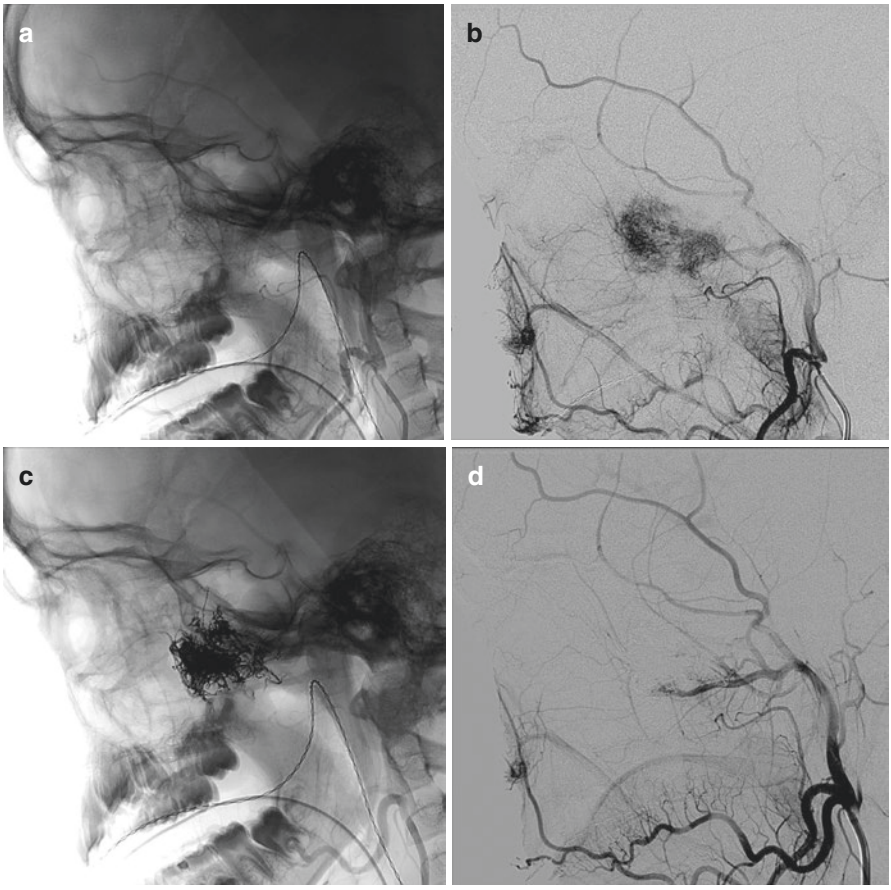

Fig. 31.4 (**a**) Native lateral angiography of the left external carotid artery prior to embolization of a JNA. (**b**) Subtracted angiography of the left external carotid artery showing multiple parasitized branches of the internal maxillary artery supplying the JNA. (**c**) Native lateral angiography showing Onyx cast s/p endovascular embolization of the JNA. (**d**) Subtracted lateral angiography demonstrating significantly reduced blood supply to the JNA s/p endovascular embolization using Onyx

Complication Avoidance

Several steps can be taken to limit the complications associated with tumor embolization. Careful analysis of the blood supply to a tumor as well as potential anastomoses with vessels near the tumor must be performed prior to performing any embolization procedure.

Continuous monitoring of embolic progression must be performed to prevent inadvertent nontarget embolization. The use of negative (blank) road maps can be used to show embolization progress, especially when a large Onyx or glue cast obscures visualization on native imaging.

The use of dual-lumen balloon catheters can also help prevent reflux and allow for better tumor penetration of embolic agents. For vessels in which a dual-lumen balloon catheter is too large or deemed unsafe, a detachable-tip microcatheter is one alternative that may prevent unintended tearing of microcatheters when using liquid embolic agents.

An alternative method for preventing reflux of a liquid embolic agent is the pressure cooker technique as described by Chapot et al. [37]. This technique involves placing two microcatheters within the same vessel supplying the tumor to be embolized and creating a proximal plug. First, a DMSO-compatible microcatheter with a detachable tip is placed within the vessel of interest supplying the tumor. To create a plug, a second microcatheter is placed next to the first catheter with its tip at the proximal end of the detachable tip of the first microcatheter. A plug is then created by pushing coils and then NBCA through the second microcatheter. The coil/glue plug is resistant to breakdown from DMSO and, thus, more resistant to reflux of Onyx. Onyx is then injected through the detachable-tip microcatheter.

The optimal timing of surgery after tumor embolization remains controversial due to the risk of post-embolization complications including the development of edema or hemorrhage within the tumor [3]. Perioperative steroid administration may prevent some of the edema-associated complications due to tumor necrosis following embolization including increased mass effect, new neurologic deficits, obstructive hydrocephalus, and coma or stupor. Bendszus et al. [3] reported a 3.2% hemorrhage rate following tumor embolization. Carli et al. [4] reported that most hemorrhages in their series occurred during or several hours after tumor embolization, and using small PVA particles (45–150 μm) was a risk factor for hemorrhage.

A potential advantage of preoperative tumor embolization is decreased intraoperative blood loss and, thus, a decreased need for transfusion of blood products. Chun et al. [5] reported decreased intraoperative blood loss when surgery was delayed more than 24 h after tumor embolization. Kai et al. [13] retrospectively reviewed 65 patients that underwent preoperative embolization of meningiomas supplied solely by the ECA and determined that the optimal time to perform surgery was 7–9 days after embolization. Oka et al. [18] reported decreased intraoperative blood loss in embolized tumors less than 6 cm in diameter but no difference in blood loss for tumors larger than 6 cm. However, in tumors with both ECA and ICA blood supply, a theoretical risk of increased intraoperative blood loss exists when only the ECA supply is embolized. This is due to the fact that the ICA supply is often deep within the surgical bed and can be challenging to visualize and secure.

Transient or permanent neurologic deficits can occur if the vascular supply to cranial nerves is embolized. The same is true if certain ECA-ICA anastomoses are embolized as embolic material can travel from ECA circulation to ICA circulation and cause reduction or cessation of blood flow to vital neurologic structures and tissue. Thus, knowledge about the vascular supply of cranial nerves as well as potential anastomoses between the ECA and ICA is crucial when embolizing tumors.

Transient facial nerve injury as well as trigeminal neuralgia has also been described secondary to traction injury on the cranial nerves as the exit the skull [38]. The accessory meningeal branch of the internal maxillary artery enters the skull through the foramen ovale and courses adjacent to the V3 segment of the trigeminal nerve. Similarly, the posterior auricular artery also travels adjacent to the mastoid segment of the facial nerve. Reflux of liquid embolic material in either the accessory meningeal artery or the posterior auricular artery can increase the amount of force required to remove a microcatheter after embolization as well as increase the amount of traction placed on the V3 segment of the trigeminal nerve or the facial nerve, respectively, and, thus, increase the potential for cranial nerve injury.

Conclusion

Preoperative embolization of hypervascular head, neck, and spinal tumors aids in reducing intraoperative blood loss as well as the ease of tumor resection by improving visualization of the surgical bed. As such, the time for tumor resection can potentially be reduced which limits the amount of time a patient is under anesthesia and the complications associated with general anesthesia. A thorough understanding of the embolic agents being used, the vascular territory surrounding the tumor, the potential vascular anastomoses, as well as the potential postoperative complications is critical to achieve the best possible outcomes with preoperative tumor embolization.

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Management of Complications Following Embolization for Intractable Epistaxis

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Checklist: Embolization for Intractable Epistaxis

Equipment needed	Procedural steps
Radiology technicians • Embolization particles – Embosphere – Gelfoam – Polyvinyl alcohol • Embolization material – Liquid embolics *n*-butyl cyanoacrylate (NBCA) glue Onyx (ethylene-vinyl alcohol copolymer) – Coils • Balloon Nursing • Staff pager numbers – Neurosurgery – Anesthesia attending – ENT • Heparinized saline bag Anesthesia • Pain management • Sedation for monitored anesthesia care (MAC) • Endotracheal intubation and mechanical ventilation capabilities (if case is initiated under MAC) Neurointerventionalist • Choice of embolization particles/material Neurosurgery • Number to operating room ENT • For unpacking in case no clear sit is identified and the need for unpacking should arise	Identification • Identify dangerous anastomoses between the ECA and the ICA or its distal branches • Recognize embolization into the intracranial circulation • Recognize wire perforation extravasation on imaging • Localize the site of bleeding Initiate and engage • Alert team • Maintain access to vessel of interest • Anesthesia: vital signs • Nursing and technologists to page for additional assistance • Technicians to open additional coils as requested • For procedure-related thromboembolization – Nursing to prepare glycoprotein IIb/IIIa inhibitors for administration intra-arterially by neurointerventionalist • Procedure-related vessel perforation – Nursing to give protamine if heparin was administered Repair • For procedure-related thromboembolism: – Intra-arterially administer glycoprotein IIb/IIIa inhibitors – If no response, consider mechanical thrombectomy via stent retriever or aspiration • Procedure-related vessel perforation – For perforation involving ECA branch, deploy coil in bleeding vessel to arrest extravasation – Continue to deploy coils while bringing microcatheter more proximally and continue coiling – Add additional coils until extravasation is controlled – No interval imaging Alternatively liquid embolic material may be used, for example, NBCA glue and Onyx

Complication Avoidance Flowchart

Complication	Cause	Remedy	Avoidance
Perforation	Excess load in system	Reverse heparin and consider deploying coils or liquid embolic material, for example, NBCA glue and Onyx	Reduce load in system prior to coiling
	Wire manipulation		Always have more than 5 mm wire extruded from microcatheter when manipulating microcatheter
	Catheter load on detachment		Remove all load from system prior to detaching coils
Thromboembolism	Insufficient anticoagulation	Administer heparin if/when deemed safe IA administration of glycoprotein IIb/IIIa inhibitors	Minimize wire time
	Dissection	If no response, consider mechanical thrombectomy via stent retriever or aspiration	Careful and gentle movement of microcatheter over wire

Introduction

Epistaxis affects an estimated 60% of people during their lifetime [1, 2]. It is found to occur most often from an anterior source rather than a posterior source [3]. The underlying etiology for epistaxis can vary from a systemic disease with an associated coagulopathy [4], to physical assault with trauma to the mucosa, nasal bone or septum, anticoagulant use, an underlying arteriovenous malformation, illicit drug use, hypertension, and/or an underlying malignancy [1, 5].

Less than 10% of patients, however, will develop significant hemorrhage requiring emergent medical treatment [2]. Conservative treatment options include electrocautery, nasal packing, and intranasal injection of hemostatic agents. For intractable epistaxis, surgical ligation or endovascular embolization can be performed. Neuroendovascular embolization has been reserved for epistaxis refractory to conventional treatment regimen [6]. Embolization involves injection of particles or glue into branches of the external (ECA) or internal carotid (ICA) arteries which supply the nasal cavity, thereby promoting occlusion of the distal vascular bed and terminating the bleeding.

Procedural Overview

Management of intractable epistaxis begins with a thorough ENT examination to localize the site of bleeding to either the right or left, anterior or posterior, and lateral or medial nasal cavity. Patients are placed under local or general anesthesia depending on patient compliance, combativeness, ability to protect the airway, and extent of the hemorrhage. A 5-F/6-F sheath is then inserted into the common femoral artery. Diagnostic cerebral angiography is performed to evaluate the external carotid artery (ECA), internal carotid artery (ICA), as well as the vertebral arteries, for the presence of underlying vascular anomalies (i.e., pial or dural arteriovenous malformations and carotid cavernous fistulas). It is also used to identify dangerous anastomoses between the ECA and the ICA or between the ECA and vertebral artery. A potential anastomosis, for example, can include one between the ECA and ophthalmic artery (OA), which could result in permanent visual deficits following embolization of the internal maxillary artery (IMA). In at least 70% of cases, angiographic findings will be normal and the epistaxis will be idiopathic [7].

Administration of intravenous heparin is controversial and should be weighed against the potential risk of exacerbation of epistaxis. In most cases the heparinized saline flush lines may provide sufficient prophylaxis against thromboembolic complications. Use of heparin should hence only be considered after taking in consideration the degree of bleeding and the ability to identify the extravasation site.

After the identification of the arterial feeder, a 5-F guide catheter is then positioned at the ostium of the ECA, and a microcatheter is navigated up through the internal maxillary artery (IMA) into the sphenopalatine artery (SPA). Distal branches of the IMA typically account for the dominant supply of blood to the nasal cavity [8]. Several embolic agents can be used at this point including a suspension of polyvinyl alcohol (PVA) particles, trisacryl gelatin microspheres (Embosphere, BioSphere Medical Inc., MA, USA) [9], gelatin sponge plugs (Gelfoam, Pfizer Inc., New York, USA), platinum coils, ethylene-vinyl alcohol copolymer (Onyx, Medtronic Inc., Dublin, Ireland), or *N*-butyl-2-cyanoacrylate (NBCA) glue [3, 8, 10] (Fig. 32.1). Following slow injection of the embolic agent into the vessel, stagnation of anterograde flow should be observed. The contralateral IMA or facial artery (FA) can be embolized as well in cases where concern for collateral blood supply is present. This, however, remains at the discretion of the treating neurointerventionalist. Anterior and posterior nasal packs can be kept in place or removed following embolization, as the current data does not support the use of one regimen over the other.

