Hot Topics in Acute Care Surgery and Trauma

Tal Hörer
Joseph J. DuBose
Todd E. Rasmussen
Joseph M. White *Editors*

Endovascular Resuscitation and Trauma Management

Bleeding and Haemodynamic Control

Hot Topics in Acute Care Surgery and Trauma

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Foreword

Research is fundamentally altering the daily practice of acute care surgery (Trauma, Surgical Critical Care, and Emergency General Surgery) for the betterment of patients around the world. Management for many diseases and conditions is radically different than it was just a few years ago. For this reason, concise up-to-date information is required to inform busy clinicians. Therefore, since 2011 the World Society of Emergency Surgery (WSES), in partnership with the American Association for the Surgery of Trauma (AAST), endorses the development and publication of the "Hot Topics in Acute Care Surgery and Trauma," realizing the need to provide more educational tools for young in-training surgeons and for general physicians and other surgical specialists. These new forthcoming titles have been selected and prepared with this philosophy in mind. The books will cover the basics of pathophysiology and clinical management, framed with the reference that recent advances in the science of resuscitation, surgery, and critical care medicine have the potential to profoundly alter the epidemiology and subsequent outcomes of severe surgical illnesses and trauma.

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Foreword

This is a textbook that is long overdue. The technology to change the paradigm in the management of vascular trauma and critically ill patients has existed for quite some time, yet its application as described in this textbook has had limited penetration. As a young vascular surgeon in the 1990s who also did a fair share of vascular trauma, I experienced the endovascular revolution in vascular surgery firsthand. It required rethinking the traditional open methods of vascular reconstructive surgery and carefully and thoughtfully replacing or supplementing many open approaches with endovascular techniques. Today, endovascular approaches have extended the vascular surgeon's scope of practice and at the same time increased the safety of vascular interventions for the preservation of life and limb. It has always seemed strange to me that the applications of endovascular techniques to vascular trauma and bleeding have not occurred at the same rapid pace.

But now, the time has come, and I would anticipate the same endovascular revolution happening in the treatment of patients who sustain traumatic vascular injury or are in need of hemorrhage control. Balloons, shunts, catheters, wires, coils, closure devices, stents, and stentgrafts are now the new tools of the trade. How these tools should be employed is the subject of this thorough and comprehensive book. Furthermore, how to best integrate these tools with the tried and tested open approaches to vascular injury and hemorrhage control is the very exciting challenge of the future. Surgeons, vascular specialists, and critical care physicians will need to reinvent themselves if they are to take advantage of endovascular technology. Applications of endovascular technology in the setting of vascular trauma and bleeding will require the development of new paradigms of care. To have a state-of-the-art textbook is a necessary foundation for expansion of endovascular techniques into this new arena.

I would like to congratulate the editors and authors for putting together this very important and timely book. I look forward to seeing how this compendium will alter the treatment of critically ill patients and extend the benefits of the endovascular approach to patients all over the world.

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Foreword

Over the past several decades, endovascular technologies have continued to evolve as valuable tools of modern vascular surgery. In my own career, I have been fortunate to play a role in this exciting evolution. In the context of this involvement, our group was able to demonstrate that resuscitative endovascular balloon occlusion of the aorta (REBOA) has the capacity to serve as a critical adjunct in the salvage of some patients with a ruptured abdominal aortic aneurysm. In the wake of this initial experience, endovascular aneurysm repair (EVAR) and selective REBOA are now being used widely to treat this acute source of non-compressible hemorrhage. It is of high interest to see this approach now expanding to other sources of non-compressible hemorrhage following bleeding after trauma and other entities. Endovascular tools continue to evolve in this regard, now being employed actively alone or in combination with other procedures, to save life and decrease morbidity.

The authors of this book summarize the current data and practice of the new concept of endovascular resuscitation and trauma management (EVTM) in this exciting new text. Trauma surgeons, surgeons, interventional radiologists, and intensivists have worked collaboratively in this effort, reviewing and analyzing advances in endovascular technologies as they apply to EVTM. Issues such as the use of early vascular access, REBOA, embolization, endografts, and other endovascular adjuncts are presented with current supporting data and research results as well as clinically relevant information from active practitioners of EVTM principles. Central to their contribution is a superb collegial collaboration between various disciplines and regions of the world, all built upon a foundational desire to better define the optimal application of endovascular technologies to benefit the patients who need them most.

Why is this book important? It summarizes our current understanding of a rapidly expanding fund of knowledge regarding endovascular and hybrid tools for resuscitation and treatment. It also presents this knowledge in a unique and focused platform which has never been done before. This evolution in care will undoubtedly continue, and this textbook is an ideal source of information for the practitioner regarding EVTM principles past, present, and future.

This volume is a “must have” for all the specialists involved in treating patients subjected to trauma and in need of resuscitation.

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Preface

In February of 2017, more than 350 medical professionals, representing diverse disciplines in surgery, trauma, anesthesia, cardiology, obstetrics, radiology, and emergency medicine and critical care from around the world, met in Örebro, Sweden, at the inaugural Endovascular Hybrid Trauma and Bleeding Management (EVTM) Symposium (#EVTM2017 http://www.jevtm.com/program-for-evtm-2017-symposium/). This international, multidisciplinary event aggregated an array of providers experienced with the management of the critically injured, ill, or bleeding patients. Through presentations, panel discussions, and moderator-led debates, the attendees advanced their understanding of the capacity for catheter-based, endovascular approaches and technologies (present and future) to improve the survival and recovery of this challenging population. The size, diversity, and international composition of #EVTM2017 and the enthusiastic nature of the discussions surpassed the projections of the event organizers. EVTM tapped and coalesced an underappreciated momentum in the area of endovascular techniques for injury, hemorrhage control, and critical care, an interest that's relatively overlooked by other, more mainstream, professional organizations.

Beyond its clinical, scientific, and new technologies content, #EVTM2017 made clear that interest in endovascular approaches to injury and critical care – compared to those applied to age-related conditions – is at the margins of many clinical disciplines, their professional organizations, and their respective meetings and publications. EVTM exposed the challenge and provided a common, cross-disciplinary forum to redress this critical gap. As an extension of the #EVTM2017, a new journal, called *Journal of Endovascular Resuscitation and Trauma Management* (*JEVTM*), was commissioned as a platform on which to continue the global discussion (www.jevtm.com). The *JEVTM* aims to capture and maintain the cross-disciplinary momentum on display at the #EVTM2017 and serve as an electronic and print forum by which to disseminate knowledge from clinical experiences as well as that stemming from structured research, development, and innovation activities. Through the publication of case reports and results from original research and by providing profiles on new technology and innovation concepts, as well as modern reviews and commentaries in this space, *JEVTM* will establish itself as a common conduit for this topic area, a conduit which courses through the established, but otherwise somewhat fixed, disciplines of trauma, surgery, cardiology, obstetrics, critical care, radiology, anesthesia, and emergency medicine. The previously held

Pan American EVTM (#panamevtm2018, Houston, Texas) and EVTM-Örebro in June 2018 continued the dynamic, interactive discussions and debates with leaders and interested professionals in this evolving field internationally.

The intent of this textbook is to provide a comprehensive review of endovascular, catheter-based approaches and technologies applied in the management of the critically injured patient and a complete review of damage control resuscitation concepts, strategies, and techniques. This textbook has incorporated the most up-to-date preclinical and clinical research into today's evidence-based (i.e., best practice) approach to trauma management for each chapter. The chapter authors were encouraged to highlight advanced endovascular applications for modern resuscitation and surgical management. We asked the leading experts in trauma, in cooperation with the World Society of Emergency Surgery (WSES), to add expert's comments on selected chapters. Our aim is to meticulously explore important issues, complexities, and controversies within the developing, cross-disciplinary, international concepts central to EVTM, in order to improve the care and outcomes of the severely injured patient globally.

Örebro, Örebro Län, Sweden — Tal Hörer
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We would like to recognize our distinguished chapter authors and coauthors who comprise an international, multidisciplinary cohort of expert clinicians, surgeons, and scientists. We greatly appreciate their dedication and contribution to this important effort regarding endovascular resuscitation and trauma management (#EVTM).

Additionally, we would like to recognize the World Society of Emergency Surgery (WSES). Their support for this project has been instrumental to its development and success.

About the Book

This text, constructed under the leadership of Tal Hörer and colleagues, provides modern practitioners with insight into the effective incorporation of techniques of endovascular resuscitation and trauma management (EVTM) into modern medical care. The field of EVTM continues to evolve, bringing together an increasingly larger and more diverse multidisciplinary group of providers interested in exploring these principles for the betterment of the patients we care for. The authors have incorporated both current science and experienced practice into each of the described elements of EVTM practices. As the first text of its kind, this work is a testament to the power of innovative collaboration and the diligent pursuit of knowledge as it pertains to define the optimal role of EVTM.

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The Concept of Endovascular Resuscitation and Trauma Management: Building the EVTM Team

1

Tal Hörer, David T. McGreevy, and Rigo Hoencamp

1.1 Introduction: Major Hemorrhage and Adjuncts for Its Detection and Control

Major hemorrhage can be essentially classified as either compressible or noncompressible hemorrhage (NCH), and continues to be the leading cause of potentially preventable death associated with trauma in both civilian and military environments [1–3]. Compressible hemorrhage, involving the extremities, can often be controlled using tourniquets and is associated with a low mortality rate [4, 5]. NCH involving the torso and junctional regions accounts for a significantly higher rate of mortality [6]. Recent publications from the conflicts in Afghanistan and Iraq have documented a prevalence of major hemorrhage from vascular trauma of up to 10%, but descriptions are limited to casualties who survived long enough to reach

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a medical (with surgical capability) treatment facility [2, 3, 7]. Major hemorrhage and NCH remain the leading causes (almost 90%) of preventable death and a major challenge in trauma care. Massive transfusion protocols may, to some extent, aid in preventing immediate collapse, but there is a pressing need for further optimization of methods for trauma and hemorrhage control [4]. Permissive hypotension has been widely used in recent years, based on the assumption that maintaining a lower blood pressure in bleeding patients by restricting the fluid resuscitation administered avoids dilutional coagulopathy and accelerated hemorrhage and might increase survival to definitive (surgical or endovascular) treatment [8].