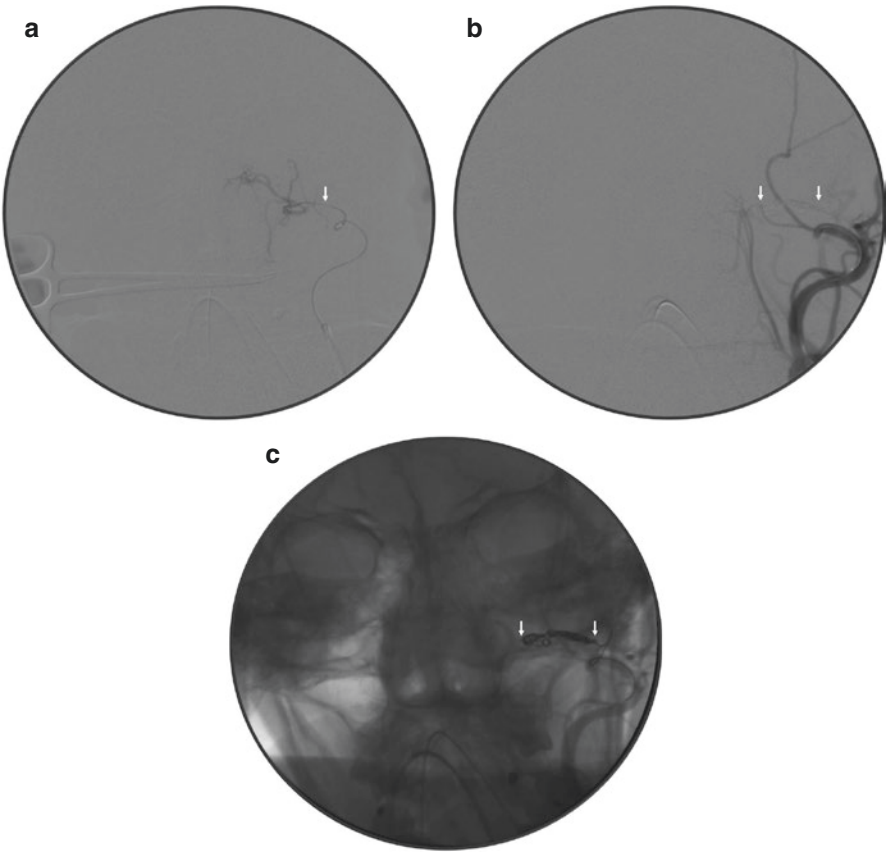

Fig. 32.1 (**a**) Pre embolization lateral superselective angiogram through the microcatheter (*arrow*) of the left IMAX revealing the sphenopalatine branches. (**b**) Post embolization lateral angiogram with coils in occluding the IMAX (*arrows*) resulting in cutoff of distal blood flow to the sphenopalatine branches. (**c**) Note coils (*arrows*) are more conspicuous on unsubtracted view

Under certain cases the exact site of bleeding cannot be identified, and in these circumstances there must be coordination with ENT to remove the nasal packing, while the patient remains on the table, and the diagnostic cerebral angiogram is repeated (Fig. 32.2).

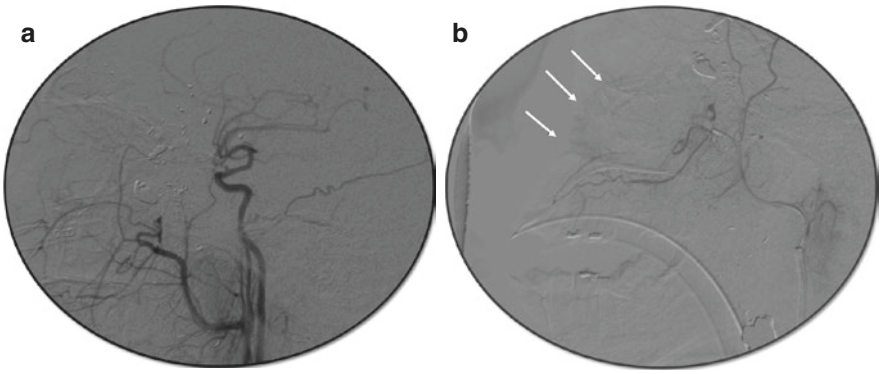

Fig. 32.2 (**a**) Lateral view angiograms of the right ECA in patient with traumatic epistaxis secondary to gunshot wound showing no active contrast extravasation with nasal packing in place. (**b**) Super-selective angiogram with microcatheter placed in the distal IMAX after removal of nasal packing. The arterial phase blush suggestive of extravasation (*white arrows*) is more clearly seen

Complications Related to Epistaxis Embolization

Complication Statistics and Clinical Outcomes

The use of embolization for the management of intractable epistaxis has been associated with an immediate success rate between 93 and 100%. However, data from retrospective analyses which consider early rebleeding have cited lower success rates between 71 and 89.2% [7, 11–14]. Clinical success rates are also dependent on the number of vessels embolized during the procedure. At the discretion of the treating neurointerventionalist, combinations of vessels that are routinely embolized include the unilateral IMA, the bilateral IMA, the IMA and the unilateral facial artery (FA), or the IMA and the bilateral FA [3]. Gottumukkala et al. reported a statistically significant, inverse correlation between the number of vessels embolized and the incidence of rebleeds as well as minor complications [15]. Fukutsuji et al. reported similar findings in a cohort of 22 patients [16].

Complication Rates and Trends

Complications associated with this procedure are typically characterized as minor (transient), major, or persistent and are observed in up to 59, 1, and 2% of cases, respectively [7, 11–13]. Minor complications can include headaches, claudication, paresthesias, and facial numbness. Headaches have been reported more commonly in patients in whom two or more arteries were embolized with Gelfoam [14]. Major complications include mucosal necrosis, transient hemiparesis, and visual field deficits. Cerebral infarction and cranial neuropathies including facial nerve paralysis are examples of persistent complications [7]. Soft tissue necrosis has been associated with the use of liquid embolic agents and embolization of more than one vessel within the same procedure [17].

Complication Avoidance: Pitfalls and Pearls

Avoidance of complications during embolization for intractable epistaxis is centered around a comprehensive understanding of a patient's unique vascular anatomy and supply to the nasal cavity. This includes identifying dangerous anastomoses between the ECA and ICA, ECA and vertebral artery, as well as identifying the predominant arterial feeders contributing to the area of extravasation or abnormal blush which would need to be embolized to prevent rebleeding from occurring. In patients with ECA-ICA anastomoses, surgical ligation may be indicated, and however more recently these cases have been managed using an endovascular approach by deploying coils proximal to the site of anastomosis to prevent the embolization particles or material into reaching the intracranial circulation. This should be discussed by the neurosurgeon or neurointerventionalist on a case-by-case basis. If embolization is performed, the embolic agent should be injected slowly to prevent reflux of the agent through the anastomoses. In the event that arterial vasospasm is detected, intra-arterial vasodilators can be administered to prevent retrograde migration of the embolic agent through these anastomoses as well. Diagnostic angiography performed prior to embolization is essential for detecting potentially treatable vascular anomalies in the context of non-idiopathic epistaxis.

Additionally, a full blood count, platelet count, and panel of coagulation tests including prothrombin time (PT)/international normalized ratio (INR) and partial thromboplastin time (PTT) should be obtained for each patient prior to embolization. These are necessary to identify patients with congenital bleeding disorders or coagulopathies who may be at an increased risk of developing intraprocedural or post-procedural thrombi. In these patients, prophylactic measures such as intravenous (IV) heparin administration prior to endovascular intervention are generally contraindicated due to the increased risk of hemorrhagic complications. As a result, these patients have an increased risk of developing intraprocedural or post-procedural thrombi. If left undiagnosed, thrombi can migrate into the anterior circulation resulting in a cerebral infarction or into the ophthalmic artery leading to visual field deficits and/or unilateral blindness.

To prevent intraprocedural vessel perforation and subsequent hemorrhage, care must be taken to detect and reduce excess load within the system. Additionally, the microwire should be extruded more than 5 mm from the microcatheter at all times prior to navigation within the intracranial vessels. Finally, the treating neurointerventionalist should ensure that all load on the system is removed prior to coiling and/or prior to deposition of the embolic agent.

Complication Management and Prevention

Vascular Supply to the Nasal Cavity and EC-IC Anastomoses

Arterial branches off of the ECA including the IMA and the FA provide a significant fraction of the total blood flow to the nasal fossa. The SPA and greater palatine arteries (GPA), both of which are derived from the IMA, supply the posterior nasal

cavity and the inferior portion of the nasal septum, respectively [3]. The superior labial artery, a branch of the FA, supplies the anteroinferior nasal cavity. The anterior and posterior ethmoidal arteries, which are derived from the ophthalmic arteries and, by extension, the ICA, supply the roof of the nasal cavity [18].

Several anatomic variants with anastomoses between these different vessels exist. For example, the ethmoidal arteries can anastomose with branches of the SPA in the posterior nasal cavity. The middle meningeal, accessory meningeal, and ascending pharyngeal arteries, which are small vessels derived from the IMA, can be sources of potential anastomoses between the ICA and the ECA [7]. In other cases, connections between the FA, SPA, and ophthalmic arteries exist. In a small subset of patients, blood supply to the ophthalmic artery can originate from the ECA in which case surgical ligation and/or cauterization should be considered prior to embolization to prevent occlusion of the retinal and posterior ciliary arteries [2]. Identification of the anastomoses in each of these scenarios during pre-procedural diagnostic angiography is *essential*. If the decision is made to proceed with embolization, and EC-IC anastomoses are present, embolic agents other than microparticles should be considered to prevent complications resulting from particle migration and occlusion of blood vessels within the intracranial circulation [19]. An alternative approach to prevent the embolization particles or material from reaching the intracranial circulation is to deploy coils proximal to the site of EC-IC anastomosis site.

Intraprocedural Thrombosis

Thromboembolic complications are believed to account for a majority of clinically relevant periprocedural complications during neuroendovascular procedures and can lead to visual deficits and/or cerebral infarctions [20]. In the setting of embolization for intractable epistaxis, the risk for thrombus formation is increased when embolization is performed using platinum coils as these provide a metal interface for thrombus formation. This effect may be exaggerated due to the more judicious use of intravenous heparinization in the setting of epistaxis. Other potential sources of thrombi include the in situ formation of thrombi or dislodgement of preexisting thrombi during endovascular manipulation [21]. Additionally, endothelial injury sustained during the procedure can induce formation of a prothrombotic or hypercoagulable state.

While initial management of acute thrombus formation typically consists of an increase in the dose of heparin delivered intravenously, newer treatment regimen incorporates intravenous and intra-arterial delivery of fibrinolytic agents (such as tissue plasminogen activator) and platelet glycoprotein (GP) IIb/IIIa inhibitors, respectively [22]. Systemic delivery of fibrinolytic agents, however, has been associated with an increased rate of complications, poorer clinical outcomes, and an increased risk of catastrophic hemorrhage [20, 22]. Platelet GP IIb/IIIa inhibitors, including abciximab (ReoPro), eptifibatide (Integrilin), and tirofiban (Aggrastat), are a relatively newer class of antiplatelet drugs which function by binding to and inhibiting receptors necessary for platelet aggregation and subsequent thrombus formation. In comparison to fibrinolytic therapies, the use of these antiplatelet

agents is believed to be generally safer for the management of acute intraprocedural thrombosis, particularly in the context of stent-assisted coiling or pipeline embolization device placement [22, 23]. Intra-arterial administration of these agents permits lower doses to be injected to localized regions within the intracranial or extracranial vasculature and is preferred over intravenous delivery.

Management of acute intraprocedural thrombosis during endovascular embolization of intractable epistaxis can include administration of a combination of these antiplatelet agents, heparin, and thrombolytic drugs. In patients with underlying coagulopathies in whom anticoagulant therapy is contraindicated, the risks and benefits of endovascular therapy must be clearly delineated on a patient-by-patient basis.

Conclusion

Endovascular embolization is routinely performed for the management of intractable epistaxis. However, the prevention and management of procedural complications is centered around a detailed understanding of an individual patient's vascular supply to the nasal cavity. Identification of vascular anomalies and potential sources of bleeding on pre-interventional diagnostic angiography is imperative. If anastomoses are detected between the ECA and the ICA, the use of microparticle-based embolic agents should be minimized to prevent distal migration of these particles and resulting ischemic complications. In patients in whom blood supply to the ophthalmic artery originates from the ECA, surgical management may be indicated. Multi-vessel embolization has been found to be associated with a lowered rate of rebleeding and should be considered in the context of epistaxis embolization. Slow injection of the embolic agent is essential for the prevention of reflux, which is particularly dangerous in patients with dangerous anastomoses. Finally, in the setting of acute intraprocedural thrombosis, newer antiplatelet agents can be delivered intra-arterially for the management of these patients.

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Sclerotherapy of Vascular Malformations

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Checklist: Sclerotherapy for Vascular Malformations (One of Two—Pre-procedure)

Equipment needed	Procedural steps
Radiology technicians • Ultrasound equipment available • 21-G or 23-G butterfly needles • 20-G or 22-G needles • Short connecting tubing • Contrast of choice (ionic) • Proper lighting is imperative at skin Nursing • Sclerosing agent of choice • Note: Bleomycin use requires tape/adhesive precautions (hyperpigmentation risk) • Note and record *maximum* dose allowed and amount used • Staff pager numbers – Ophthalmology (orbital lesions) – ENT (lesions of the pharynx and tongue) Anesthesia • General anesthesia • Monitor airway pressures (EtOH- induced pulmonary hypertension) Neurointerventionalist • Proper lighting	Prep • Sterile prep and drape Procedure • Ultrasound guidance or palpation • Identify "flash" of blood in butterfly • Confirm compartment with contrast under subtraction • Inject agent • Assess for blanching of skin • Compress venous outflow • Keep needle *in situ* for 1–2 min before removing Monitor • Electrophysiology for facial nerve • Pulmonary hypertension assessment • When using ethanol, note careful quantity administered to avoid intoxication

Checklist: Sclerotherapy for Vascular Malformations (Two of Two—Skin/Soft Tissue Injury)

Equipment needed	Procedural steps
Radiology technicians • Bacitracin ointment Nursing • Vital signs • Consider pain medication • Dry sterile dressing with minimal adhesives • Staff pager numbers – Plastic surgery – ENT Anesthesia • Pain management Neurointerventionalist • Sterile dressings	Identification • Recognized blanching of the skin Procedure • Immediately stop injecting agent • Do not remove needle as this will track ethanol or other agent through the skin and increase necrosis • Monitor electrophysiology (if being used) • Anesthesia: monitor for evidence of pain Post-procedure • Apply antibiotic ointment and dressing • Consider plastic surgery consult

Complication Avoidance Flowchart

Complication	Treatment	How to avoid
Mild to moderate pain and edema	Pain meds and steroids	Common and expected posttreatment side effect
Severe pain and edema—potential airway compromise or outflow obstruction, intraorbital lesions	Pain meds, IV steroids, airway maintenance, elevate head of bed; if airway/orbit at risk, ICU monitoring for 48 h and supportive care, ENT/plastics/ophthalmology consult as needed	Don't overdo; choose less aggressive agents (bleomycin); consult ENT/plastics/ophthalmology for lesions involving or close to airway/orbit
Skin and soft tissue minor injury (skin blistering)	Simple dressing, ointment	Making sure of intravascular position of tip of the needle before injecting the agent; don't overdo
Skin and soft tissue extensive and/or deep injury (necrosis, ulceration)	Wound care, antibiotic ointment, occasionally topical collagenase or superficial debridement, and in extreme cases complex reconstructive plastic surgery	Making sure of intravascular position of tip of the needle before injecting the agent; don't overdo
Nerve injury, neuropathy	Expectant and supportive management, gabapentin (?) and duloxetine (?), possibly in severe cases	Making sure of intravascular position of tip of the needle before injecting the agent; don't overdo; facial nerve monitoring
Ethanol intoxication, pulmonary hypertension, seizures, and cardiopulmonary arrest	Supportive care, ICU management	Limit the amount of the agent (ethanol) per session
Localized intravascular coagulopathy (LIC)—usually very large and extensive venous malformations	Low molecular weight heparin, hematology consult	Pre-op labs: D-dimer (abnormally elevated) and fibrinogen (abnormally low); hematology consult
Venous thrombosis in case of sclerosing agent reaching deep venous system	Anticoagulation	Don't overdo; limit the amount of sclerosing agent; compress outflow vein when injecting the sclerosing agent
Hemoglobinuria	Simple IV hydration, but occasionally with adjunctive urine alkalinization, or IV furosemide; watch for signs of acute renal injury	Don't overdo; limit the amount of sclerosing agent

Introduction

Advances in interventional techniques have revolutionized the treatment of congenital vascular malformations of all types. Traditional open surgical extirpation of these lesions carries the very real risks of excessive blood loss, incomplete excision of the lesions—often resulting in recurrent pathology—wound-healing complications, and frequently suboptimal aesthetic outcomes. While surgery is still indicated in some cases, interventional treatments have far and away become the first-line

approach in a nearly universal paradigm shift toward less invasive techniques that also typically result in diminished associated morbidity.

The two main groups of vascular malformations—low-flow lesions and high-flow lesions—each carry distinctive risk profiles with regard to the basic pathophysiology of the lesions, as well as how the lesions are approached for treatment and more specifically to the complications associated with the various endovascular treatment protocols currently in use. In other words, a low-flow vascular malformation that is treated with direct percutaneous approach using a sclerosing agent has different risks than a high-flow lesion that is approached via transarterial route using liquid embolic or sclerosing agents. As such, they should be considered separately.

Procedural Overview

- Prep and drape the area for percutaneous approach in a sterile fashion
- Anesthesia support (for either MAC or GA)
- Have ultrasound equipment available
- Make sure you have the sclerosing agent of choice available
- If using bleomycin, tape/adhesive precautions are necessary due to the risk of hyperpigmentation
- Be aware of maximum amount limit per session of some sclerosing agents
- Depending on the type of lesion: butterfly needles 21- or 23-G
- Depending on the type of lesion: 20- or 22-G
- Short connecting tubing
- The checklist for high-flow lesions should respect also all the requirements for usual transarterial and/or transvenous catheter techniques
- If the lesion is close to the airway, have ENT/plastics on standby in case airway is compromised
- If the lesion is intraorbital, have ophthalmology on standby in case decompression is needed

Low-Flow Vascular Malformations

When approaching venous and lymphatic malformations, in an attempt to minimize the complications of treatment, it is important to consider the angioarchitecture of the lesion prior to intervention. Since no arterial inflow is present, the use of catheter angiography for diagnosis (or treatment) is ineffective and thus unnecessary. MRI with contrast is currently the imaging technique of choice in these cases due to its incomparable soft tissue visualization, allowing for accurate definition of the location and extent of the lesion, and its relationship with important adjacent structures such as nerves, orbits, and the airway. MRI often unveils lesions that are much larger than the clinical exam suggests and is particularly important in the planning of craniofacial and head and neck lesions because of the aforementioned reasons [1]. Detailed knowledge of the anatomy of the lesion allows the clinician to account for peculiarities of flow and intimate association with vital structures, thereby

potentially preventing disastrous unintended results from errant infiltration, local tissue swelling and necrosis, or systemic side effects.

As treatment of low-flow lesions is typically accomplished through direct puncture and injection of a sclerosing or embolic agent, selection of the appropriate agent must be carefully considered when attempting to effectively minimize the complications of intervention. Each carries its own set of associated risks, and since the agents used to treat low-flow vascular malformations differ slightly between venous and lymphatic malformations, they should be discussed separately.

Direct puncture is the approach of choice for low-flow lesions but can also be very helpful and successfully used in high-flow lesions. When treating superficial venous or arteriovenous malformations, we usually prefer to use butterfly needles (21- or 23-G). Blood return through the butterfly tubing needle indicates intravascular position. The system is flushed with saline, and then gentle contrast injection using a 1 mL syringe is performed to confirm position of the needle. For small lymphatic malformations, we prefer a small angiocath to decrease the risk of traversing the cyst during aspiration (which may occur using a butterfly needle due to its sharp tip). A small amount of contrast is then administered to fill the cyst(s). At any time, if contrast extravasation is noted, the needle/angiocath needs to be repositioned and the steps above repeated. Please see further technical aspects and agents specific to each type of lesion below.

Venous Malformations

The procedure is done in the angiography suite, and the lesion is accessed with direct puncture under ultrasound guidance. After slow venous return is seen through the needle, venography is performed to verify correct placement of the needle, and confirm the absence of extravasation into surrounding soft tissues, or drainage into the adjacent venous system.

If fast drainage is seen into important regional veins that cannot be protected with direct pressure, sclerotherapy should be performed very carefully, and in such cases, placement of a transvenous occlusion balloon and closure of the communication with coils can be performed to help minimize unintended local or systemic morbidity.

Regarding the choice of sclerosing agents, the most commonly used in the USA are ethanol, bleomycin, and sodium tetradecyl sulfate (STS). Ethanol is widely used and is highly effective but carries a greater risk of complications. Most commonly complications are relatively minor and transient and include swelling, skin blistering, and peripheral nerve injury. Posttreatment edema is essentially an accepted side effect, occurring in over 50% of patients in multiple large series (Fig. 33.1) [2]. In most patients, this can be minimized by treatment with IV corticosteroids at the time of the intervention and frequently a tapered oral dosing regimen once discharged [3]. Swelling can occasionally become a more serious issue when dealing with craniofacial lesions adjacent to vital structures, putting the patient at risk for airway compromise or venous outflow obstruction. These scenarios should be managed attentively with ICU monitoring and supportive care—maintenance of the

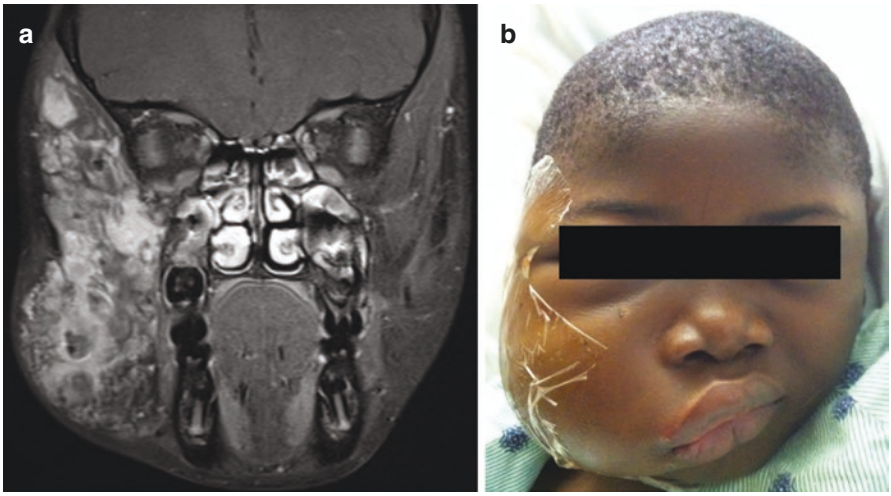

Fig. 33.1 A patient with an extensive right craniofacial venous malformation (**a**) who underwent five sessions of percutaneous sclerotherapy to achieve a good cosmetic/functional result. After the fourth session, the patient developed extensive swelling of the right side of the face (**b**) that was treated with steroids and pain management resolving completely after 4 days

airway, elevation of the head of the bed, and corticosteroids. Likewise, in the extremities, there is the rare risk of developing a compartment syndrome. In these cases, elevation of the affected extremity is given, but time is of the essence, and the slightest suspicion of a developing compartment syndrome should trigger a surgical consultation and may result in the need for fasciotomy.

Skin and soft tissue injury is also a relatively common complication of intervention with ethanol [4]. The typical presentation is of relatively minor skin blistering, especially when dealing with lesions that are particularly superficial in the skin. Most of these cases heal quickly and without additional complications with simple dressings or even no treatment at all. At times, the damage can be more extensive, and there can be necrosis of the skin and subcutaneous tissue, resulting in more extensive ulceration or deeper wounds (12–28% incidence) [4]. Again, the vast majority of these cases are minor and will heal with basic local wound care—daily dressing changes and antibiotic ointment. Occasionally topical collagenase or superficial debridement may also be necessary. Rarely, there may be extensive necrosis of adjacent soft tissue with substantial consequences. Treatment of these patients can require extensive debridement of devitalized tissue and complex reconstructive procedures, and plastic surgery consultation is indicated in order to minimize functional and aesthetic morbidity [4].

Adjacent deeper structures can also be affected by intervention. Nerve injuries—from peroneal nerve weakness to facial nerve paresis and vocal cord paralysis—can occur in up to 10% of patients, but these are usually transient and self-resolving [2, 4]. Permanent nerve injury is rare but has been reported [2, 4]. Unfortunately, expectant management is the mainstay for these patients. Neuropathy is mostly associated with the use of ethanol, as opposed to STS or Onyx [2, 4].

When treating venous lesions, the clinician must also be vigilant to the possibility of a resulting venous thrombosis (VT). This can occur when small communicating veins are present between a malformation that is adjacent to the deep venous system. If there is drainage of the sclerosing agent through the communicating vessels, a VT may occur [4]. This can have significant consequences and morbidity, including pulmonary embolism and death. The standard treatment in these patients is immediate anticoagulation with a low molecular weight heparin, with transition to long-term anticoagulation using an oral agent such as warfarin or rivaroxaban for 6 months [4].

Systemic complications are also possible and must be accounted for in these patients. Hemoglobinuria is common (up to 2/3 of all patients), mostly transient, and managed in most cases with simple IV hydration but occasionally with adjunctive urine alkalinization or IV furosemide as well [2–4]. Rhabdomyolysis can occur with intramuscular lesions, and patients must be monitored closely for signs of acute kidney injury. Again, these patients are managed with IV hydration and nephrology consultation as needed. Acute ethanol intoxication is a concern mostly in pediatric patients who are both smaller in body mass and typically naïve to ethanol consumption. Nevertheless, this complication can usually be prevented by careful dosing of the agent, and, in the event of intoxication, supportive care [3]. More serious systemic issues are extremely rare but can include pulmonary hypertension, seizures, and cardiopulmonary arrest [2–4].

In considering alternative sclerosing agents, bleomycin has been shown to provide good results and has an excellent safety profile [5–7]. Relative to ethanol, there are considerably less associated complications and post-procedural swelling—and most tend to be transient and minor [5–7]. Sodium tetradecyl sulfate (STS) has also been used extensively with good results [7–9]. And studies have demonstrated an incidence of approximately 10% for minor transient complications and almost no major complications [7–9].

Special consideration must be given when treating lesions located in the orbit or airway, since marked swelling from sclerotherapy may cause compartment syndrome or compromise the airway. In these cases, it is prudent to consider a sclerosing agent that will cause less swelling, such as bleomycin. Another option for these cases is preoperative embolization using liquid embolic agents like n-BCA (Codman), Onyx (Medtronic), or Phil (Microvention). These embolic agents cause minimal or mild swelling and can facilitate more complete surgical excision of localized lesion [10].

Another clinical scenario that requires special attention is the treatment of patients with large, extensive, or multifocal venous malformations. The physiology of these lesions predisposes the patient to a form of localized intravascular coagulopathy (LIC) that is frequently chronic in nature. Under the circumstances of sclerotherapy or surgical intervention, LIC can acutely progress to disseminated intravascular coagulopathy (DIC), a disastrous and potentially fatal consequence of treatment [11–13]. It is essential that these patients be identified prior to intervention through clinical history and exam, as well as obtaining lab values for D-dimer (which is generally abnormally elevated) and fibrinogen (which is generally abnormally low). It is recommended that these patients receive pre-procedural LMWH for 10 days, which is continued posttreatment for 10 days as well [11–13]. A hematology consult may also be warranted.