The Modern American College of Surgeons Advanced Trauma Life Support (ATLS) principles emphasize early diagnosis and management of airway problems and major bleeding control [9]. ATLS provides a protocolized approach that affords effective initial assessment and resuscitation and is the golden standard for trauma care around the world [5]. In the past two decades, endovascular procedures and techniques have revolutionized the way that vascular surgery is performed today [10–12]. With improved endovascular devices (e.g., stent grafts, embolization agents, balloon-occlusion catheters) and diagnostic imaging technology (e.g., Computed Tomography [CT] or CT Angiography [CTA], ultrasound, angiography, Doppler), minimally invasive surgery can now be performed for hemorrhage control [13–16]. The use of these modern endovascular modalities for bleeding patients initially began with the treatment of aortic aneurysmal disease [10, 17, 18] and has since been adopted into trauma. For many years, there have been anecdotal reports of centers treating bleeding patients with basic endovascular methods, but the continued evolution of technology and the arrival of the "endovascular era" has heralded a new age [19]. Parallel to this, EndoVascular resuscitation and Trauma Management (EVTM) has been a consistently evolving multidisciplinary concept for acute trauma care [20–24]. It aims to combine modern endovascular techniques and procedures with traditional ATLS and Definitive Surgical Trauma Care (DSTC) [25] for early multidisciplinary evaluation, resuscitation, and definitive management of hemodynamically unstable patients. It has been suggested that using the EVTM concept may result in faster bleeding control, minimized blood loss, and less extensive surgical insult [23]. It may also help surgical teams to assemble the necessary resources and save precious time. It can be used in austere environments with limited resources to focus medical resources and attention on the appropriate needs of the patient [26]. At present, ATLS and DSTC do not provide guidance on the use of endovascular modalities and EVTM, but it will be included to some degree in future editions of the DSTC. The same is true for modern courses such as the Damage Control Surgery (DCS) course [7], which concentrates on damage and surgical bleeding control. However, EVTM is a skillset that is rapidly being embraced as a contemporary adjunct to conventional ATLS and DSTC, and is now part of the clinical guidelines in an increasing number of major trauma centers around the world [23]. Some examples are the use of Thoracic Endovascular Aortic Repair (TEVAR) for traumatic aorta injury, iliac/aorta endografts for bleeding control, and kidney, spleen, and liver injury embolization [27–34]. Intraluminal balloon occlusion for hemorrhage control, or Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA), is one of the EVTM tools seeing greater clinical use and this will be further discussed in other chapters in this book.

Since endovascular and imaging technology has improved, bleeding can now be detected and treated rapidly. CT/CTA was previously known as the "tunnel of death," when scanning time was long, image quality was low, and the interpretation of images was slow, which can also be said for ultrasound imaging. Modern CT/CTA and ultrasound are fast with very high resolution, having high specificity and sensitivity for the mapping of bleeding injuries [35, 36]. CT on rails and CT in the ER has further facilitated the feasibility of using these techniques in even more patients, although CT is yet to be avoided as a gold standard for hemodynamic unstable patients for obvious reasons [37].

However, despite these developments contributing to advanced methods for bleeding control and hemodynamic stabilization, as a community, there is a need to better share lessons learned, to collaborate, and to further define the optimal utilization of EVTM principles in victims of trauma.

1.2 The Concept of EndoVascular Resuscitation and Trauma Management

Over the past 20 years, a collection of tools and techniques used in endovascular surgery and interventional radiology have been gathered and combined with the fundamental principles of traditional trauma care to form the EVTM concept [23, 38] (Fig. 1.1). This concept does not replace traditional surgical or other solutions, but instead incorporates all available tools into a common trunk. The main points of the EVTM concept are listed in Table 1.1. It is based on a multidisciplinary approach to early evaluation, resuscitation, and hybrid

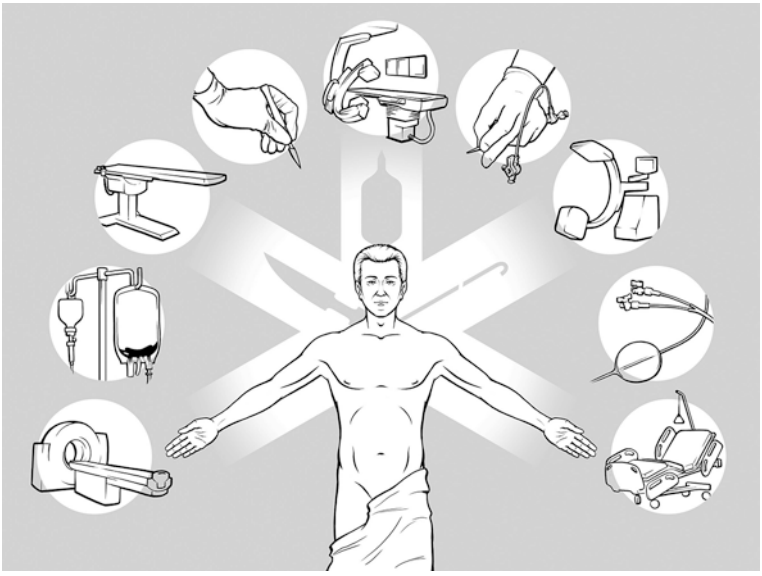

Fig. 1.1 The EVTM concept. Multidisciplinary and patient centered

Table 1.1 Main points of the EVTM[a] concept

• Early multidisciplinary team approach (hospital dependent)
• Early femoral arterial (and venous) vascular access during primary survey (AABCDE[b] principle)
• CTA[c] scan if possible. Always for hemodynamically stable patients (Trauma/bleeding protocol)
• REBOA[d] (partial/intermittent) if needed for temporary hemodynamic stabilization and bleeding control (REBOA is only a bridge to definitive care.)
• Hybrid mindset: endovascular tools and open surgery complement each other
• All procedures are performed on a sliding table (angiography table)
• Using modern CTA scans and ultrasound techniques for continuous patient evaluation in the direct postoperative period
• Vascular access maintenance and closure principles

Applicable from the prehospital scenario to the post-operative ICU period and adjustable to individual centers

[a]EndoVascular resuscitation and Trauma Management

[b]Airway, Access, Breathing, Circulation, Disability, Exposure

[c]Computed Tomography Angiography

[d]Resuscitative Endovascular Balloon Occlusion of the Aorta

definitive management of hemodynamically unstable patients (trauma and non-trauma). The application of EVTM is highly dependent on the skillset and capabilities of the managing team or center and the resources available, and therefore can and should be modified accordingly. The establishment of early arterial vascular access is essential for endovascular resuscitation. Puncturing the common femoral artery (CFA), which is the cornerstone access vessel, concurrent with airway assessment, saves time in the treatment of acute trauma. A modification has been suggested to the traditional "ABCDE" mnemonic advocated in the ATLS protocol. An EVTM-enabled provider should instead consider using "AABCDE" (Airway and simultaneous vascular Access, Breathing, Circulation, Disability, and Exposure) as an initial approach to trauma evaluation and treatment [21, 23, 38]. This mnemonic may better represent actual modern trauma practice, since hemorrhage control is vital in the "Golden hour." Controlling catastrophic bleeding is the major life-saving skill in trauma and vascular surgery, equivalent to airway management. The use of an AABCDE-centered concept for truncal or junctional injuries might be exceptionally useful in both civilian and military environments. The earlier CFA access is established the better (even with a 4–5 French sheet), preferably occurring during the resuscitation phase. The more the patient deteriorates, the harder it will be to get arterial access; therefore, the EVTM concept also recommends considering gaining bilateral access in major trauma cases. Upon circulatory collapse, it is directly possible to upgrade to a larger sheath (7 French) for REBOA placement. Apart from its endovascular bailout benefit, it provides a possibility for invasive blood pressure monitoring, blood analysis, arterial fluid resuscitation, and medical therapy. Other advantages of early CFA access are listed in Table 1.2.

Table 1.2 Additional advantages of early CFA[a] access

• The CFA[a] is a major available vessel that can be cannulated relatively easily
• The femoral area is usually not used during primary survey in the majority of centers
• Vascular access for angiography, embolization, endografting, etc.
• A relatively minimally invasive procedure
• Very fast in experienced hands
• Can be done by ultrasound, blindly, or surgical cut-down

[a]Common Femoral Artery

Another fundamental element of the EVTM concept is the multidisciplinary hybrid approach to the selection of temporary and definitive hemostatic solutions. Open and endovascular surgery are not two conflicting entities in treating a hemodynamically unstable patient, but rather complement each other in reaching hemorrhage control and definitive treatment. For example, the traditional treatment for intra-abdominal bleeding is laparotomy with abdominal packing. However, an EVTM-minded team might consider simultaneous CFA access and REBOA in Zone I for proximal control (minimizing distal exsanguination) and definitive treatment by transcatheter embolization or laparotomy. Simultaneous and concurrent activity is key. By joining forces, sharing knowledge, and profiting from broad expertise, blood loss is minimized and time to definitive hemorrhage control is reduced. This collaborative endeavor can only be successful with complete transparency, and clear communication and leadership. However, there is not always an indication to use the EVTM concept, so you should not use it just because you can. EVTM must always be considered but only used in the optimally selected patient at the right time, and if the expertise and resources are present. Recently, the concept was further extended to include more than just bleeding patients. Now, endovascular Cardio-Pulmonary Resuscitation (eCPR) and Extracorporeal Membrane Oxygenation (ECMO), as well as other hemodynamic instabilities, can be considered part of the EVTM approach [39].

1.3 Building the EVTM/REBOA Team: Resources Needed for Optimal EVTM

Major trauma and bleeding are two of the most challenging conditions for physicians to deal with, when decisions are not easy and are made under time pressure. The responsibility of having to make these decisions is demanding, regardless of experience. In the new era of EVTM, all phases of trauma care, from initial resuscitation, decision making, and ultimately definitive treatment, involve team work with a specific role for every member. One question is who should be part of an EVTM team and what resources are needed. The answer to this is quite simple: there are no restrictions on who should be part of the EVTM team, but only those with appropriate training should be performing endovascular procedures. The essence of

endovascular resuscitation is that much of the treatment can be accomplished with relatively basic (innovative) tools. Advances in the field of imaging and endovascular technology have allowed for a fundamental shift in the treatment of trauma patients. However, high-level technology is not of any use if it cannot be seamlessly integrated into the existing trauma system. The concept may be modified depending on the team members present, location, available resources as well as other factors.

A vital part in the management of NCH is locating the source of exsanguination. With the CTA bleeding protocol (or trauma protocol) and new CT technology, a total body scan takes no longer than a minute to perform (up to 2 min, if a venous phase is included). A CT scan is now faster, more reliable, readily available, and can be performed on patients where it was previously not considered feasible [40]. The major time-consuming part of a modern CT-scan is not the technical part, but rather the time for transfer and positioning, which can be improved with training and standard procedures [41]. Performing a CTA provides information by locating the source of bleeding and giving an insight into the overall injury of the trauma patient within a very short time. These factors together make the modern CT scan a very powerful tool in trauma care. Most modern Level-1 trauma centers therefore place their CT scanners either directly adjacent to or in the trauma bay. Focused Asset Sonography in Trauma (FAST) has also become widely available and is used routinely in many emergency services [42].

1.3.1 Why Waste Time on Imaging?

What is the point of locating the source of exsanguination using a CT scan if the patient deceases during the process? It is better to open the patient and manage the source. This was previously the adage and, in some circumstances, it still is. However, today, EVTM and faster imaging technology allows you to get the best of both worlds [20].

For example, in the right patient, an EVTM-enabled provider may consider placing a REBOA in a hypovolemic patient to stabilize blood pressure and minimize distal exsanguination, allowing time for CTA imaging to facilitate definitive surgical management. This is a clear example that should be debated and clarified by scientific research. A practical example of EVTM would be to insert a CFA sheath during primary survey before performing a CT scan on a stable patient, allowing immediate access for REBOA, endografting or embolization if hemodynamic deterioration occurs.

The modern hybrid operating theaters have opened the door for effortlessly combining open and endovascular surgical procedures with live imaging technology. Time is a major factor in trauma and bleeding patients. Allowing an EVTM team to simultaneously perform multiple procedures, without delay or need for transportation, is a significant advantage [43]. These hybrid suites are state of the art, usually located close to the operation rooms or trauma bay, and are ideal locations to treat trauma patients. Another option is the conversion of a surgical suite

to a semihybrid operating theatre. Using a simple C-arm and a proper surgical table enables imaging during surgery. For REBOA or simple embolization, a C-arm fluoroscopic X-ray system is more than sufficient. In prehospital or initial care, REBOA can also be inserted without any form of radiologic control [44]. This implicates that EVTM principles should not only be used in high economic/modern centers, but also austere (military) environments and rural underdeveloped locations [45–47].

1.4 Optimal Provider Training and Challenges to Skillset Acquisition and Maintenance

As with all training for trauma care providers, teaching the concept has to rely on literature, simulated scenarios, porcine and cadaver hands-on experience, or virtual reality [9, 25, 48–50]. Real patients are not acceptable for practice, especially since most endovascular resuscitation procedures are time-sensitive in a trauma environment. There is therefore a need to specifically educate and train physicians in EVTM issues, especially as it has not been incorporated into the ATLS or in DSTC course 2018 in The Netherlands. Endovascular resuscitation methods for hemorrhage control are complex procedures and can be enormously challenging. Becoming familiar with the tools and the EVTM concept is paramount in order to deliver optimal endovascular care and EVTM team work.

Generally, trauma surgeons and emergency physicians are those responsible for trauma patients upon hospital admission. However, EVTM is not and should not be provider specific, but instead a concept understood by all those involved in order to find common ground. At Level-1 trauma centers, experts within basic or advanced endovascular methods for resuscitation will be present; however, other care facilities might not have such expertise available. Optimal provider training should therefore aim at introducing the EVTM concept to the medical care provider, focusing on establishing basic vascular access and use of REBOA [51]. All participants should be familiar with a vascular access kit and the Seldinger technique in order to follow the suggested AABCDE mnemonic [52]. In a stress-free environment, establishing vascular access may seem like a walk in the park. However, in a patient with hypovolemic shock, imminent circulatory collapse with no palpable femoral pulsations, or even ongoing CPR, it might not be so straightforward. In these cases, it is important that the EVTM provider also has basic knowledge of additional appliances such as ultrasound and fluoroscopy to facilitate the procedure as needed. Obviously, open cut-down is used when applicable and senior team members should be able to perform this bailout procedure [53].

Of the tools used in EVTM, REBOA is one of the most important, but it is still to some extent controversial. This endovascular technique uses the inflation of a compliant balloon in the aorta to limit the flow of blood distally, potentially increasing coronary and cerebral perfusion and stabilizing the patient [16]. If used in the right way, by the right person with appropriate training, and in the right patient, it may be the difference between life and death, acting as a bridge to definitive treatment.

Acquiring the appropriate knowledge and hands-on training may be challenging in the current stream of superspecialization, with endovascular workshops and courses being sparse. The Basic Endovascular Skills for Trauma (BEST) and Endovascular Skills for Trauma and Resuscitative Surgery (ESTARS) courses are run in the United States, and are mostly attended by trauma surgeons [49, 50]. The Diagnostic and Interventional Radiology in Emergency, Critical Care, and Trauma (DIRECT) educational workshop in Japan was established as a multidisciplinary collaborative attempt to diminish the gap between trauma surgeons, emergency medicine physicians, and interventional radiologists involved in trauma care [48]. The EVTM Workshop in Örebro, Sweden (http://www.jevtm.com/workshop/), is the only European EVTM workshop. It is defined as a workshop and not a course as it allows both organizers and attendees to mutually exchange knowledge, experience, and ideas in order to stimulate further development. This is all part of a multidisciplinary approach to introducing the EVTM concept and basic endovascular techniques into trauma management. To further contribute to the cause, the organizers of the Örebro EVTM workshop also help to build similar workshops worldwide.

Teamwork is an essential part of the EVTM doctrine, with quality of care being based on technical skills, material, and teamwork. Therefore, during the workshops, special emphasis is given to (international) collaboration and judgment-free learning. With continued experience, however, the collaborators of this textbook believe that EVTM is poised to become an integral element of hybrid trauma care in the earliest phases after injury. It is, therefore, our aim to introduce and/or facilitate the implementation of the EVTM concept around the world, in order to limit death caused by exsanguination. This integral approach might cause a paradigm shift in trauma care and is only possible with a dedicated team and a clear vision. The mission of the EVTM International Collaboration Workgroup is to gain insight into the safety and the effect of EVTM. An example of implementing the EVTM concept in a trauma patient can be seen in Fig. 1.2. This demonstrates a modern multidisciplinary team approach to trauma management.

Expert's Comments by Ernest E. Moore

The resuscitative balloon occlusion of the aorta (REBOA) revelation may be the beginning of the EndoVascular resuscitation and Trauma Management (EVTM) revolution. The authors of the this chapter have nicely described the current state of EVTM and the implications of the widespread adoption of REBOA. The team concept is perhaps more important in EVTM than any other emergent intervention, because unique equipment is required, and conditions necessitating alternative equipment may occur rapidly. The implementation of EVTM will be regionally dependent as the composition of physicians with the required technical skills, and assistants who are familiar with the equipment, within an institution will vary substantially. Within the spectrum of essential technical skills, perhaps, there should be a distinction of three levels of expertise. The basic skills include

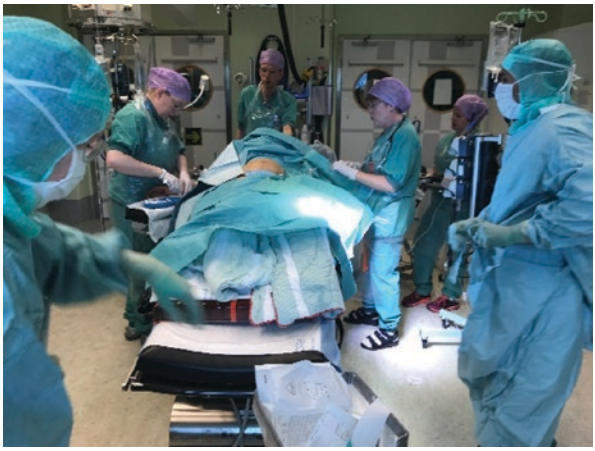

Fig. 1.2 Practical example of EVTM in a trauma patient: Patient with an unstable pelvic bleeding. Hybrid setup with a sheath placed in left femoral artery before anesthesia induction, pelvic packing, explorative laparotomy packing, angiography, and orthopedic leg extension-fixation, all performed in the same place by a multidisciplinary team. Setup—notice the angiotable. Left femoral artery sheath for REBOA and/or embolization

vascular ultrasonography, common femoral artery sheath placement, subdiaphragmatic aortography, and pelvic angioembolization. The intermediate level includes selective angioembolization of solid organs and stenting of the aorta and junctional vascular injuries. Advanced techniques include stenting of aortic branches and carotid/vertebral arteries. There is little debate that a hybrid operating room (OR) is essential to acquire optimal imaging, ensure safety of those involved in these procedures, and allow rapid open access if needed. While the C-arm in a trauma OR may be a reasonable starting point, this provides suboptimal imaging and inadequate radiation protection. The CT-hybrid model, established by the Japanese, is appealing in that it provides the additional resources to comprehensively manage the critically injured patient. Assuming appropriate skills are acquired, which physician should lead EVTM is highly controversial at this time. I submit that it should be those who are on call, have the appropriate skills, and are physically in the hospital 24/7. In the United States, this is relatively straightforward; the U.S. trauma surgeon is in the emergency department (ED) to initiate treatment of the most seriously injured, continues with operative care, and provides management in the intensive care unit (ICU). The challenge in the United States is appropriate training, particularly in the current framework of trauma and acute care surgery (TACS) fellowships. Unfortunately, the current fellowship training is inadequate to acquire basic EVTM skills, and most trainees are unwilling to add an additional 2 years of formal vascular training. Thus, we need to develop trauma-specific EVTM fellowships to ensure appropriate training for basic and intermediate EVTM capabilities in additional to open operative procedures. Similarly, military surgeons need this preparation. The challenges may be

greater in Europe, because the "visceral surgeon" usually provides trauma coverage and does not typically supervise ED and ICU care. The solution will undoubtedly vary across the world, but critically injured patients deserve access to regional centers with EVTM capabilities. The authors have begun to build the foundation for a new era of trauma care.

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Principles of Modern Trauma Resuscitation

2

Rowan R. Sheldon and Matthew J. Martin

2.1 Background on Hemorrhage and Resuscitation

Hemorrhage accounts for nearly 40% of civilian trauma deaths and up to two-thirds of preventable military battlefield deaths [1–3]. In addition to the already high morbidity and mortality associated with major hemorrhage, there has been an increasing realization that some widely accepted and utilized resuscitation practices were actually contributing to the development or worsening of coagulopathy, excess hemorrhage, and increased late complications, including acute respiratory distress syndrome and abdominal compartment syndrome. This civilian data coupled with the experience over the past decade-plus of US and NATO military combat operations has led to a renewed focus on optimizing the management of the massively bleeding trauma patient. This has included the development of new strategies for early hemorrhage control coupled with major changes in the approach to resuscitation of the bleeding trauma victim. When performed correctly, resuscitation maintains adequate tissue oxygenation and restores end-organ perfusion without compromising hemostasis or exacerbating hemorrhage and end-organ injury. When performed incorrectly, however, resuscitation can exacerbate physiologic derangement, worsen metabolic acidosis and coagulopathy, and push patients closer to cardiovascular collapse.

An additional major advancement in the care of the injured patient has been the development and continued refinements of minimally invasive and endovascular

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techniques, procedures, and devices. Historically, endovascular techniques in the trauma patient were mainly limited to diagnostic angiography performed during the in-hospital phase of care to identify select major vascular injuries. This was then followed by basic endovascular interventions for bleeding, such as coil or gelfoam embolization. The past decade has now seen a rapid and continued explosion of endovascular trauma management techniques, including endovascular interventions and stenting for major vascular injuries, and endovascular interventions for aortic balloon occlusion (REBOA) to temporize patients with non-compressible truncal hemorrhage. However, the use of these techniques must still be paired with smart and effective resuscitation strategies that work synergistically to achieve hemostasis, stabilization, and end-organ perfusion and decrease morbidity and mortality. In select cases, these endovascular techniques may help achieve earlier hemostasis while simultaneously creating additional resuscitation challenges due to factors such as ischemia-reperfusion injury following REBOA application. Therefore, the modern trauma practitioner must be well versed in the current best evidence-based resuscitation practices and have an appreciation for how to apply and adjust them to an individual patient based on the type and severity of injuries, the physiologic response and degree of shock, and the impact of any endovascular or open interventions. This chapter seeks to describe the evolution of current optimal trauma resuscitative strategy, explore best practices, and identify future directions for improvement.