Lymphatic Malformations

Lymphatic malformations are divided into macrocystic, microcystic, and combined lesions. Similar to venous lesions, interventional treatment is performed through direct puncture of the lesion under ultrasound guidance. After the catheter is in good position, the lymphatic malformation is completely aspirated, and the sclerosing agent is then administered slowly through the catheter to approximately 80–90% of the aspirated volume. In larger lesions, the sclerosing agent is allowed to dwell for 2–6 h, and depending on the size of the lesion, the procedure can be repeated every day for several days.

Several agents are currently used in the treatment of lymphatic malformations, including ethanol, STS, doxycycline, bleomycin, and OK-432. Currently, the preferred agents are doxycycline and bleomycin due to their excellent results with macrocystic lesions and preferred safety profile.

Doxycycline is an effective agent for lymphatic malformations, with an excellent safety profile. Complications are infrequent (0–10% incidence) and minor, involving local soft tissue swelling, blistering, or localized alopecia, and resolve with minimal treatment [14, 15]. Major complications are rare, but there are incidents reported of significant transient neuropathy [15]. Microcystic lesions also appear to be associated with a higher rate of complications relative to macrocystic or mixed lesions, and increasing doses of doxycycline are associated with an increased risk of complications [14].

In one large series, bleomycin has been reportedly associated with posttreatment deaths from pulmonary complications, though certain etiology in these cases was unclear. Patients have also required emergent intubation for airway compromise, emergent tracheostomy, and orbital decompression after treatment of craniofacial lesions with OK-42, demonstrating once again that craniofacial lesions deserve special consideration, and may be associated with a more difficult posttreatment course. Minor issues with this agent included fever, erythema, and local pain [16].

High-Flow Vascular Malformations

High-flow vascular malformations (HFVM) pose a very difficult therapeutic challenge. They are locally aggressive lesions that can present in several different ways, from being completely asymptomatic lesions to significant bleeding, pain, neuropathy, or congestive heart failure [17–27]. Diagnosis is made based on clinical history and confirmed with ultrasound, Doppler, MRI, and contrast-enhanced MRA [19, 20]. Catheter angiography is still considered the gold standard in the evaluation and treatment planning of these lesions since it provides, with great spatial and temporal resolution, detailed information of the angioarchitecture [18]. Several therapeutic strategies have been employed, including surgery, embolization, or a combination of both [17–27]. Unfortunately, curative treatment is frequently not possible, and control of symptoms is often the aim of treatment. As such, the avoidance of treatment-related morbidity is a significant concern.

For high-flow vascular malformations, transarterial, transvenous, and direct access can be used. Whenever possible, the goal of interventional treatment should be complete occlusion of the nidus or fistulous connections. In cases where

transarterial access can be used, the microcatheter should be advanced to a location as close to the nidus/fistulous connections as possible. As with low-flow lesions, it is important to understand the angioarchitecture of the lesion—including the presence of supply to normal tissue, venous drainage, and transit time, as well as reflux into the feeding arteries. If supply to normal tissue is observed, embolization at that location should be avoided if possible to diminish the risk of tissue necrosis. In cases where the transarterial route cannot be used due to severe tortuosity or proximal occlusion from prior embolization or surgical procedures, direct puncture or venous approach can be performed. Because of the extensive collateral supply that develops to feed head and neck and craniofacial HFVMs, it is imperative that the operator be aware of potential dangerous anastomosis between the external carotid branches and the ophthalmic, internal carotid and vertebral arteries, since unwanted embolization of these territories will result in catastrophic outcomes (Fig. 33.2). The operator should also have clear understanding of the external carotid supply to the cranial nerves to avoid neuropathy or loss of function due to embolization. Particular to the transarterial access, there are complications that are not encountered on direct percutaneous access including access site complications (hematoma, pseudoaneurysm, retroperitoneal hemorrhage, fistula, occlusion, dissection), renal failure, arterial/vascular complications (dissection, perforation, occlusion, vasospasm), and stroke.

Selection of embolic agents for the treatment of HFVM, again, plays a role in potential complications and morbidity. Coils, ethanol, n-BCA, and Onyx have all been used successfully to treat high-flow lesions, and it is important to understand the technical particulars of each agent, which have been described elsewhere [17–27]. As with venous lesions, ethanol seems to be associated with the highest rate of cure and permanent occlusion, even in extensive lesions. Likewise,

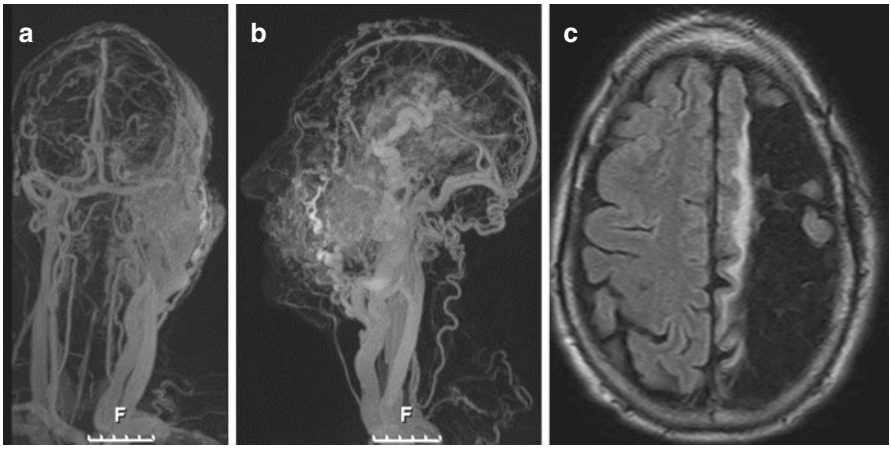

Fig. 33.2 A patient with a long-standing extensive left craniofacial HFVM (**a** and **b**) who underwent several treatments, both endovascular and surgical, throughout his life. During endovascular transarterial treatment in the 1980s, the patient suffered unwanted embolization of his left MCA territory (resulting in a large left MCA infarct—**c**) sustaining significant permanent neurological deficits which persist to this day

it is also associated with a higher risk of complications in HFVMs, encompassing a similar range of findings, including minor issues such as skin blistering and neuropathy and in extreme cases cardiopulmonary collapse and death [17–20, 22, 24, 25].

Similar to the treatment of venous malformations with ethanol, patients frequently experience posttreatment swelling, which can last for several days [22]. Again, this is treated initially with IV corticosteroids, followed by a tapered dose of oral corticosteroids. Skin blistering and minor cutaneous or mucosal necrosis are also relatively common in the treatment of HFVMs with ethanol, seen in 14–37% of cases [17, 18, 22, 28]. Most of these issues resolve quickly with simple dressing changes, though some patients may require a plastic surgery procedure to promote healing or a short course of antibiotics if an infection develops [22, 28].

Deeper tissue can be affected, and at times minor muscle necrosis may occur. Again, these wounds typically heal with minimal treatment and consequence, depending on the anatomy involved [22]. Peripheral neuropathy—either sensory or motor—is relatively common, though it is also usually minor and transient [17].

Hemoglobinuria is common with ethanol (up to 30%) and, as previously described, treated with alkalinization of the urine, IV hydration, and/or IV furosemide, depending on the judgment of the clinician [17]. Systemic ethanol toxicity can be more of a concern when treating facial HFVMs, especially in children (as noted previously), since the posttreatment blood levels seem to be higher with these lesions in particular, possibly due to the inherent difficulty in achieving adequate venous occlusion in the head and neck [6].

Major complications are uncommon (less than 5%) but can include permanent nerve injury, acute kidney failure due to rhabdomyolysis, and severe infection due to tissue necrosis that can result in significant aesthetic and functional morbidity [17].

Other embolic agents like n-BCA and Onyx have been successfully used in the management of HFVMs alone or in combination with surgery [21, 26, 27]. These embolic agents are effective in controlling symptomatic lesions (such as hemorrhage), and their safety profiles are generally more favorable compared to ethanol. For example, Onyx has only a 0–3% incidence of minor skin ulceration in one series and in some series a 0% incidence of more serious complications [21, 27, 29]. One of the concerns with liquid embolic agents is that, because Onyx and n-BCA are foreign bodies, if an ulceration develops and the embolic agent is exposed, despite appropriate wound care and antibiotic therapy, it may take several months for the ulcer to heal, and it usually happens only after the exposed agent is totally expelled (Fig. 33.3) [29]. Onyx is also an excellent option for high-flow craniofacial lesions because of the lesser degree of posttreatment swelling observed in these areas adjacent to the airway and other vital structures [21, 29, 27].

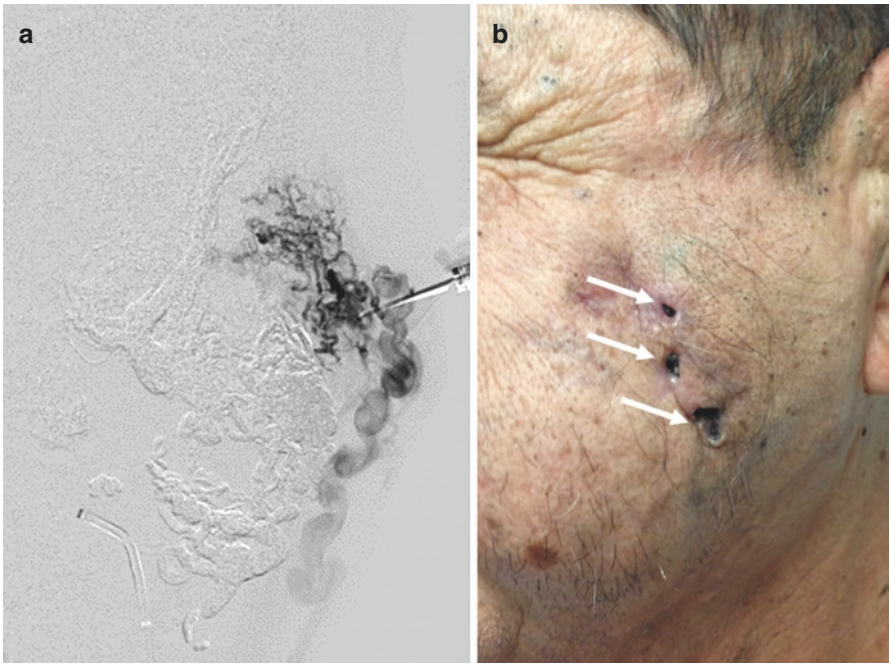

Fig. 33.3 A patient with left craniofacial HFVM who presented with hemorrhage and was treated with sessions of transarterial, transvenous, and direct access using liquid embolic agent (Onyx). After a session where direct puncture was used to inject the embolic agent, (**a**) the patient developed three small areas of ulceration 1 month after the procedure (*arrows*—**b**). Note the exposed embolic material. These ulcerations were treated with wound care, antibiotic ointment, and transcutaneous removal of the Onyx with complete healing after 4 months

Conclusions

1. Prevention is key. Pre-procedural due diligence and detailed knowledge of the angioarchitecture of these lesions can allow the clinician to create a detailed and customized approach to each case that can avoid unexpected and potentially disastrous complications.
2. Selection of the sclerosing agent plays a significant role in potential complications. Ethanol may achieve a higher rate of cure but also poses a greater risk for local and systemic morbidity and should be used only by operators that are experienced with the use of this agent.
3. Most cutaneous complications that may result are minor and will resolve with simple local wound care.
4. Major tissue necrosis, though rare, may require substantial reconstructive procedures and should be treated by a plastic surgeon.

5. Lesions of the craniofacial region are associated with some measure of increased risk due to the intimate relation to the airway and other vital structures and the difficulty in controlling outflow. Supportive measures should be in place to treat impending airway compromise.
6. Awareness of potential dangerous anastomosis between the external carotid branches and the ophthalmic, internal carotid and vertebral arteries is critical since unwanted embolization of these territories will result in catastrophic outcome (blindness, stroke, or even death). The operator should also have clear understanding of the external carotid supply to the cranial nerves to avoid neuropathy or loss of function due to embolization. Systemic complications are a very real risk (mostly with ethanol) and in some cases relatively common depending on the extent of the lesion. These issues—ethanol toxicity and hemoglobinuria—should be treated appropriately as they arise.

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Part IV

Radiosurgical Procedures

Radiation Physics: Stereotactic Radiosurgery for Arteriovenous Malformations

34

Krishna Amuluru and Christopher G. Filippi

Introduction

Cerebral arteriovenous malformations (AVM) are collections and anastomoses of arterial and venous vasculature. Left untreated, AVMs possess an annual rupture rate of 3–5%, with higher rates of bleeding in AVMs that have previously ruptured or contain intranidal aneurysms [1, 2]. In AVMs without a history of hemorrhage, the annual risk is slightly lower at 2%; however after a sentinel bleed, the annual risk of bleed increases to nearly 18% [1, 3]. The combination of an early age of presentation and the estimated annual risk of hemorrhage lends to a high lifetime risk of morbidity from untreated AVMs [4]. Accordingly, the traditional management of AVMs has been aggressive intervention.

The treatment of cerebral AVMs requires a multidisciplinary approach that includes microsurgery, endovascular embolization, stereotactic radiosurgery (SRS), and/or a combination thereof [5]. Surgical resection remains the gold standard for the definitive eradication of the majority of these lesions. However, many AVMs are not amenable to surgical resection because of the morbidity related to their deep or critical brain locations [6]. For these particular lesions, recent advances in both endovascular techniques and SRS have allowed new treatment strategies, potentially with enhanced efficacy and improved outcomes.