2.2 A History of Resuscitation Strategies

Modern trauma resuscitation has evolved significantly over the past 100 years and has been particularly impacted by the experiences and evidence gained from the high volume of severely injured patients during times of war. World War I brought about the first use of whole blood in severely injured patients. After improving blood typing [4, 5], prolonged storage [6], safe transport [7], and rapid administration [8], battlefield hospitals in 1918 were reportedly transfusing between 50 and 100 pints (approximately 25–50 L) of blood to an average of 50 wounded each day [7]. Limitations on broad field use spurned the development of lyophilized plasma at the beginning of World War II [9, 10]. With greater ease of transport and storage, plasma became the resuscitative bridge to higher levels of care. A fundamental understanding that plasma lacked oxygen-carrying capability [11], however, meant that resuscitation switched to a whole blood-based model as soon as possible. The primacy of whole blood resuscitation led to the first large-scale studies demonstrating improved survival through rapid transport to surgical care [12, 13].

As physiologists gained greater understanding of the consequences of extreme fluid deficits in hemorrhagic shock [14], the military began to advocate aggressive large volume resuscitation. The widespread implementation of this strategy in Vietnam saw both improved survival and decreased renal failure [15, 16]. While improving circulatory support, however, the new strategy gave rise to acute respiratory distress syndrome, otherwise known at the time as DaNang lung or shock lung [17]. Despite the complications, high volume resuscitation continued to predominate.

Tenants of damage control resuscitation
1. Minization of isotonic crystalloid fluids
2. Permissive hypotension
3. Transfusion of balanced blood products
4. Goal-directed correction of coagulopathy

Fig. 2.1 Tenants of damage control resuscitation

Further study then began demonstrating a distinctive pathology of trauma-associated coagulopathy. The derangement arose from both a biochemical and a dilutional etiology [18–20]. In this setting, it was found that aggressive resuscitation not only worsened coagulopathy, but increased the incidence of abdominal compartment syndrome, acute respiratory distress syndrome, multiple organ failure, and death [21–23]. In parallel with the advent of damage control surgery came damage control resuscitation. As evidence compounded, it led the US Army to publish a suggested resuscitation algorithm which recognized the metabolic consequences of inappropriate fluid resuscitation and suggested the judicious use of permissive hypotension resuscitation [24]. In its current iteration, damage control resuscitation focuses on four key components: minimization of isotonic crystalloid, permissive hypotension, transfusion of a balanced ratio of blood products, and goal-directed correction of coagulopathy (Fig. 2.1).

The most recent military experience gained from over a decade of sustained combat operations in Iraq and Afghanistan has also provided a significant body of evidence supporting the use of whole blood as a primary resuscitative measure for patients with traumatic hemorrhage. Although whole blood is rarely used in the civilian environment due to concerns about safety, storage, and cost-effectiveness versus component therapy, it has been widely utilized by the United States and most NATO countries during this conflict. Although initially performed out of necessity due to the unavailability of component products in austere combat medical treatment facilities, the use of fresh whole blood has been embraced by the military as the superior approach to the massively bleeding patient. Transfusion of warm fresh whole blood automatically replaces red cells, plasma (including fibrinogen and clotting factors), and platelets in a 1:1:1 ratio. In addition, it avoids any of the adverse effects demonstrated with prolonged storage of blood products, also known as "storage lesion," that may decrease their efficacy and safety. More recently, the military and some civilian trauma centers have begun to use stored whole blood as a primary resuscitative blood product. Although there is no true "universal donor" blood type when using whole blood, the current data supports the use of type O blood with low-titer levels of antibodies. Further data is required to demonstrate the ultimate benefits and patient selection for using fresh and/or stored whole blood, but this remains the resuscitation product of choice in select military and other austere settings.

2.3 Finding the Appropriate Ratio

The critical importance of ensuring adequate oxygen delivery cannot be overstated. It is clear, however, that equally important in the balanced transfusion of blood products after trauma is the correction of the patients altered physiology and coagulopathy. When blood component therapy was first initiated en masse in the civilian sector, there was an emphasis on the administration of large quantities of stored packed red blood cells in an attempt to maximize oxygen delivery and to base the transfusion of plasma or platelet products on the later development of laboratory coagulation abnormalities or clinical signs of severe coagulopathy. A common standard of care was to provide 1 unit of fresh frozen plasma (FFP) for every 6 units of packed red blood cells (PRBCs) and 1 unit of platelets for every 10 units of PRBCs [25], with the plasma and platelets typically being given in a delayed fashion. This approach, however, underestimated the combined insult to the coagulation cascade that occurred as a result of dilution, consumption, and dysfunction. In addition, this approach did not fully appreciate that coagulopathy is frequently present at the time of admission or shortly thereafter in the most severely injured patients. As a consequence, any delays in focused intervention will often fail to correct the now irreversible coagulopathy or will lead to preventable excess morbidity and mortality due to hemorrhage.

Continued reviews over the years have demonstrated that higher ratios of FFP/PRBCs portend improved results in trauma patients. Duchesne et al. found that patients who experienced trauma requiring surgery and massive transfusion showed dramatically improved survival with a 1:1 FFP:PRBC ratio as opposed to those who received a 1:4 ratio (74% vs. 12.5%, $p < 0.0001$) [26]. Among the most influential early studies on using higher ratio transfusion strategies was a review of military combat data by Borgman et al. that found a stepwise improvement in mortality with increasing ratios of FFP:PRBCs. In this analysis, patients receiving 1:8, 1:2.5, and 1:1.4 showed mortality rates of 65%, 34%, and 19%, respectively ($p < 0.001$) [27] (Fig. 2.2).

While the preponderance of the evidence was highly suggestive that a higher plasma/PRBC ratio was better for patients, the retrospective nature of the data raised

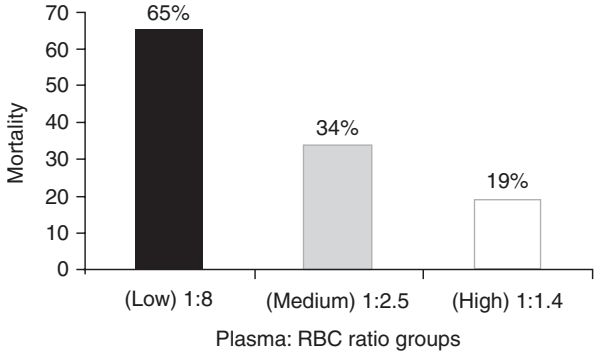


Fig. 2.2 Mortality associated with low, medium, and high plasma to RBC ratios transfused at admission following combat trauma. (Reprinted with permission from: Borgman M et al., J Trauma. 2007;63:805–13)

concerns. In order to identify study patients, prior studies collected patients who met the classic definition of massive transfusion—those receiving at least 10 units of PRBCs in a 24-h period. To meet this threshold, however, patients would have to survive long enough to utilize this higher number of units. The concern for survivor bias was later substantiated when Snyder et al. studied FFP/PRBC ratio as a time-dependent covariate in a multivariate cox proportional hazards model. What they found was that if you controlled for the timing of component administration, the 24-h survival difference between high FFP/PRBC and low FFP/PRBC ratios disappeared [28].

To combat survival bias, clinical researchers sought to find a well-validated definition that could enable prospective data collection. Savage et al. prospectively analyzed severely injured patients receiving at least 1 unit of PRBCs and analyzed their outcome and need for massive transfusion. They found that patients who received 3 units of PRBCs in any given 60-min period had a twofold increased risk of death. They concluded that this threshold, now defined as the critical administration threshold (CAT), could be utilized to allow for improved prospective data collection and study in the highest-risk patient populations [29].

The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) Study then utilized this new CAT metric to prospectively analyze 905 patients arriving to ten US Level-1 trauma centers. The PROMMTT trial found that those who had received an FFP/PRBC ratio greater than 1:2 early on in their resuscitation demonstrated better survival at both 30 min and 6 h [30]. This trial, however, also had limitations. While the demographics and injury severity of the analyzed groups were similar, the lack of randomization raised additional concern for selection bias and other unmeasured confounders. The 2015 Pragmatic, Randomized, Optimal Platelet and Plasma Ratios (PROPPR) trial was a randomized attempt to compare 1:1:1 FFP/platelets/PRBCs ratio to a 1:1:2 ratio. After analyzing 680 patients, the authors found a significantly increased rate of hemostasis at 24 h among the 1:1:1 group compared to the 1:1:2 group (86% vs. 78%) and decreased death due to exsanguination (9% vs. 15%). When analyzed for 6-h, 24-h, or 30-day mortality, however, no such significance was observed. Also of importance, however, was the fact that even though the 1:1:1 group received a significantly greater amount of blood products over the first 24 h, there was no significant difference among the two groups in regard to ARDS or multiple organ failure [31].

Based upon this data, the trauma community has coalesced around the balanced administration of FFP, platelets, and PRBCs. The Eastern Association for the Surgery of Trauma (EAST) and the Department of Defense (DoD) Joint Trauma System (JTS) have both published clinical practice guidelines recommending the administration of blood products with a ratio approaching 1:1:1 [32, 33]. The American College of Surgeons Trauma Quality Improvement Program (ACS TQIP) suggests a slight flexibility, recommending administration somewhere between 1:1:1 and 1:1:2 [34]. One constant throughout, however, is that all of these societies place an emphasis on the early and empiric administration of plasma and platelets as part of a "balanced" resuscitation strategy, as opposed to delaying administration based on subsequent development of laboratory evidence of coagulopathy or

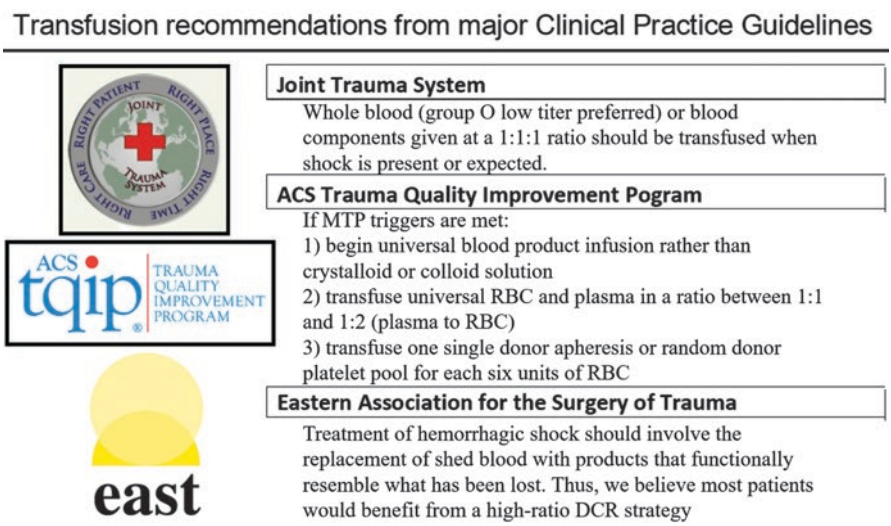


Fig. 2.3 Transfusion recommendations according to clinical practice guidelines from major trauma societies

clinical signs of coagulopathy (Fig. 2.3). In addition, if component products are not available or feasible, such as seen in the military or other austere environments, then whole blood transfusion should be utilized as an appropriate means of achieving a 1:1:1 ratio resuscitation. Figure 2.4 demonstrates an algorithm for utilization of a high ratio damage control resuscitation approach in the fully resourced setting, as well as in the resource constrained or austere environment utilizing fresh whole blood. Finally, data analysis from the experience with stored whole blood (low-titer type O) in the military and in select civilian institutions will be critical to identifying whether this is equivalent to warm fresh whole blood and/or component therapy in bleeding trauma patients.