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In this chapter, we explore the role of SRS, its indications, and predictors of success and failure. We focus on the avoidance and management of the complications of SRS including treatment failure, hemorrhage after treatment, and radiation-induced necrosis, for which detailed knowledge of the technical nuances of SRS is required.

Procedural Overview

Stereotactic radiosurgery is the term coined by Lars Leksell to describe the application of a single, high dose of radiation to a stereotactically defined target volume, such as an AVM [7, 8]. When an AVM is treated with radiosurgery, radiation injury to the nidus leads to progressive thrombosis and obliteration, thereby eliminating the risk of hemorrhage resulting in a durable cure [7].

Compared to microsurgical and endovascular treatments, SRS is advantageous due to its noninvasive nature, its minimal risk of acute complications, and the fact that it can be performed as an outpatient procedure requiring no recovery time for the patient [7]. The primary disadvantage of radiosurgery is that cure is not immediate, and thus an interval period of approximately 24–36 months exists during which the risk of hemorrhage remains [1, 9]. As a result, radiosurgery is not typically used in AVMs that present with hemorrhage [10]. Other disadvantages of radiosurgery are potential long-term adverse effects of radiation exposure.

Techniques of SRS

A number of different SRS technologies have been developed to achieve AVM obliteration, including Gamma Knife, linear accelerators (e.g., CyberKnife, Synergy S, and Trilogy), and particle beam [7].

The Gamma Knife is a dedicated radiosurgery machine, invented by Lars Leksell and his colleagues in 1968, in Sweden. Current Gamma Knife equipment contains 192 cobalt-60 sources, held in a hemispherical array, each of which emits high-energy photons (gamma rays). Each source creates an independent beam path, all of which coincide at the target, delivering a high dose of radiation. Every individual beam path has a small dose, thus creating a steep dose gradient with little risk to normal tissue [7].

The adapted linear accelerator (LINAC) was pioneered by Osvaldo Betti and is a device that uses microwave energy to accelerate electrons to very high speeds [7, 11]. The electrons collide with a heavy metal alloy in the head of the machine. The majority of the collision energy is lost as heat, but a small percentage results in high-energy photon radiation. These photons are virtually identical to those produced by the spontaneous decay of radioactive cobalt in the Gamma Knife. They are collimated and focused on the radiosurgical target. By rotating the gantry of the LINAC in different angles, a set of multiple convergent noncoplanar wide arcs is obtained [7].

Particle beam, such as proton beam, therapy uses a synchrotron to accelerate protons to interact with the target tissue. Proton beam therapy is often distinguished

from the Gamma Knife and LINAC by the use of protons, which have more mass [1]. Because of a unique physical property called the Bragg peak effect, this results in a steep radiation dose falloff allowing for the use of higher doses deposited at a predictable depth, thus minimizing damage to neighboring tissue [7].

Although several different stereotactic radiosurgery technologies exist, studies have suggested that the quality of Gamma Knife and LINACs as well as the efficacy, outcomes, and complications of the technologies are essentially similar [1, 12, 13].

Dose Planning

Dose planning involves dose optimization to improve efficacy while minimizing radiation damage to surrounding tissue. Every neurological location has its own radiation dose tolerance threshold that must be taken into account for dose selection. Treatment of non-eloquent locations may allow for larger doses, but this can also lead to an increased risk of radiation damage. Stereotactic and volumetric axial plane imaging in conjunction with digital subtraction angiography is needed to obtain a complete conformal dose plan [6]. Magnetic resonance imaging with digital subtraction angiography remains the gold standard by which a true conformal dose plan can be formulated to optimize safety and to increase the chance of obliteration [14, 15].

Doses at the margin of an AVM typically vary from 16 to 25 Gy in a single procedure, and obliteration rates tend to improve when the marginal dose equals or exceeds 17 Gy [6]. The margin dose should be anywhere from 50 to 80% of the delivered dose at the center of the target to protect adjacent parenchyma and to achieve satisfactory obliteration rates [16].

Newer imaging modalities such as blood-oxygen-level-dependent functional magnetic resonance imaging (BOLD-fMRI) and diffusion tensor imaging (DTI) have recently been implemented in modern neuronavigation systems to identify the primary motor cortices and corticospinal tracts during treatment planning for high-grade gliomas [17]. There are a limited number of studies that have used DTI and diffusion tensor-derived tractography along with BOLD to identify eloquent cortex and critically important white matter pathways in planning optimal treatment strategies in patients, including children, with arteriovenous malformations, who are undergoing stereotactic radiosurgery [18–21]. More robust research studies are needed to demonstrate the utility and benefit of functional MRI and DTI as quantitative metrics for routine treatment planning for radiosurgery.

Patient Selection

In determining the role of SRS for AVM patients, various scales are used to guide treatment. In unhemorrhaged AVMs, case selection can be guided by a number of AVM grading scales, such as the Spetzler-Martin scale and the modified Spetzler-Martin scale (mSM) (Table 34.1) [22, 23]. Microsurgery remains the gold standard for AVM treatment, and microsurgery is generally recommended for mSM Grades I to IIIA [1].

Table 34.1 AVM grading scales

Spetzler-Martin AVM grading scale						
	Size		Eloquence of adjacent brain		Venous drainage	
Score =	1 (<3 cm) 2 (3–6 cm) 3 (>6 cm)	+	0 (non-eloquent) 1 (sensorimotor, language, or visual cortex; hypothalamus or thalamus; internal capsule; brainstem; cerebellar peduncles or nuclei)	+	0 (superficial only) 1 (deep)	
Modified Spetzler-Martin AVM grading scale)						
	Size		Eloquence of adjacent brain		Venous drainage	Modifier (if grade 3)
Score =	1 (<3 cm) 2 (3–6 cm) 3 (>6 cm)	+	0 (non-eloquent) 1 (sensorimotor, language, or visual cortex; hypothalamus or thalamus; internal capsule; brainstem; cerebellar peduncles or nuclei)	+	0 (superficial only) 1 (deep)	A (>3 cm) B (<3 cm)
Modified Pittsburgh radiosurgery-based AVM grading scale (RBAS)						
	Volume		Age		Location	
Score =	0.1 × volume (cc)	+	0.02 × age (years)	+	0.5 ×	0 (frontal, temporal, parietal, occipital, intraventricular, corpus callosum, cerebellar) 1 (basal ganglia, thalamus, brain stem)

Although the Spetzler-Martin grading system is designed to predict outcome following surgical resection of AVMs, factors critical to successful AVM radiosurgery are not inherent to this grading system, thus limiting its optimal correlation with radiosurgical outcomes [23, 24]. Thus in 2002, a radiosurgery-based scale was developed by the Mayo Clinic and the University of Pittsburgh Medical Center with a purpose to include factors associated with successful single-session radiosurgery, termed the radiosurgery-based AVM scale (RBAS) (Table 34.1) [25, 26].

The RBAS was developed using linear regression modeling based on patients having radiosurgery using stereotactic angiography alone for dose planning and used three factors (patient age, AVM volume, and AVM location) [23, 25]. For these patients, the risk of symptomatic T2-weighted imaging changes varies with location since location determines the maximum dose deliverable to the nidus without clinically significant damage to neighboring structures [26]. The scale was later modified to a simpler, two-tiered description of location (based on deep, e.g., basal ganglia/thalamus/brainstem vs. other site) [26].

Cases scoring <1 on the RBAS have a 90% chance of AVM obliteration without a new neurologic deficit, whereas cases scoring >2 have >50% chance of such an outcome [1]. Since its publication, the RBAS has been shown to correlate with outcomes in pediatric AVM patients, patients with deep AVMs, and patients whose AVMs were treated using LINAC-based radiosurgery [23, 27–29].

Patients with a history of a prior bleed may not be good candidates for SRS, due to the latency period before obliteration [1]. Radiosurgery requires a median of 20 months to achieve subtotal (>95%) obliteration in AVMs, and thus an interval period exists during which the risk of hemorrhage remains [1, 9, 10]. However, sometimes SRS can be an appropriate choice in patients who present with a prior hemorrhage if the risks of microsurgery or observation are also high.

In certain situations, traditional single-dose radiosurgery does not offer a viable solution, such as geometrically complex AVMs or extremely large AVMs. Large AVMs may require high doses or may be suboptimally treated with subtherapeutic doses to the nidus. Proposed solutions have included volume fractionation and dose fractionation radiosurgery, in which the nidus is treated in multiple sessions, allowing lower radiation of normal tissue while maintaining therapeutic doses to the nidus. Further investigations are needed to identify the interval risk of hemorrhage and to determine a threshold where risk is balanced with benefits of staged treatment [5, 7].

SRS: Factors that Influence Success

To determine the factors that affect the outcome of SRS, one must acknowledge that varying definitions of successful treatment of an AVM exist, which include considerations of nidus obliteration, hemorrhage prevention, and/or symptom management. With this in mind, obliteration rates are consistently improved in AVMs with smaller volumes and in cases utilizing higher marginal doses [1, 5, 6, 23, 24, 30]. In large trials examining small-volume AVMs located in less functional brain regions, the 3–5-year total obliteration rates after a single SRS procedure range from 71 to 90% [1, 24, 30].

The most important factor for AVM obliteration is the dose, with the marginal dose being the most significant predictor of success [5, 31, 32]. Increasing marginal dose of radiation correlates with increasing rates of nidus obliteration, as determined by MRI [1]. At a threshold of 15 Gy, the odds ratio of successful obliteration is 3.7 (Fig. 34.1) [33]. Increased AVM size is consistently associated with decreased obliteration rates and increased treatment-associated deficits [24, 34].

Other factors that may influence dose selection, and thus successful obliteration rates, include hemodynamics of the lesion (high- vs. low-flow fistulae, venous drainage stenosis), diffuse vs. compact nidus, and/or the presence of intranidal aneurysms [1, 5, 7]. The presence of prior hemorrhage has also been shown to be a predictor of fewer posttreatment complications in several studies, although the reasons for this finding remain unclear [32, 35]. Although the number of draining veins and pattern of venous drainage (i.e., superficial vs. deep drainage) are associated

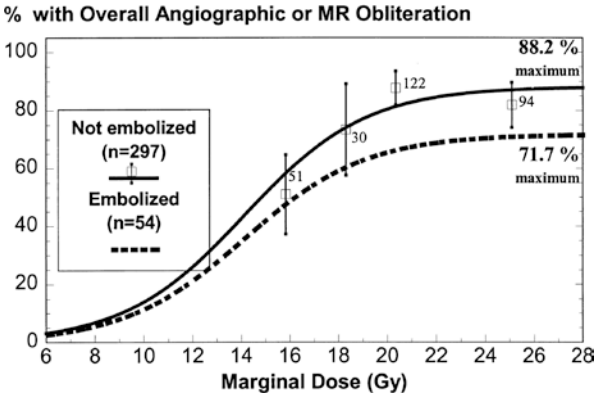

Fig. 34.1 Model of nidus obliteration as a function of marginal dose in patients without prior embolization. This illustrates the dramatic increase in obliteration rate observed around 15 Gy and the flattening of the curve around 18 Gy, which is the approximate dose typically used in AVM SRS (From Flickinger JC, Kondziolka D, Maitz AH, et al. An analysis of the dose-response for arteriovenous malformation radiosurgery and other factors affecting obliteration. Radiother Oncol 2002; 63(3):347–54; with permission)

with microsurgical success, it is not clear if these factors influence the success of SRS [1, 22]. Proximity to eloquent structures is associated with decreased obliteration rates but is not associated with hemorrhage rates [26, 33].

Complications of SRS

Failure of SRS

Identified predictors of failed SRS are incomplete angiographic definition of the nidus due to recanalization after embolization, visually occult nidus due to subacute hematoma, or the presence of intranidal arteriovenous fistulae [5]. Nidus outside the prescription isodose line and large-volume, high-grade AVMs can correlate with relatively low marginal dose. Deeply located AVMs demonstrated lower obliteration rates than peripheral lesions. The presence of these factors may result in underdosage to the AVM and thereby contribute to treatment failure [24, 28, 36–38].

Hemorrhage After SRS

The major drawback of radiosurgical AVM treatment is the persistent risk of hemorrhage during the latent period (typically 24–36 months) between treatment and AVM obliteration [7]. There is currently no consensus whether the risk of hemorrhage during the latent period differs from the risk of untreated lesions. Most studies suggest that the risk of hemorrhage remains unchanged until obliteration, with reported bleeding rates ranging from 1.6 to 9% [5, 10, 39]. Other studies have shown

both increased and decreased hemorrhage risk during the latency period [40–43]. Thus, the true risk of hemorrhage in the latent period is currently unknown, and only microsurgical resection can immediately and completely eliminate the risk of AVM bleeding.

Radiation Necrosis

Radiation damage to neighboring healthy tissues of the brain can occur when large volumes of brain tissue are irradiated. Symptoms are heterogeneous and influenced by focal mass effect and midline shift, including headache, nausea, and somnolence. The diagnosis of radiation necrosis typically involves multimodality imaging. CT typically reveals low attenuation in the nidus bed and the surrounding tissue, representing edema. MR imaging shows abnormal T2 prolongation (edema) surrounding the AVM lesion with associated focal mass effect and, depending on location, midline shift, and post-contrast imaging shows heterogenous peripheral enhancement with cystic degeneration and/or necrosis. Perfusion imaging with a relative cerebral blood volume (rCBV) threshold of 2.1 has been shown to result in a sensitivity of 100% and specificity of 95.2% when distinguishing radiation necrosis from other similarly appearing diagnoses [44].

^{18}Fluorodeoxyglucose-positron emission tomography (FDG-PET) has been used and investigated on the principle that radiation necrosis would have decreased uptake, although methodologies and protocols vary in regard to comparison to normal tissue. Other nuclear medicine modalities have been investigated, namely, thallium-201 (Tl) single-photon emission CT (SPECT) [45]. Despite numerous studies assessing novel imaging techniques for radiation necrosis, the studies are all small, and there is no established radiographic method or "gold standard" to diagnose radiation necrosis.