2.3.1 Component Therapy

Multiple studies have found a correlation between injury severity and the extent of acute coagulopathy in trauma [19, 35] and a growing body of evidence is suggesting that this increase is secondary to an endogenous process (Fig. 2.5) [36]. As described by Simmons et al. in 2014 [36], trauma results in damage to the endothelial layer of the blood vessel causing an increase in cellular surface expression of thrombomodulin (TM) and endothelial protein C receptor (EPCR) [18, 37]. Significant trauma also causes a release of thrombin. While normally found at the site of injury, overwhelming tissue trauma can cause thrombin's systemic release. TM, EPCR, and thrombin then bind to protein C, causing activation and a 5–20-fold upregulation in activity [38]. Activated protein C then causes cleavage of factors V and VIII, factors essential in fibrinous clot formation, and upregulation of fibrinolysis through

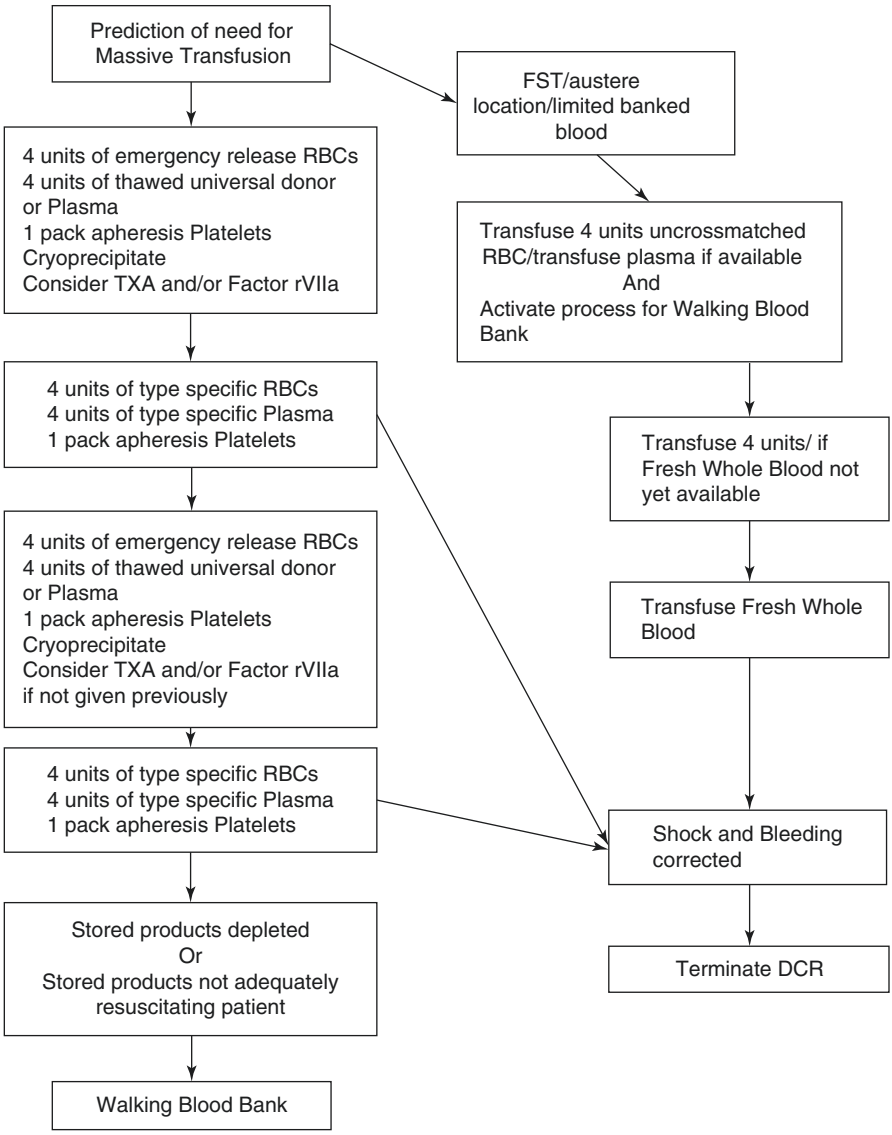


Fig. 2.4 An algorithm for utilization of a high ratio damage control resuscitation in both a fully resourced setting and a resource-constrained environment. (Reprinted with permission from: Martin M, Beekley A, Eckert M (eds), Front Line Surgery, 2nd Edition, Springer Publishing, 2017)

inhibition of plasminogen activator inhibitor 1 [39]. FFP has also been shown to either partially improve or to entirely prevent significant endothelial injury and glycocalyx shedding that is associated with hemorrhagic shock and the administration of crystalloid fluids.

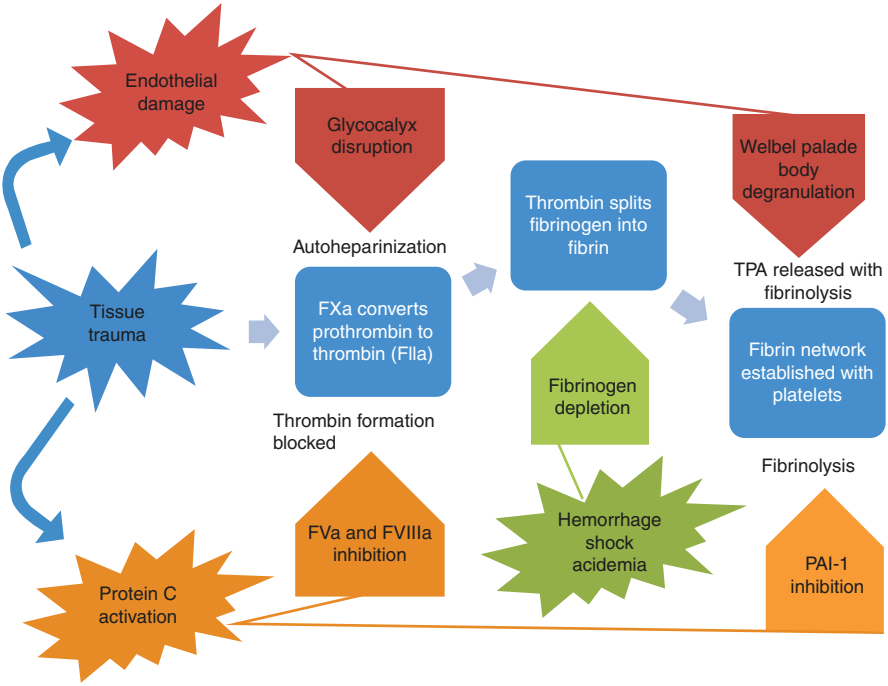


Fig. 2.5 Changes in trauma-induced coagulopathy affect multiple vital functions in the coagulation cascade. Blue, normal coagulation; red, endothelial glycocalyx disruption coagulopathy; orange, activated protein C coagulopathy; green, fibrinogen depletion coagulopathy. (Reprinted with permission from: Simmons J, et al. Trauma-induced coagulopathy. Curr Anesth Rep. 2014;4(3):189–99)

FFP performs a vital role in both intravascular volume expansion and the correction of trauma-induced coagulopathy. Administration of plasma has been shown to statistically increase the levels of fibrinogen, factor II, factor V, factor VII, factor IX, factor X, and factor XII [40], and, as noted in our discussion of the PROPPR trial above, higher ratios of FFP/PRBCs demonstrated improvement in hemostasis [31]. Despite these findings, the complexities of trauma-induced coagulopathy suggest that FFP alone may be inadequate at correcting all of the physiologic derangements of trauma victims. Specifically, FFP does not target the destruction of factors V and VIII or stem the tide of fibrinolysis that accompanies major trauma (Fig. 2.6).

2.3.1.1 Tranexamic Acid

Fibrinolysis is a normal physiologic mechanism by which the body seeks to break down clots and to recanalize obstructed vessels and remodel the body after injury. When the body loses control of this process, however, the effects can be catastrophic [41]. Hyperfibrinolysis has been independently associated with higher mortality in patients with severe trauma [42]. In a retrospective review of major traumas, severe hyperfibrinolysis (those with complete clot dissolution at 30 min) portended a 100% mortality [43]. With this scientific underpinning, tranexamic acid (TXA) has sought

Blood product	Volume (per unit)	Shelf-life	Indications	Dosage & response
Red blood cells	250-300mL	35-42 days	Symptomatic anemia, active bleeding, massive transfusion	1-2 units, depending on hemodynamic stability; 1 unit should increase hemoglobin by 1 g/dL in *non-bleeding* patients
Platelets (single donor or pooled-donor)	200-300mL	3-5 days	Thrombocytopenia, active bleeding, massive transfusion	1-2 units depending on severity of thrombocytopenia; 1 unit should increase platelet count by 20,000 to 40,000 platelets/μL
Cold-stored platelets	200-300mL	5-10 days (and potentially longer)	Same as above	Same as above
Frozen plasma	250-300mL	1 year (24 h after thawing, stored at 1-6 °C)	Multiple clotting factor deficiencies, active bleeding, liver failure, massive transfusion, warfarin reversal, plasma exchange	10-15 mL/kg of body weight; intrinsic INR of 1.3-1.7 in each unit of plasma
"Thawed" Plasma	250-300mL	5 days	Multiple clotting factor deficiencies, active bleeding, liver failure, massive transfusion, warfarin reversal, plasma exchange	10-15 mL/kg of body weight; intrinsic INR of 1.3-1.7 in each unit of plasma
Liquid plasma	250-300mL	26 days	Active bleeding, massive transfusion	10-15 mL/kg of body weight; intrinsic INR of 1.3-1.7 in each unit of plasma
Cryoprecipitate	10-20mL	1 year (4-6 h after thawing stored at 20-24 °C)	Hypofibrinoginemia DIC, liver failure, Von Willebrand's disease, massive transfusion	5-10 pooled units; fibrinogen level should increase by 5-10 mg/gL per unit transfused
Fresh warm whole blood	450-500mL	24-72 h	Massive transfusion, insufficient availability of blood Components	Variable dose based on severity of bleeding
Stored Whole Blood	450-500mL	35-42 days	Massive transfusion, insufficient availability of blood components	Variable dose based on severity of bleeding

Fig. 2.6 Characteristics of blood products and components. (Reprinted with permission from: Salim A, Brown C, Martin M, Inaba K (eds). Surgical Critical Care Therapy, 1st Edition. Springer Publishing, 2018)

to arrest the hyperfibrinolytic mechanisms found in trauma. TXA had previously been found to be far more potent than ϵ-aminocaproic acid and had been in use since the 1960s in the treatment of bleeding from hereditary coagulopathies, orthopedic surgery, and GI hemorrhage [44, 45]. Its utility in trauma, however, came to the forefront with the publication of the CRASH-2 trial in 2010.

The CRASH-2 trial was a randomized, controlled, multi-center trial that studied 20,211 adult trauma patients with, or at risk of, significant bleeding within 8 h of their injury. After randomization to receive either TXA or a matching placebo, the patient was then followed for all-cause mortality, death due to hemorrhage, total blood products administered, and complications such as vascular occlusive events. The investigators found that TXA administration demonstrated a significant reduction in all-cause mortality (RR 0.91, $p = 0.0035$) and death due to hemorrhage (RR 0.8, $p = 0.0036$), with no statistical change in number of blood products administered (6.06 U vs. 6.29 U) or vascular occlusive events (1.7% vs. 2.0%) [46].

This was refined in 2011 as the CRASH-2 collaborators further analyzed their data. Patients were stratified based upon the time from injury to treatment. Early treatment with TXA (less than 1 h from injury) demonstrated a significantly reduced risk of death due to bleeding (RR 0.68, $p < 0.0001$). Treatment given between 1 and 3 h from injury also reduced the risk of hemorrhagic death (R 0.79, $p = 0.03$). Treatment after 3 h, however, demonstrated an association with an increased risk of death due to hemorrhage (R 1.44, $p = 0.004$). However, this finding was only seen on post-hoc analysis and the randomization scheme did not include time from injury and thus remains a subject of debate. But based on this finding, the CRASH-2 collaborators concluded that TXA was effective at minimizing hemorrhagic death in severe trauma, but only when it is given within 3 h of injury [47].

This data was then validated in a military setting in the Military Application of Tranexamic Acid in Trauma Emergency Resuscitation (MATTERs) study. Through a retrospective observational cohort study, a Role 3 Echelon surgical hospital in southern Afghanistan compared TXA administration with no TXA in patients receiving at least 1 unit of PRBCs after arrival within 1 h of combat injury. This study found that not only did the TXA group have a lower unadjusted mortality rate than the no-TXA group (17.4% vs. 23.9%, $p = 0.03$), but among those who required massive transfusion, the reduction in mortality was nearly 50% (14.4% vs. 28.1%, $p = 0.004$) [48]. A subsequent military study in severely injured pediatric combat trauma victims, the PEDTRAX study, similarly found an overall survival benefit and improved neurologic outcomes associated with TXA administration [49].

The trauma community and the military have now largely embraced TXA as an adjunctive measure to decrease hemorrhagic death (Fig. 2.7). The clinical practice guidelines of EAST, the DoD JTS, and the ACS TQIP suggest empirically treating casualties at high risk of hemorrhagic shock as long as TXA can be administered within 3 h of surgery [32–34]. For eligible casualties, the suggested dosing is 1 g intravenously administered in 100 mL of normal saline over 10 min, followed by another 1 g delivered over 8 h. However, in practice, many groups have adopted a protocol of giving the initial 1 g bolus dose and either not administering the follow-on infusion or re-dosing via bolus for patients with ongoing or inadequately controlled hemorrhage.

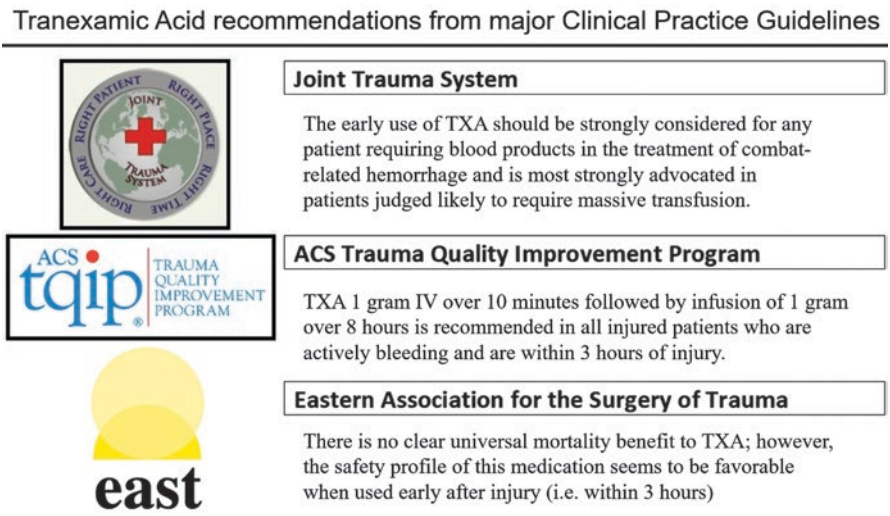


Fig. 2.7 Tranexamic acid recommendations according to clinical practice guidelines from major trauma societies

2.3.1.2 Cryoprecipitate and Fibrinogen Concentrates

Fibrinogen plays a critical role in maintaining hemostasis after traumatic hemorrhage. As traumas progress, however, levels of fibrinogen are rapidly depleted. In cases of severe trauma, fibrinogen levels are frequently observed to decline even before a patient reaches treatment [50, 51]. Subsequent resuscitation has then been seen to exacerbate this depletion by diluting the remaining substrate [52]. Low levels of fibrinogen have long been associated with uncontrolled hemorrhage and hypofibrinogenaemia and, even in atraumatic patients, can lead to continued bleeding and hemarthrosis [53]. Prior studies suggested that a threshold of fibrinogen levels of 100 mg/dL was required to allow for normal coagulation [54]. Observational reviews, however, have demonstrated continued bleeding at these levels, thereby resulting in clinical practice guidelines in the United States recommending maintaining levels greater than 180 mg/dL [33, 55].

FFP contains levels of fibrinogen capable of raising serum fibrinogen levels, but even high volume plasma transfusion (30 mL/kg) has only demonstrated average post-transfusion fibrinogen values of 100 mg/dL [40]. The amount of fibrinogen in any given unit of FFP is also not controlled and may be highly variable. Cryoprecipitate, however, carries 4–8 times the amount of fibrinogen in the same volume [56]. The CRYOSTAT-1 study demonstrated the ability to maintain fibrinogen levels over 180 mg/dL in severely injured patients by utilizing early cryoprecipitate in a balanced trauma resuscitation but was unable to demonstrate a mortality benefit [57]. A follow-on multicenter randomized study, CRYOSTAT-2, is ongoing and pending the reporting of results. The MATTERs II study showed a reduction in mortality when cryoprecipitate was used in trauma resuscitation (OR 0.61, $p = 0.02$) in a battlefield setting but did not have the laboratory capabilities to track fibrinogen

levels. Combining this data, it is highly suggestive that the elevation of fibrinogen resulting from the addition of cryoprecipitate to balanced resuscitation strategies is responsible for a reduction in mortality and morbidity. An alternative to rapidly replacing fibrinogen in the bleeding patient is the administration of fibrinogen concentrates. These products are pharmacologic preparations of purified and concentrated fibrinogen that can rapidly and more effectively replace fibrinogen compared to FFP or even cryoprecipitate. They are shelf stable, require no cross-matching, and can be immediately available for use in the injured patient without special preparation. The major drawback to these products is their cost, which is significantly higher than either FFP or cryoprecipitate in terms of cost per dose. Whether they are ultimately cost-effective remains an area of debate, and will require further study to analyze their impact (if any) on improved outcomes.

Currently, more studies are underway to further elucidate the connection between early aggressive fibrinogen supplementation and outcomes. The FEISTY study is an exploratory, multicenter, randomized controlled trial comparing fibrinogen concentrates to cryoprecipitate for fibrinogen supplementation in traumatic hemorrhage using thromboelastographic to guide and dose supplementation [58]. The FlinTIC study is a randomized controlled trial seeking to evaluate the utility of fibrinogen concentrates in the prehospital setting [59]. While we anxiously await the results of these two studies, there has been sufficient evidence for the DoD JTS to suggest the early use of cryoprecipitate as part of a balanced resuscitation. They suggest that a 10-unit bag of cryoprecipitate be included in the first pack of any massive transfusion protocol with an overall goal of approximating a 1:1:1:1 PRBC/FFP/platelet/cryoprecipitate ratio [34].

2.3.1.3 Factor Concentrate-Based Resuscitation Strategies

As described above, the United States has largely adopted a strategy of damage control resuscitation using conventional blood products (PRBC, FFP, PLTs) in a 1:1:1 ratio or using whole blood in highly select settings. An alternative approach that has mainly been utilized by European centers is the use of purified factor concentrate products either as augmentation of the plasma component of resuscitation or to entirely replace the need for FFP and cryoprecipitate [60]. The main factor concentrates utilized in these strategies include fibrinogen factor concentrate (FFC), which has been previously described, and prothrombin complex concentrates (PCC). PCC products are purified and concentrated solutions containing primarily the vitamin-K-dependent clotting factors. The preferred PCC is now the 4-factor PCC solution, which contains factors II, VII, IX, and X, as well as the antithrombotic factors proteins C and S.

Arguments for this factor-based approach to resuscitation include the fact that factor concentrates can more rapidly and effectively replace depleted fibrinogen and clotting factors, have no risk of viral transmission or transfusion reactions, and require no cross-matching or prolonged preparation [61–63]. Arguments against this approach include concerns over the high cost of these products and the lack of well-controlled studies demonstrating their safety and efficacy in massively bleeding trauma patients. However, there is an increasing body of evidence

and experience indicating that this strategy is at least as effective as using standard blood products and may be superior in terms of resource utilization, avoidance of transfusion, and in select outcome measures [60]. Several retrospective series have demonstrated that an FC-based approach resulted in significantly improved hemostasis and less requirement for PRBC transfusion and was associated with decreased rates of post-resuscitation complications and organ failure [61, 63–65]. More recently, a 2017 prospective randomized trial (RETIC Trial) randomized 100 severely injured patients with evidence of coagulopathy on rotational thromboelastometry (ROTEM) to either an FC-based resuscitation strategy or an FFP-based approach [66]. The study demonstrated that the FFP-based approach was associated with a significantly higher failure to correct coagulopathy and required rescue therapy in 52% versus only 4% in the FC-based group. In addition, the need for massive transfusion was significantly lower in the FC-based group, prompting the study to be terminated early due to safety concerns with the FFP-based approach. Figure 2.8 demonstrates an algorithm outlining the approach to utilizing an FC-based resuscitation strategy based on viscoelastic testing. However, it should be noted that this approach requires the use of thromboelastography (TEG) or ROTEM and running multiple simultaneous assays, which may not be readily available at many centers. A simplified and empiric FC-based approach using only clinical parameters that has been proposed is shown in Fig. 2.9 and emphasizes the sequential approach of stopping hyperfibrinolysis (TXA), enabling clot formation with FFC and platelets, and then increasing thrombin generation potential with PCC.

2.3.1.4 Factor VIIa

In the 2000s, recombinant factor VIIa gained support as an adjunctive tool for cessation of massive hemorrhage. In 2005, a randomized prospective trial demonstrated an average reduction of 2.6 units of PRBCs per patient ($p = 0.02$) but failed to see a difference in mortality or critical complications [67]. Excitement then grew as a 2007 retrospective review of trauma admission to a combat support hospital in Iraq demonstrated a 20% reduction in trauma patients requiring massive transfusion. Again, however, no statistical significance could be drawn in regard to outcomes [68]. At this time, it appeared that rFVIIa could prove useful in the armamentarium against massive hemorrhage, but its large cost per dose and underpowered studies limited its acceptance. Finally, in 2012, a Cochrane review of 29 randomized controlled trials and 4290 patients gained the power necessary to suggest the actual effect on clinical outcomes. The aggregate data continued to demonstrate a minor decrease in blood loss (mean difference −297 mL) and PRBC transfusion requirements (MD −261) with rFVIIa treatment. Unfortunately, however, there was no statistical reduction in mortality (RR 0.85; 95% CI 0.72–1.01), and there was a trend towards an increase in thromboembolic adverse events (RR 1.14; 95% CI 0.89–1.47). As such, it led the authors of the review to conclude "…The data supporting the off-license use of recombinant FVIIa are weak. The use of rFVIIa outside its current licensed indications should be restricted to clinical trials" [69].