MR scans show postradiosurgery imaging changes in the brain surrounding AVM in approximately 30% of patients, depending on the treatment volume and, to a lesser extent, the dose administered (Fig. 34.2). Fortunately, these effects are asymptomatic in two-thirds of the affected patients, thus symptomatic postradiosurgery sequelae develop in only approximately 9% of patients [16, 31, 46, 47].

Flickinger and colleagues examined the complications from AVM radiosurgery and demonstrated the importance of lesion location and dose. With respect to location, the frontal lobe harbors the lowest risk, while the pons and midbrain bear the highest risk [46]. The total volume of tissue receiving 12 Gy or more (including the target), termed the "12-Gy volume," was found to accurately reflect the risk of developing postradiosurgery imaging changes [46, 47]. A postradiosurgery imaging expression (PIE) score was constructed to help predict the development of symptomatic postradiosurgery injury from location and dose/volume which appears best represented by the 12-Gy volume [48]. The risks of developing permanent symptomatic sequelae from AVM radiosurgery are well predicted according to the PIE location-risk score and the 12-Gy volume [46].

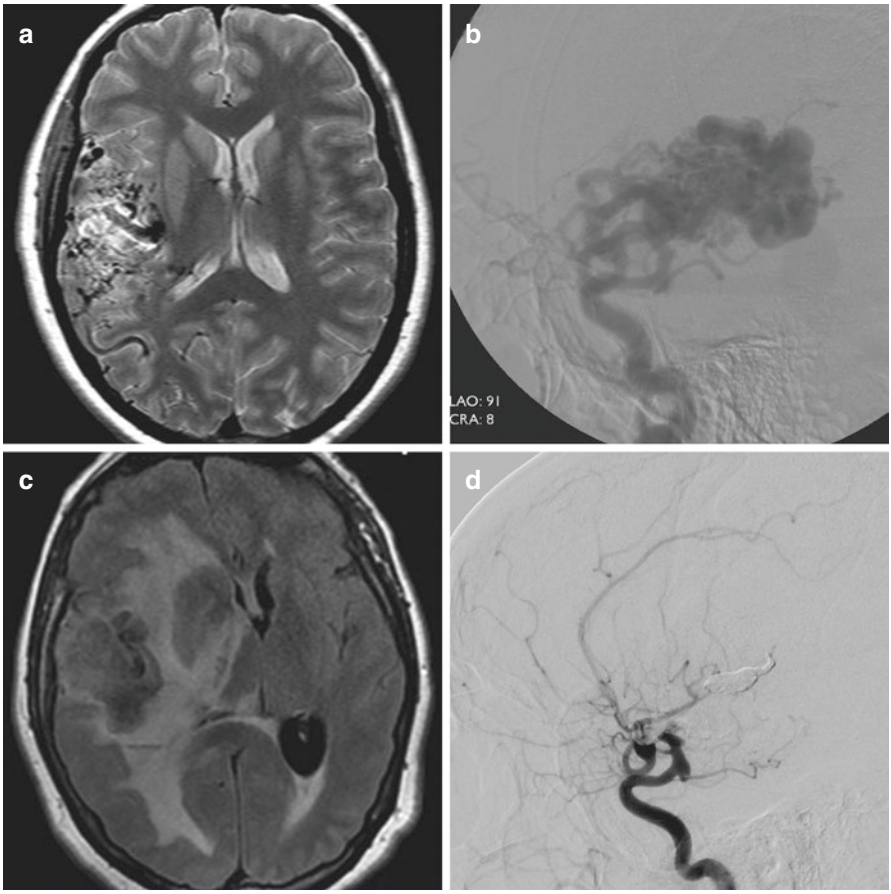

Fig. 34.2 (**a**) MRI brain, axial T2 image and (**b**) right internal carotid artery (ICA) digital subtraction angiogram (DSA) in lateral view showing a right parietotemporal AVM, Spetzler-Martin grade-III. The patient underwent a three-staged embolization, followed by SRS. (**c**) MRI brain, axial FLAIR image on 4-year follow-up showing subcortical T2 shortening in the right frontal, temporal, and parietal lobes and internal capsule representing edema along with midline shift. (**d**) Four-year follow-up DSA of right ICA in lateral view showing obliteration of AVM nidus, along with radiation vasculopathy changes involving the cortical branches of the anterior and middle cerebral arteries

Cerebrovascular Complications

Stereotactic radiosurgery may lead to a spectrum of radiation-induced vasculopathies, some of which are well-known complications of traditional radiotherapy [49]. Reports on radiation-induced vasculopathies after SRS treatment for AVMs have described vascular dysplasia, cerebral artery stenosis, de novo aneurysm and pseudoaneurysm formation, dural arteriovenous fistula formation, and venous stenosis

and/or occlusion [7, 50]. Many cases can be asymptomatic, while others may be the underlying cause of unexplained delayed hemorrhage following confirmed angiographic obliteration of AVMs treated with SRS [51].

Late-Onset Complications

Late-onset complications after SRS for AVM obliteration have been reported, of which the majority are asymptomatic. Follow-up studies examining patients 10–23 years after SRS have documented cyst formation at the previous AVM site, contrast enhancement at the former lesion site (without AVM recanalization), and increased T2 MR signal at the former lesion site. The absence of clinical symptoms in these patients may indicate that such late radiographic abnormalities are of limited clinical importance [7, 50, 52, 53].

Management of SRS Complications

Management of Treatment Failure

Even with the optimal SRS treatment plan, at least 12% of AVMs are not entirely obliterated, some of which may be treated with repeat SRS [1]. Several groups have reported on the use of repeat radiosurgery as a salvage technique after failed AVM radiosurgery. Obliteration rates have ranged from 56 to 71%, which are similar to the averages for primary SRS [5]. Neurological complications range from 5 to 18%, which are equal or slightly higher than the rates of complications for primary SRS. Hemorrhage rates may also be higher considering the longer latency time periods [54–56].

Management of Radiation Necrosis

Radiation necrosis is not always a progressive process, thus observation can be considered for patients who are asymptomatic or if the affected region is small [45]. Because radiation necrosis is associated with significant cerebral edema, first-line treatment usually involves high-dose glucocorticoids, tapered slowly over 1–2 months [45]. Resection is reserved for steroid-refractory radiation necrosis or in situations in which the diagnosis is unclear. Other management options include anticoagulants such as heparin and warfarin, which presumably arrest and reverse small vessel vascular injury, controlling the necrosis [45].

In some cases, radiation necrosis is a continuous process in which endothelial cell dysfunction leads to tissue hypoxia and necrosis, with the concomitant liberation of vasoactive compounds such as vascular endothelial growth factor (VEGF) [57]. Recent studies have explored the role of bevacizumab, a humanized

monoclonal antibody directed against VEGF in the treatment of radiation necrosis of the brain. Some studies have shown that treatment with bevacizumab may improve functional outcomes and radiographic features of radiation necrosis in patients treated with SRS for brain tumors [57, 58]. Currently, there are very limited studies examining the effect of bevacizumab in patients with radiation necrosis after SRS for the treatment of AVMs.

Another well-tolerated option is the combination of pentoxifylline and vitamin E, which can be used over an extended time frame. Rarely, barbiturates, hypothermia, or hyperbaric oxygen therapy is used, although data on these therapies is limited. There is stronger evidence, however, that hyperbaric oxygen may be used as a prophylaxis to prevent radiation necrosis [45].

Conclusion

The continued challenge in the treatment of AVMs will be to provide a treatment strategy that can achieve an optimal outcome while minimizing patient morbidity. Conclusive studies regarding the natural history of the disease and the results of randomized studies on the outcomes of radiosurgical treatment of AVMs are required. Until then, optimal treatment strategies will likely remain highly individualized. An intimate knowledge of the radiation physics underlying SRS is required in order to effectively select appropriate patients and to avoid and manage the complications of treatment.

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Radiobiology of Stereotactic Radiosurgery in the Treatment of Arteriovenous Malformations

35

Rachel Pruitt and Michael Schulder

Introduction

Stereotactic radiosurgery (SRS) has been defined as the use of concentrated ionizing radiation delivered to a stereotactically defined point in space [1, 2]. SRS was used to treat patients with arteriovenous malformations (AVMs) as early as the 1970s [1]. As many as 500,000 people in North America have AVMs [3]. With SRS, angiographic cures fall between 60 and 90% [3–5]. A consideration of the radiobiology of SRS will explain why tumors and vascular lesions respond to radiation differently, and why patients with AVMs are ideal candidates for radiosurgery.

Effect of Irradiation on AVMs

Obliteration of AVMs through radiation occurs as damage to the endothelium leads to an inflammatory reaction, which in turn leads to progressive luminal narrowing and AVM obliteration [4, 6, 7]. This typically occurs weeks to months after treatment, occurring in conjunction with localized radiation necrosis. Normal vessels rarely occlude as the result of radiation treatment. This suggests that the vessels of AVMs must be somewhat radiosensitive, making them ideal candidates for SRS.

The technical goal of any SRS treatment, and no less so in patients with AVMs, is to deliver irradiation selectively to the lesion without inducing damage to surrounding tissue. What makes the treatment of patients with AVMs very different from those with neoplasms is that the surrounding tissue and microenvironment around an AVM are very similar to the lesion being treated [7]. Thus, while in patients with malignant lesions the hypoxic environment, poor repair mechanisms, and proliferative capacity make fractionated treatment an ideal option, for patients

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with AVMs, single-dose radiosurgery has been shown to be uniquely effective [8]. The radiobiological principles of radiation demonstrate how AVMs are ideal candidates for SRS therapy.

Classically, the biologic principles of radiation therapy are defined as the four Rs: reoxygenation, repair, redistribution, and repopulation [2, 9]. In this chapter, we will explore these concepts, how SRS differs from fractionated radiation therapy, and how these principles are applied differently in the treatment of malignant and vascular lesions.

Reoxygenation

Reoxygenation is most relevant when treating patients with malignant neoplasms as these tumors rapidly proliferate, causing them to outgrow their vascular supply. In turn, this creates a microenvironment of hypoxic cells. In contrast, benign vascular lesions are not rapidly expanding and therefore do not develop regions of hypoxia.

At different doses of irradiation, different cell populations are susceptible. For example, at low doses (i.e., <10 Gy), the response is dominated by oxygenated cells, whereas above doses of approximately 10 Gy, hypoxic cells are predominantly affected (Fig. 35.1) [7].

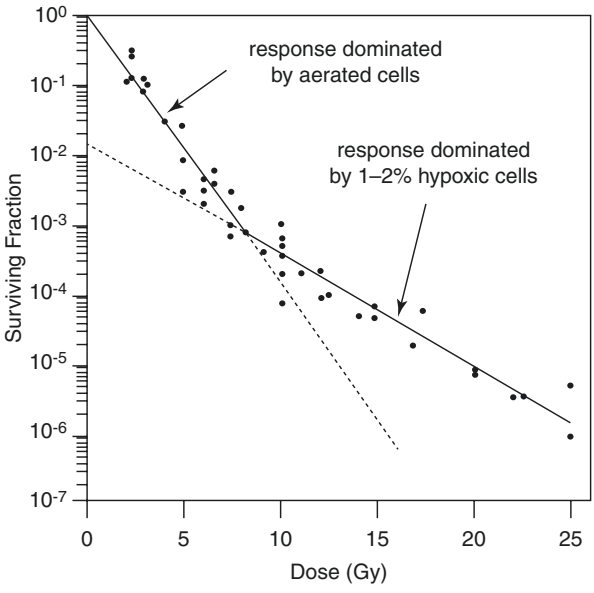

Fig. 35.1 Fraction of surviving cells after a single radiation dose in small mouse lymphosarcomas irradiated in vivo. The shallow initial part of the curve is due to the presence of aerated oxygenated cells, whereas the steeper slope at higher doses is caused by the presence of l–2% of hypoxic cells [7]

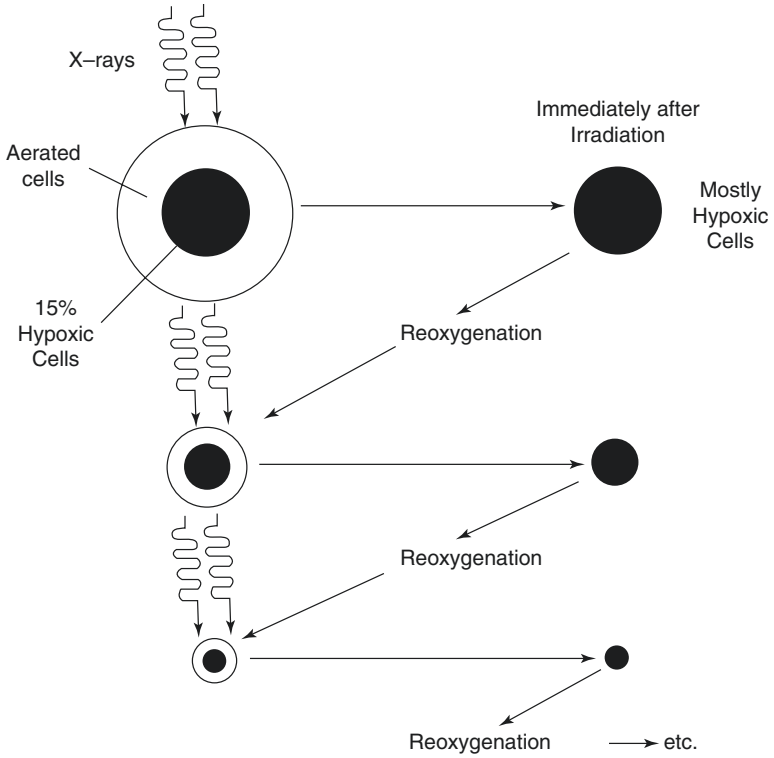

Fig. 35.2 Schematic illustration of the process of reoxygenation: Almost all tumors initially contain a mixture of aerated and hypoxic cells. A single radiation dose will kill a larger fraction of aerated than oxic cells because they are more radiosensitive (Fig. 35.1). Thus, after irradiation, a larger fraction of cells are hypoxic. But after a short period of time, the tumor tends to return to its original proportion of oxic and hypoxic cells, allowing many of the previously hypoxic (but now aerated) cells to be killed by a second, and subsequent, dose fractions [7]

Another difference between malignant and vascular lesions is that malignant lesions will revascularize [9]. As such, with malignant lesions, the ratio between oxygenated and hypoxic cells remains relatively constant. With each treatment, the oxygenated cells are killed, and reoxygenation allows for them to repopulate (Fig. 35.2) [7, 9]. For this reason, malignant lesions are amenable to multiple fractionated doses of radiation as each treatment shrinks the size of the lesion by killing off the oxygenated population and allows for reoxygenation of the hypoxic population, which in turn makes another set of cells vulnerable to radiation. In contrast, vascular lesions do not have a hypoxic component and as such are in many ways more amenable to single high-dose treatment.