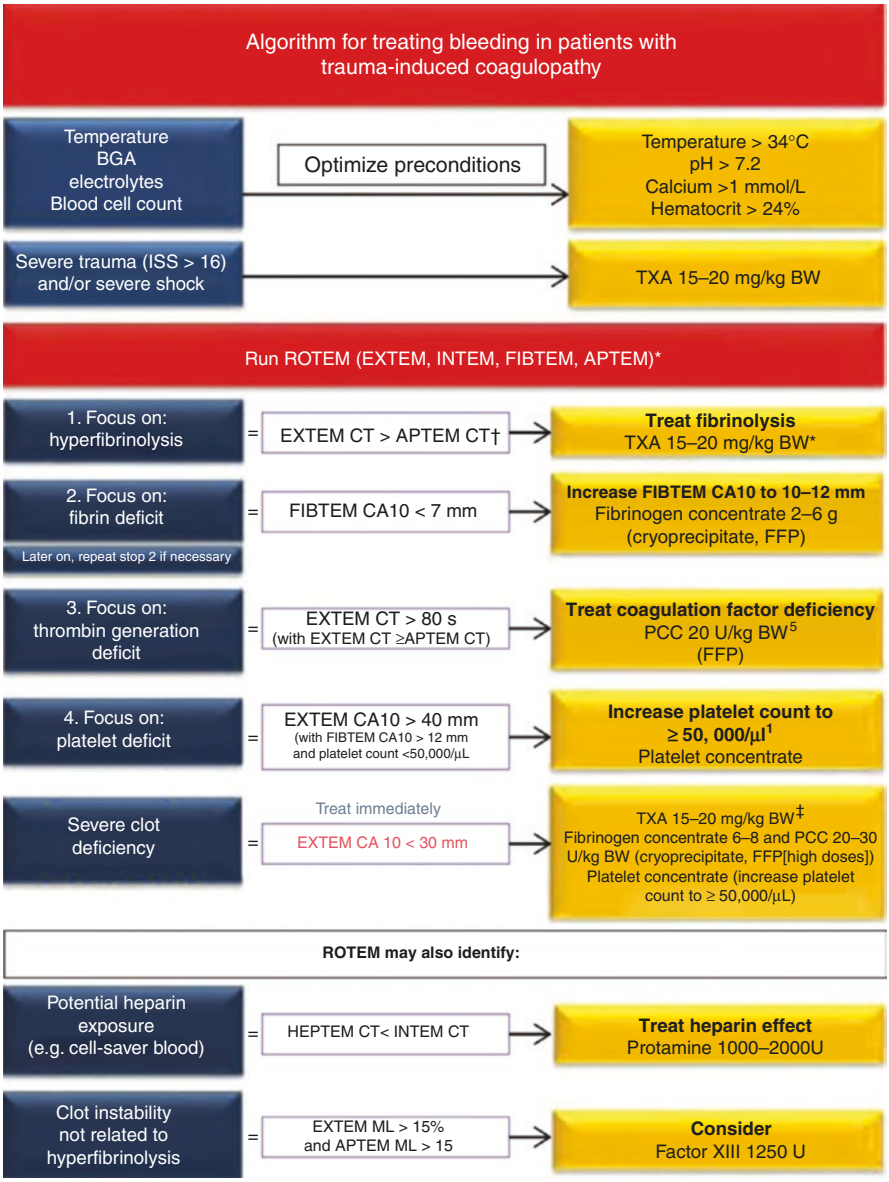


Fig. 2.8 Algorithm for treating bleeding in patients with trauma-induced coagulopathy using factor concentrates based on ROTEM guidance. (Reprinted with permission from: Tobin et el. Current Opinion in Anesthesiology. Wolters Kluwer Health, Inc., 2015)

Since that time, the only FDA-approved use for rFVIIa has remained the treatment of critical bleeding or surgery in hemophiliac patients with known inhibitors to factors VIII or IX (Fig. 2.10). ACS TQIP states that "recombinant VIIa is generally not recommended for management of refractory hemorrhage in trauma" [33].

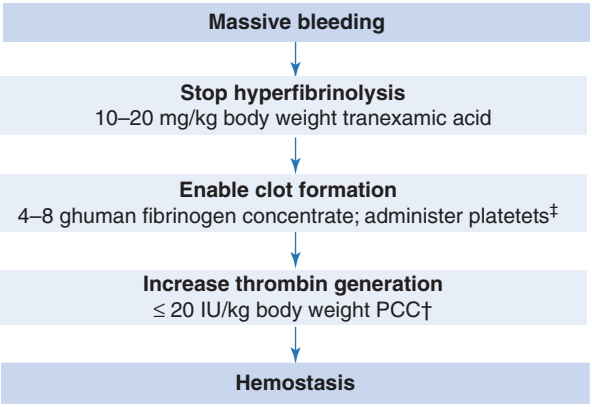


Fig. 2.9 A simplified algorithm for empiric factor-based resuscitation using clinical criteria. (Reprinted with permission from Grottke et al., Annual Update in Intensive Care and Emergency Medicine 2015. Springer Publishing, 2015)

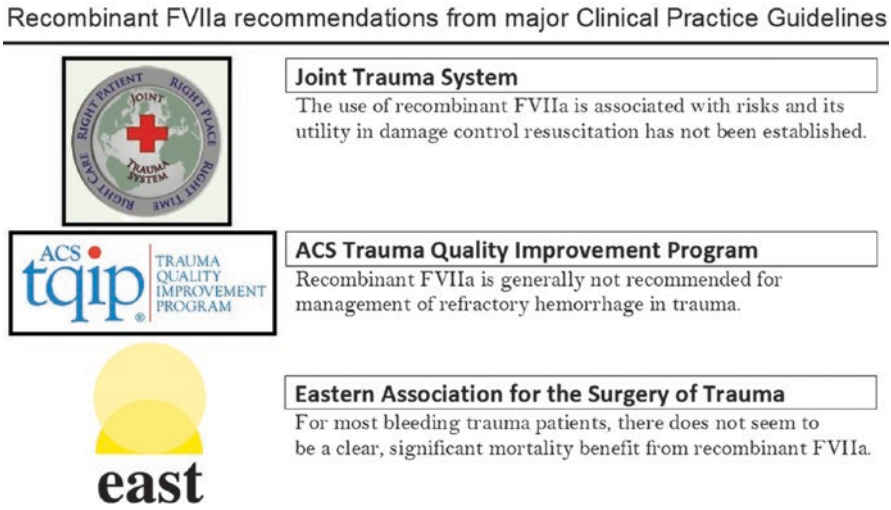


Fig. 2.10 Recombinant FVIIa recommendations according to clinical practice guidelines from major trauma societies

2.3.2 Indications and Alternate Endpoints

There have been myriad advances in our ability to resuscitate the severely injured trauma patient. Multiple studies have demonstrated improved outcomes from having and following a protocol, regardless of what that protocol is [70]. While most physicians can grasp the idea of a 1:1:1:1 ratio transfusion, knowing when to start and stop a massive transfusion can prove to be a more nebulous concept. There have been multiple attempts to create prospective scoring systems to allow a provider to

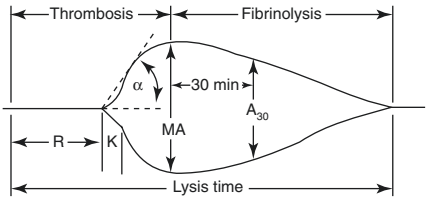
Components of the assessment of blood consumption (ABC) score
Penetrating mechanism
Positive focused assessment with sonography for trauma
Arrival blood pressure less than 90 mmHg
Arrival pulse greater than 120 bpm

Fig. 2.11 Components of the assessment of blood consumption (ABC) score. Each factor is worth 1 point. A score greater than 2 shows a high correlation with the need for massive transfusion following trauma. (From Cotton et al. J Trauma. 2010;69(Suppl 1):S33–39)

predict the need for massive transfusion and call for early assistance. Early attempts such as the Trauma Associated Severe Hemorrhage (TASH) score [71] and the McLaughlin score [72], however, relied on laboratory values thereby severely limiting their utility. Instead, the ACS TQIP now suggests the use of the Assessment of Blood Consumption (ABC) score (Fig. 2.11) [73]. The score consists of four variables (pulse > 120, SBP < 90, penetrating torso injury, and positive FAST) each worth one point apiece. When Cotton et al. validated this scoring system in a multicenter trial, they found that a score of 2 was associated with a sensitivity between 75% and 90% and a specificity between 67% and 88%. The utility of the scoring system, however, was grounded in its simplicity and rapidity.

After initiating resuscitation, it is important to remember the principles explored above. At their most basic, these principles include hypotensive resuscitation, correction of the underlying physiology, and appropriate use of hemostatic adjuncts. Growing evidence has suggested that the use of TEG or ROTEM may allow for a more targeted correction of an individual patient's physiologic derangement. These methods of viscoelastic hemostasis testing in whole blood produce easily identifiable nomograms [74] that provide useful information regarding specific blood product deficiencies [75]. Both methodologies have already been used extensively in spinal and cardiac surgery [76, 77]. These experiences have suggested that they provide for early identification and treatment of deficiencies and result in less intraoperative blood loss and reduced transfusion requirements.

The success of viscoelastic assays in surgery suggested that this utility might extend to damage control resuscitation. In 2009, the United Kingdom Defense Medical Service used ROTEM in Afghanistan as part of a feasibility study. While they made no remark on differences in transfusions or survival, the deployed medical combat team noted that the ROTEM identified significantly more patients as coagulopathic (64% vs. 10%, $p = 0.0005$) when compared to standard laboratory testing at the time of admission [78]. Later studies demonstrated that the greater specificity in identifying coagulopathy allowed for more judicious use of blood products [79]. As experience with TEG and ROTEM in trauma expanded, viscoelastic assays began demonstrating differences in outcomes. Gonzalez et al. performed a single-center randomized controlled trial directly comparing massive transfusion guided by TEG or by conventional coagulation assays (CCA). After enrolling 111 patients, the study found that survival in the TEG group was significantly higher than in the CCA group (36.4% vs. 19.6%, $p = 0.027$) [80].