Repair

Repair of DNA damage occurs between radiation treatments. Radiation causes such damage, either to a single strand of DNA or a double-strand break. Single-strand breaks are usually considered repairable, as the information remains intact on the other DNA strand. In contrast double-strand DNA breaks are not repairable as with both strands broken, there is no "template" from which to copy, and the information is lost.

At low doses of radiation, single-strand breaks are common, and repair can occur. At higher doses, double-strand breaks predominate. Thus, as you increase the dose of radiation, the percent of cells surviving decreases. When examining survival curves, the "curve" of the graph is the result of repair. The more linear the graph, the less repair has occurred.

This concept becomes important when examining the differential response to radiation between patients with AVMs and those with malignancies, as the survival curves are different between "normal" cells and cancer cells. Cancer cells lack many repair mechanisms and thus are not as effective at repairing DNA damage. Thus, their survival curves are more linear. This means that these "early responders" will respond to radiation at lower doses than the "late-responding" normal cells.

This difference between the ability to repair DNA is illustrated as part of the linear quadratic equation where survival is modeled as *S*:

$$S = \exp(-\alpha D - \beta D^2)$$

In this model, *S* is the surviving fraction, alpha is a coefficient for the cellular radiosensitivity (non-repairable damage), and beta is a coefficient for the cellular repair mechanisms (repairable damage) [9]. As beta increases, the time for repair increases, and the cell proliferates more slowly as is seen with normal tissue. Thus the differences between early- and late-responding tissues can be seen with differences in the alpha/beta ratios. As beta becomes smaller, the alpha/beta ratio is larger, as in cancer cells or early-responding tissues. In contrast, as the alpha/beta ratio is smaller or beta is larger, the time to repair is larger, modeling late-responding tissues [7].

As you decrease the dose or increase the fractionation, there is an increase in cell survival. This fractionation spares late-responding tissues more than early-responding tissues, as demonstrated by Fig. 35.3. This is part of the argument as to why it is less advantageous to fractionate radiation for patients with AVMs and why they are ideal candidates for single-treatment radiosurgery. The goal of fractionation in malignant disease is to preferentially treat the tumor, giving the cells

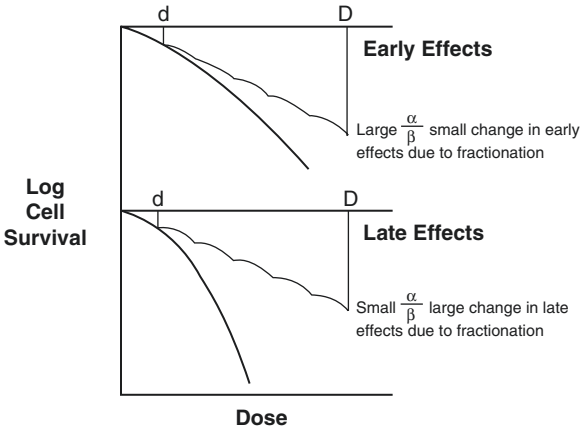

Fig. 35.3 The gamma-ray dose-response curve for late-responding tissue (e.g., AVM obliteration, cerebral necrosis) is "curvy," that is, has a small alpha/beta ratio (estimated here to be around 0.6 Gy); for early-responding endpoints such as tumor control, the dose-response curve is straighter, that is, the alpha/beta ratio is larger. Consequently, dose fractionation spares late-responding tissues more than early-responding tissues [7]

time to reoxygenate and giving normal tissue time to repair. In contrast, with AVMs, the vascular lesion and the surrounding normal tissue are biologically similar. Thus there is little advantage added to fractionation [7].

Redistribution

Redistribution refers to the redistribution of cells in the cell cycle after radiation [2, 9]. Cells have repair checkpoints built into critical points in the cell cycle. The response to radiation at these checkpoints is dose dependent, as at lower doses the DNA is able to be repaired, and the cells are able to progress through the cell cycle (however redistributed, as cells exposed to radiation take longer to repair at these checkpoints). In contrast, at higher doses, DNA damage is irreparable, and the cells arrest in whichever stage of the cell cycle they happen to be (Fig. 35.4).

SRS uses high doses of irradiation. In the case of AVMs, the higher doses are associated with higher rates of obliteration; thus, the doses used for treatment cause arrest in all stages of the cell cycle [8, 11]. At these doses, redistribution is unlikely to play a role in the cell populations.

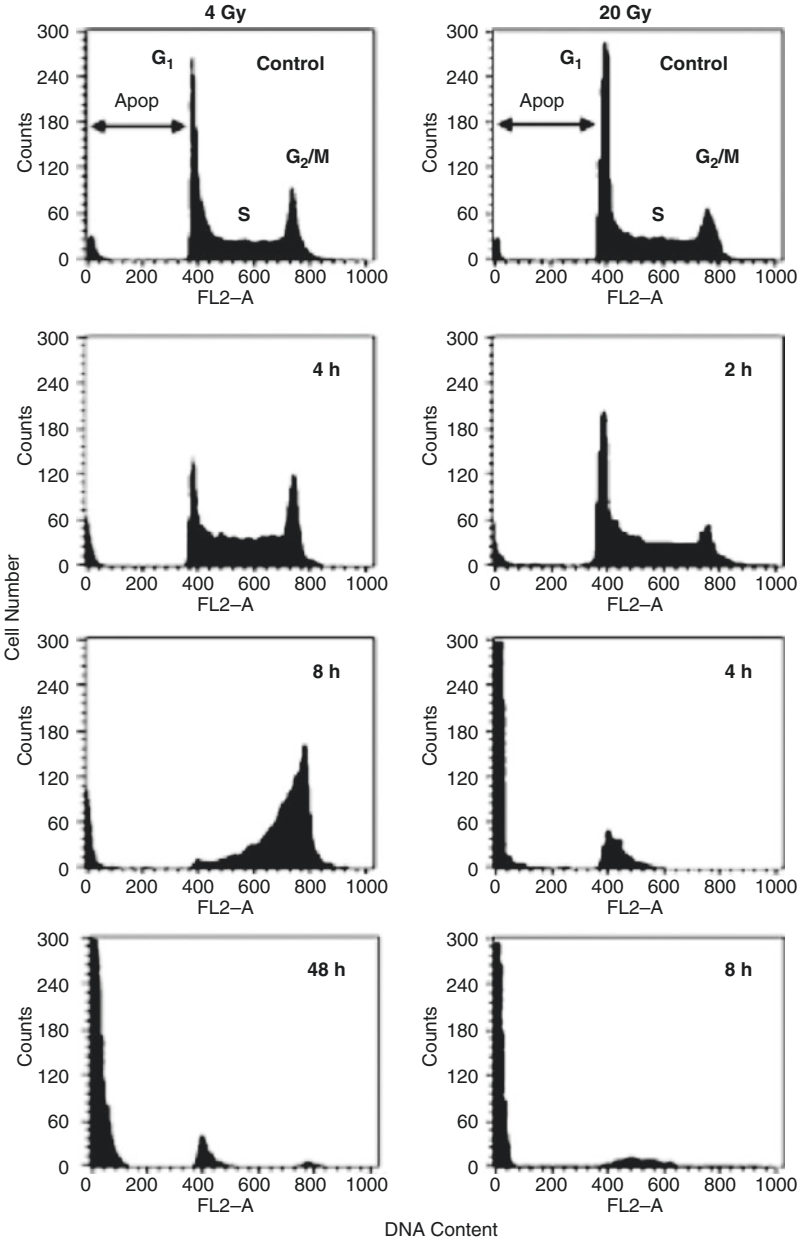

Fig. 35.4 Cell cycle progression of HL-60 cells after irradiation. Cells were irradiated with 4 or 20 Gy, and the cell cycle progression (DNA histograms) was measured with flow cytometry. Most of the cells were in late S and G2 phases 4 h after 4 Gy irradiation and then died of apoptosis as indicated by the large increase in the sub-G1 fraction. When irradiated with 20 Gy, no cell cycle progression occurred, and the cells died of interphase death in the cell cycle phases, where the cells were at the time of irradiation [10]

Repopulation

Repopulation refers to the regeneration of cells. Again, this concept is especially important in the treatment of patients with malignant lesions in the setting of fractionated radiotherapy. Cancer cells proliferate more rapidly than normal cells (and this holds especially true for the central nervous system, where relatively little new cell formation occurs) so that repopulation can lead to treatment failure. In the setting of patients with AVMs, in whom there is no proliferation of the AVM cells and in whom a single high dose of SRS is given, this concept is less applicable [9].

Conclusions

The first use of SRS to treat patients with AVMs was in the 1970s. The same radiobiological principles that made patients with AVMs ideal candidates for single radiation treatments apply today. When treating patients with malignant neoplasms, fractionating at lower doses may be advantageous, allowing tumors time to revascularize and normal tissue time to repair. However, AVMs do not have a hypoxic component and have a microenvironment similar to their surrounding tissues, making them ideal candidates for high-dose, single-fraction SRS treatment.

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Radiosurgery for Arteriovenous Malformations

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Amparo Wolf and Douglas Kondziolka

Checklist: Radiosurgery of AVM

Equipment needed (at time of radiosurgery or follow-up)	Procedural steps
Gamma Knife radiosurgery unit Interventional suite for cerebral angiogram Leksell stereotactic frame Gamma Knife planning station Nursing • Local anesthetic • ± Conscious sedation Radiation oncologist Neurosurgeon MRI or CT scan	Identification • Based on CT or MRI, recognize complications including hemorrhage, radiation injury, or delayed cyst formation. Initiate and engage • If large hemorrhage, it may require surgical evacuation or external ventricular drain. Notify nursing and/or OR staff Repair • Surgical evacuation if large hemorrhage or insertion of external ventricular drain • Corticosteroids for edema/radiation injury • Cyst aspiration for large delayed cysts Close follow-up imaging as needed

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Complication Avoidance Flowchart

Complication	Predisposing factors	Remedy	Avoidance
Hemorrhage	Presence of aneurysm, AVM volume and flow rate, morphology of venous drainage, prior hemorrhage	Observation, external ventricular drain, surgical evacuation of hematoma	Tx aneurysms endovascularly or surgically prior to SRS if feasible
Edema/ radiation injury	Radiation dose Volume of irradiated tissue (12 Gy volume)	Corticosteroids, bevacizumab	Reduce margin dose for larger volume AVMs and depending on location
Delayed cyst formation	Potentially prior embolization, prior SRS, brain edema, large nidus, maximum dose, lobar AVMs, complete AVM obliteration	Observation, cyst aspiration, cystoperitoneal shunt	None

Introduction

Stereotactic radiosurgery (SRS) is a minimal access, widely used approach to manage patients with an intracranial arteriovenous malformation (AVM). It can result in the total obliteration of AVM blood flow, thereby eliminating the risk of intracranial hemorrhage. Long-term results, compiled by the International Gamma Knife Research Foundation, in 2236 patients that had undergone radiosurgery for cerebral AVMs, showed an overall obliteration rate of 65% (50–85%) at a median time of 3.5 years [1]. Younger patients with smaller AVM target volumes and higher margin doses are more likely to achieve total closure [1]. The mechanisms underlying the eventual obliteration of AVMs after SRS include endothelial injury, myointimal proliferation, collagen deposition, and vessel hyalinization leading to vascular thrombosis and occlusion [2].

The overall morbidity of SRS in AVMs is low, but new neurological deficits can occur. Complications can arise and include most commonly delayed hemorrhage, hemodynamic effects on the regional brain from AVM vessel closure, radiation injury to the adjacent brain, and delayed cyst formation. This chapter reviews the principles of complication avoidance and management in the radiosurgical treatment of AVMs.

Procedural Overview

On the morning of SRS, patients are fitted with a Leksell stereotactic frame under local anesthesia and mild intravenous conscious sedation. Children and younger adolescents are typically placed under general anesthesia. Contrast-enhanced MRI including 1 mm MP-RAGE and long relaxation time sequences are acquired. Subsequently, patients undergo stereotactic digital subtraction angiography (DSA).

MR imaging and biplane stereotactic angiograms are coupled in the planning software for optimal conformal dose planning aimed at targeting the malformation nidus. Radiosurgical planning is performed by the neurosurgeon along with the radiation oncologist. Isocenters of different sizes (4 mm, 8 mm, or 16 mm) are utilized to develop a conformal plan. Dose selection depends predominantly on the location and the size of the AVM [3]. Doses at the margin of an AVM are typically 16–25 Gy. The margin isodose is between 50 and 80% to shield adjacent parenchyma while maintaining a high obliteration rate. After radiation delivery, the stereotactic frame is removed. Antiepileptics such as phenobarbital are commonly administered the day of the procedure in the setting of lobar AVMs in order to reduce the risk of an early seizure. Similarly, a dose of methylprednisolone may be given after radiosurgery. Patients are generally discharged the same day of the procedure. Follow-up with MRI is routinely performed at 6 months to assess for perinidal edema and then yearly. DSA is recommended at 3–4 years or earlier to confirm AVM obliteration if suggestive on MRI.

Complication Avoidance

Hemorrhage

There continues to be a risk of hemorrhage after SRS during the latency period until complete obliteration is achieved. In most studies, the hemorrhage rate during the latency period is not significantly different from the pre-SRS hemorrhage rate or is lower at an annual risk of approximately 1–3% [1, 4, 5]. The timing of SRS after AVM hemorrhage has not been shown to predict hemorrhage after SRS [4, 6]. However, patients whose radiosurgery was delayed more than 6 months in order for the hematoma to reabsorb had a higher risk of re-hemorrhage prior to SRS [4]. As such, it is generally recommended to perform radiosurgery within 6 months after an initial bleeding event.

Approximately 3–50% of AVMs have associated aneurysms (depending on the detail provided by angiography), with an increased annual bleeding risk varying from 7 to 11% [7, 8]. Similarly, AVMs containing high-flow arteriovenous fistulas (AVF) may be associated with a higher incidence of perioperative hemorrhage. Surgical or endovascular management of these vascular lesions may be warranted prior to undergoing SRS to minimize the risk of hemorrhage. In a study of patients with Spetzler-Martin grade 1 and 2 AVMs having undergone SRS, the presence of a coexisting aneurysm was the only factor associated with an increased hemorrhage rate after radiosurgery [9].

There are several risk factors for hemorrhage following SRS that may differ from those associated with bleeding prior to treatment and include patient age, AVM size or volume, radiation dose and coverage, and AVM flow rate [10–12]. Lower hemorrhage rates have been reported after radiosurgery in patients with lower Spetzler-Martin grade (I–III), smaller nidus volume, and increased margin dose [5, 13, 14]. Some studies have shown that patients presenting with a hemorrhage prior to SRS

are more likely to hemorrhage after SRS [1]. The morphological characteristics of the AVM may also predispose to hemorrhage including venous stenosis or occlusion of a high-flow draining vein. Hemorrhage early after radiosurgery can occur, believed to arise from acute draining vein thrombosis [15, 16]. Aside from the margin dose, there are no solid treatment predictors of hemorrhage after SRS. One hypothesis is that higher doses of radiation to the draining vein(s) may be associated with higher rates of hemorrhage due to their faster occlusion, particularly in the setting of a single draining vein. However, no studies have directly addressed this.

Hemorrhage after documented obliteration is rare, reported in <1% of AVMs [17, 18]. Approximately 60–80% of obliterated nidi will continue to enhance to some degree with gadolinium administration years after obliteration [19, 20], without AV shunt present on angiography. Histological evaluations may show signs of AVM vascular channels which may be vessels within the granulation tissue [20].

To summarize, in order to minimize the risk of AVM hemorrhage after SRS, certain recommendations can be made. Firstly, consider treatment of an aneurysm or fistula prior to AVM using endovascular or surgical technique. Secondly, it is important to develop a conformal plan, tailoring the radiation to the nidus and not to include areas of arteriopathy outside of the AVM in addition to the draining vein.

Radiation Injury

The aim of AVM radiosurgery is to accurately target the AVM nidus to achieve obliteration while avoiding serious complications due to suboptimal planning. Transient increased perinidal T2 signal changes consistent with edema may develop within months to 1 year after SRS. This is often asymptomatic. AVMs located near critical structures are more likely to result in symptomatic effects if edema develops. Radiation-induced imaging changes, defined as increased perinidal T2-weighted signal on follow-up MRI, were reported in almost 30–60% of patients and symptomatic in 3–11% [1, 21, 22]. Only 1–5% of patients will have permanent deficit including headache, seizures, or focal neurological deficits [1, 21, 22]. Vascular injury may be the underlying cause of perinidal edema including endothelial cell damage followed by breakdown of the blood-brain barrier. Alternatively, the transient changes could be hemodynamic as the regional brain adjusts.

The extent of radiation injury depends on numerous factors, the most important of which are radiation dose and the volume of irradiated tissue. Patients receiving a margin dose greater than 24 Gy are at the greatest risk of developing radiation-induced changes, including symptomatic and permanent injury [1]. Other factors may include the type of tissue radiated including the amount of the normal brain, history of prior radiotherapy, the location of the AVM, a single draining vein, and an individual's susceptibility to radiation injury [1, 23, 24]. Radiation injury may be more pronounced with premature occlusion of the draining vein due to early venous thrombosis [25]. Some studies have reported that patients who develop radiation-induced imaging changes are more likely to achieve complete obliteration [23, 26].

The development of permanent symptomatic sequelae from AVM radiosurgery depends predominantly on location and volume irradiated [3]. The locations with the highest risk of symptomatic AREs are the pons, midbrain, and thalamus, while the lowest risk is the frontal lobe. The total volume of tissue receiving 12 Gy or more (V12—12 Gy volume) has been correlated to the risk of developing post-radiosurgery imaging changes [3].

In order to avoid permanent radiation-induced injury, dose selection is crucial. When planning, it is important to balance the rate of obliteration achieved at higher doses with the risk of permanent radiation injury, varying with location (Fig. 36.1).

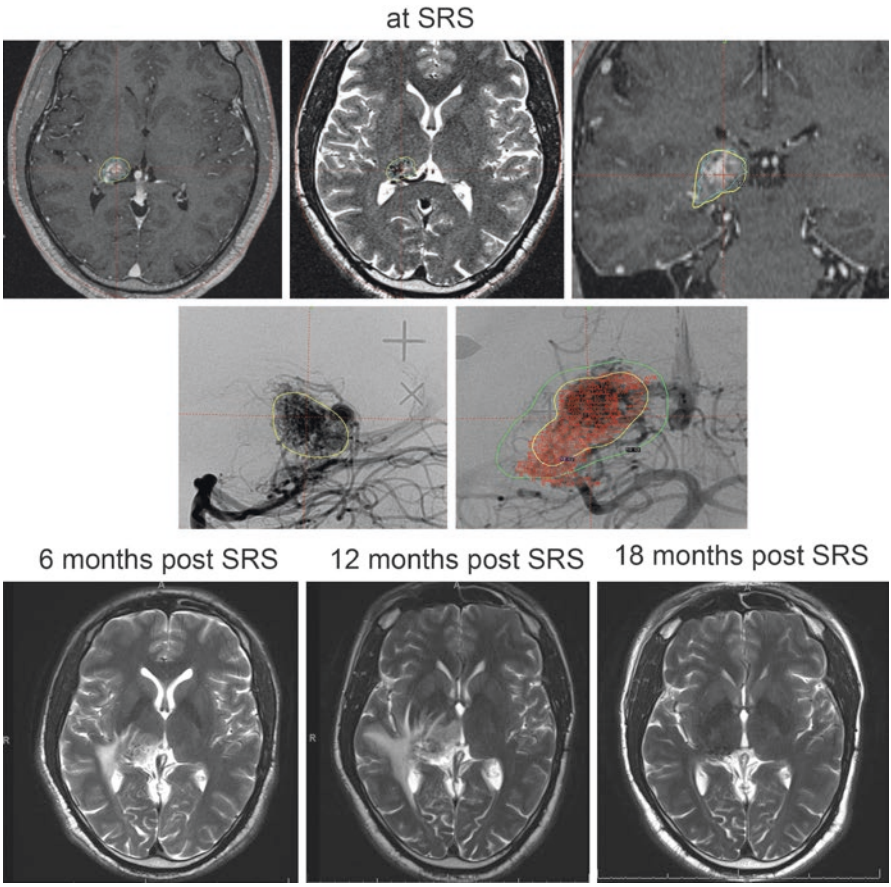

Fig. 36.1 A 45-year-old male underwent SRS for a right thalamic AVM. (**a**) MRI with gadolinium and DSA depicting the radiosurgery plan. Margin dose = 19 Gy at 50% isodose, volume = 2.22 cm^3. (**b**) At 6 months post-SRS, there is significant regional edema which is more pronounced at 12 months post-SRS. The patient was placed on a tapering course of corticosteroids. By 18 months, there is resolution of the edema and near obliteration of the AVM

Delayed Cyst Formation

Late radiation-induced changes, such as cyst formation, have been reported after AVM radiosurgery (Fig. 36.2). The interval from radiosurgery to cyst formation varies from months to many years. Depending on the location of the cyst, it can cause focal neurological signs or, if large enough, symptoms of increased intracranial pressure (ICP). The prevalence of cyst formation is 1.1–5.5% [27–29]. There may be a higher prevalence in unruptured AVMs, since normal perinidal brain parenchyma is generally more vulnerable to radiation than gliotic tissue [29]. Or else, a cyst could form in the encephalomalacic brain in an old hemorrhage cavity. An increased risk of late cyst formation has been reported in patients having undergone prior embolization or repeat radiosurgery or in patients who developed brain edema after SRS [30]. Large nidus volume, a high maximum radiation dose, lobar AVMs, and complete AVM obliteration may also predispose to cyst formation [31].

The exact mechanism of cyst formation is not known but may relate to the breakdown of the BBB with an exudate producing a growing cyst. Its development may occur in several steps including inflammation of the perinidal parenchyma,

BBB breakdown due to inflammation, formation of dilated capillary vessels, serum protein exudation forming a perinidal cavity, neoangiogenesis in the wall of the cavity forming nodule, and repeated hemorrhage into the cavity from the neoangiogenic vessels, eventually resulting in osmotic cyst expansion or chronic encapsulated hematomas [19, 32].

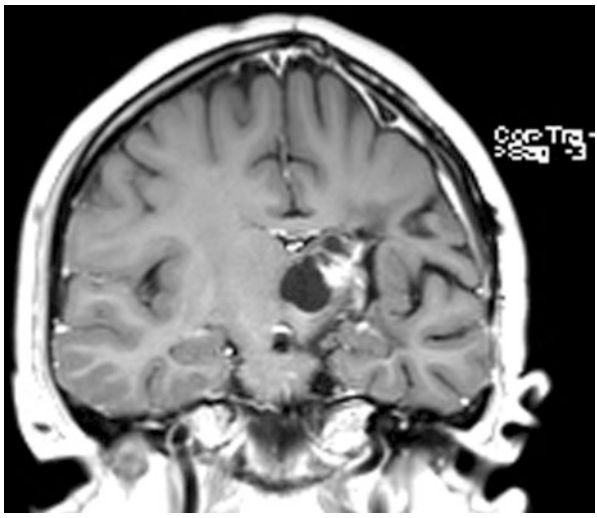

Fig. 36.2 Coronal T1-MRI with contrast showing a left thalamic AVM after two radiosurgery procedures that led to complete AVM obliteration. This young woman had a prior large AVM hemorrhage and cranioplasty. Late follow-up imaging showed asymptomatic cystic changes adjacent to the obliterated AVM that continues to be monitored

Complication Management

Hemorrhage

Large symptomatic hemorrhages may require a craniotomy with evacuation of the hematoma. Cardiorespiratory support and monitoring in the intensive care unit may be required for larger hemorrhages resulting in increased ICP and reduced level of consciousness. Intraventricular hemorrhages may necessitate insertion of an external ventricular drain. Smaller hemorrhages that are minimally symptomatic may be monitored with serial imaging.

Radiation Injury

Corticosteroids (e.g., dexamethasone) are the first-line treatment for brain edema or radiation injury. However, prolonged usage of corticosteroids can lead to side effects including weight gain, hypertension, osteoporosis, and cataracts, among others, and thus they should not be used for an extensive duration. Surgery may be required in patients who are refractory to corticosteroids and remain symptomatic.

Alternative treatments reported include pentoxifylline and Vitamin E. The combination of oral pentoxifylline and vitamin E has been reported to benefit patients with radiation injury in other organ systems. A pilot study on 11 patients with brain tumors reported a mean decreased edema volume of 72 mL with the treatment of pentoxifylline 400 mg twice a day and Vitamin E 400 IU twice a day [33]. Side effects include nausea and abdominal discomfort. Further studies may help better understand the effect and mechanism of pentoxifylline and Vitamin E in adverse radiation events.

A few studies, including a randomized double-blind placebo-controlled trial, have reported a beneficial effect of bevacizumab in radiation injury, resulting in improved functional outcomes in patients having undergone SRS for brain metastasis and other brain tumors [34–36]. One case report demonstrated control of severe, corticosteroid refractory edema in a patient having undergone radiosurgery for an intracranial AVM [37]. There are systemic side effects reported for bevacizumab which include sinus thrombosis, pulmonary embolus, hypertension, and wound dehiscence among others.

Delayed Cyst Formation

Cyst formation can be self-limiting and thus be observed over time with serial imaging. Surgical management of a cyst may be required when causing progressive focal neurological symptoms or increased ICP. Surgical options include cyst aspiration under stereotactic image guidance, craniotomy for cyst fenestration, and potentially a cystoperitoneal shunt for recurring cysts.

Conclusion

Radiosurgery is an important treatment tool in the management of AVMs. It is a minimally invasive approach to its management, and permanent complications are relatively rare. However, we must be aware of the complications of hemorrhage, radiation injury, and delayed cyst formation. These complications can often be managed medically; however at rare times, surgical intervention may be required including in the setting of a large hemorrhage or a symptomatic delayed cyst.

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