E	Hypercoagulability
D	Fibrinolysis
C	Thrombocytopenia
B	Hemophilia
A	Normal tracing

TEG	Interpretation	Treatment
R	Time to amplitude > 2 mm Rate of initial fibrin formation ~Plasma clotting factor activity ↑Deficiencies or inhibitors ↓Hypercoagulability	↑R: 2-4 U FFP
K-time	R time to amplitude > 20 mm Time to form strong clot with cross-linking Influenced by: Clotting factors Fibrinogen Platelets	↑K/↓α: 2-4 U FFP Consider: Cryoprecipitate rVIIa PLTs
α angle	Speed of clot strengthening Similar information to K-time Decreased with: ↓Fibrinogen ↓Platelets	
MA	Maximum amplitude Final clot strength Influenced by:	↓MA: Give PLTs
LY30	Clot stability % decrease from MA after 30 min	↑LY30: consider DIC therapy

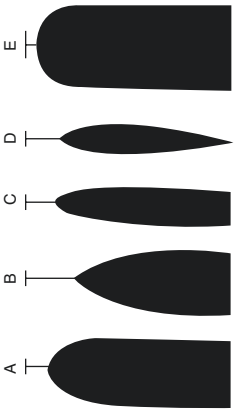


Fig. 2.12 A guide to resuscitation decisions based upon viscoelastic testing. (Reprinted with permission from: Martin M, Beekley A, Eckert M (eds), Front Line Surgery, 2nd Edition, Springer Publishing, 2017)

Although these data support the safety and potential outcome benefit of using a TEG-guided resuscitation strategy, they were limited by the small sample size and the use of a CCA-guided approach as the comparison arm. Further studies directly comparing TEG-guided versus an empiric 1:1:1 (damage control resuscitation) approach and with larger samples are needed to clarify this issue. Figure 2.12 shows an example of utilizing viscoelastic testing results to guide resuscitation decisions and which products to administer for select TEG abnormalities. Despite this promising trend and the clear benefits of viscoelastic testing in coagulation research, the evaluation of viscoelastic assays to guide clinical decisions remains in its infancy. A preponderance of the research to this point suggests that it may take a larger role in the future of goal-directed therapy, but this is yet to be decided.

Conclusion

Hemorrhagic shock continues to represent the most common cause of preventable death in both civilian and military settings and requires novel and innovative approaches to early hemorrhage control and resuscitation. Among the most promising developments of the past decade has been the explosion in interventional and endovascular techniques to diagnose, intervene, and even treat truncal hemorrhage. However, these must always be coupled with a sound and evidence-based approach to resuscitation and restoration of oxygen delivery and normal

coagulation function. By utilizing the principles described in this chapter—limiting crystalloid fluids, hypotensive resuscitation, balanced resuscitation, and rapid surgical intervention—we are better armed to improve survival in hemorrhagic shock. Despite this, however, the optimal treatment of the hemorrhagic trauma patient remains a work in progress. At present, there is evidence to support selecting one of three primary approaches to resuscitation of massive hemorrhage: (1) ratio-based approach using standard blood products, (2) viscoelastic testing-based approach guided by TEG or ROTEM, and (3) factor concentrate-based approach guided either by clinical parameters or TEG/ROTEM. Current guidelines and best practice must be continually updated as our collective experience generates more data, and new technologies must be validated and integrated as appropriate.

Expert's Comments by Federico Coccolini and Fausto Catena

As clearly stated by the authors, hemorrhage accounts for almost half of preventable civilian trauma deaths, increasing to two-thirds in the military setting.

For this reason, studies focusing on widely used and accepted resuscitation techniques are demonstrating a possible correlation with an increase in the rate of complications.

In fact, if performed incorrectly, resuscitation and hemostatic strategies may be harmful.

Knowledge and improvements in the field of post-traumatic damage are the results of a combination of civilian and military learning, coming from different countries and regions. The World Society of Emergency Surgery (WSES) is strongly trying to encourage a more equal sharing of knowledge between all trauma and emergency general surgery experts. For this reason, the most recent development in hemorrhage control gained using endovascular strategies must be given great consideration together with the need to consider an adequate, up-to-date, non-harmful resuscitation strategy. Indeed, not all countries are equal and the device accessibility in different settings is far from homogeneous. In this chapter, the authors have encompassed all the different aspects and historical details of resuscitation in trauma with hemorrhage control. This will give potential readers the possibility to increase their knowledge about this topic and gain all the necessary information in order to make improvements in their local setting.

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Endovascular Management of Cervical Vascular Trauma

3

Todd Simon and Kevin Brown

3.1 Blunt Cerebrovascular Injuries

Traumatic vascular injuries involving the carotid and vertebral arteries have long been a frustrating problem. Injuries often resulted in asymptomatic periods with little to no evidence of vascular injury. Left untreated, these injuries often resulted in catastrophic morbidity as they frequently produced embolic strokes which carried an extremely high morbidity and up to 50% mortality [1].

Over the past two decades, there has been a renaissance of data and subsequent developments which have changed the screening, diagnosis, and treatment of these blunt injuries. This research has not only improved the early detection and diagnosis, it has increased the diagnostic accuracy and reduced the incidence of stroke thereby improving outcomes in these complex patients.

Unfortunately, much still remains to be elucidated before optimal results can be achieved. First, there is conflicting/inconsistent data supporting digital subtraction angiography (DSA) vs. computed tomography angiography (CTA) for screening of these injuries. To further complicate matters, the ideal treatment regimen has yet to be determined. Due to the frequency of multiple injuries including head and spinal injuries, ideal medical management with antithrombotic agents to prevent stroke is often contraindicated. Additionally, open surgical repair, which has the potential to negate the need for such medical management, is often extremely difficult due to the

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location of these injuries, which are often near the skull base or within the vertebral canal. Endovascular techniques have evolved over time and have become more and more attractive because they can make these difficult exposures feasible from an intraluminal approach.

In this section we will discuss blunt cerebrovascular injuries (BCVI) and the growing body of data regarding endovascular treatment options. This will be followed by a discussion about the equally difficult subject of penetrating cervical vascular injuries.

3.2 Epidemiology and Presentation

Blunt carotid and vertebral artery injuries, collectively termed blunt cerebrovascular injuries (BCVI), can be some of the most difficult injuries to diagnose and treat in the setting of trauma. Historically, BCVI were present in 0.1% of patients admitted for trauma [2]; however, with aggressive screening protocols, the prevalence has been shown to be closer to 1.6% of all patients with trauma and as high as 2.7% of patients with severe multisystem trauma [3].

It has been theorized that most of these injuries are due to one of three mechanisms. First, high energy cervical motion can result in hyperextension, hyperflexion, or rotational motion that can injure the carotid or vertebral arteries. Hyperflexion can cause injury to the ipsilateral carotid due to impingement by the angle of the mandible or the styloid process. Hyperextension can stretch the contralateral carotid artery at the entrance to the skull base or over the C1–C3 vertebral bodies causing intimal tearing. Bony fracture or subluxation of either the skull base, mandible, or cervical vertebral bodies can cause direct injury to the carotid or vertebral arteries. Lastly, direct blows to these arteries can result in injury [4]. Intimal tears create the potential for vessel dissection leading to expansion of a false lumen and subsequent vessel stenosis or occlusion. Pseudoaneurysm development can also result via further vessel wall injury or by degenerative processes. Both dissections and pseudoaneurysms can expose tissue factors and other prothrombotic mediators resulting in platelet aggregation and thrombus formation. This thrombus can result in worsening stenosis or dislodge and embolize to the cerebral circulation causing ischemia, infarction, and stroke. Enlarging pseudoaneurysms can also cause mass effects resulting in worsening vessel stenosis thereby reducing blood flow to the brain. In the case of an incomplete circle of Willis, this can result in a stroke.

BCVI can present in a variety of ways. Some manifestations of BCVI include ipsilateral headache, neck pain, Horner's syndrome, soft tissue injury/ecchymosis (seat belt sign), and bruit [4]. Fortunately, most blunt carotid and vertebral artery injuries initially present without neurologic symptoms [5–8]. In a large series from the Denver group, comprised of 418 patients with blunt cerebral vascular injuries, only 29% of patients were found to have neurologic deficits on presentation [9]. This was corroborated by Biousse and colleagues who evaluated 80 patients with extracranial carotid dissections, with 33% presenting with neurologic symptoms [10]. Symptom onset can be delayed for weeks; however, Biousse et al. found 82%

of those that eventually developed symptoms did so within 7 days and the majority of patients develop symptoms within 72 h [9, 10].

As previously stated, it was believed that these injuries were rare; however, the broad and varied presentation combined with the devastating morbidity of a missed injury has driven the implementation of increasingly liberal screening criteria [4].

3.3 Screening and Diagnosis

The difficulty in diagnosing blunt cerebrovascular injuries on physical examination alone has driven researchers to develop liberal screening criteria in order to accurately and expeditiously screen blunt trauma patients. Biffl et al. first developed screening criteria in the 1990s [6]. All blunt trauma patients underwent four-vessel cerebrovascular digital subtraction arteriography using the criteria below:

Hard signs:

- Active hemorrhage from any orifice
- Expanding hematoma
- Bruit in patients <50 years of age
- Evidence of infarct on cerebral imaging
- Unexplained central or lateralizing neurologic deficit, TIA, or amaurosis fugax
- Horner's syndrome

They later expanded the criteria in 1996 to also include associated mechanism of injury which were shown to put patients at risk for hyperextension/rotation or hyperflexion as well as high energy fractures of the skull base and midface. This was again broadened in 2011 when Cothren et al. [11] found that 20% of blunt cerebrovascular injuries did not meet the prior criteria. Table 3.1 summarizes the Denver group's current screening criteria.

CTA is a widely available, fast, and efficient imaging modality that can diagnose blunt carotid and vertebral artery injuries as well as musculoskeletal and soft tissue injuries of the head and neck. CTA is also noninvasive and caries only the risk of radiation and contrast-induced complications. While CTA has become the primarily accepted imaging modality among most major trauma centers, there is some data which argues that it may not be the ideal modality to screen for these injuries.

Digital subtraction angiography (DSA) has long been the "gold standard" for diagnosing BCVI; however, it is an invasive procedure with the risk of access site complications and/or stroke due to wire and catheter manipulation within the aortic arch, great vessels, and carotid/vertebral arteries. DSA is also more expensive and takes significantly longer to perform and, depending on local resources and expertise, might not be readily available. For these reasons, both the Eastern Association for the Surgery of Trauma (EAST) and the Western Trauma Associations (WTA) have recommended CTA as an acceptable modality for BCVI screening. These recommendations, however, referenced only two studies which utilized and compared DSA with CTA for every patient. Other studies which have compared these

Table 3.1 Screening criteria (Adapted from Burlew et al. [9])

Date published	Criteria
1996	Signs/symptoms – Hemorrhage – Cervical bruit – Expanding hematoma – Focal neurologic deficit – Neurologic examination not consistent with imaging – Stroke on secondary survey Risk factors associated with high energy mechanism – LeForte II or III facial fractures – Basilar skull fractures involving the carotid canal – Petrous fractures – Diffuse axonal injury and GCS < 6 – Near hanging with anoxic brain injury
2005	Risk factors associated with high energy mechanism – Cervical spine fracture with subluxation – Cervical spine fracture of C1–C3 – Fractures extending to transverse foramen
2011	Risk factors associated with high energy mechanism – Mandibular fractures – All basilar skull fractures – TBI with thoracic injuries Potential criteria – Thoracic vascular injuries or cardiac injuries – Scalp degloving injuries – Complex frontal skull fractures with orbital involvement

modalities directly have varying sensitivities for CTA from 41% to 98% [11]. These disparate findings suggest that more evidence needs to be collected before we can declare CTA as the ideal imaging modality to diagnose blunt injuries. A recent study published by DiCocco et al. [12] examined 684 patients over a 29-month period with both CTA and DSA using previously published screening criteria and found CTA sensitivity of 51% with a 6% rate of "poor quality" CTA. Even removing these poor-quality CTAs from the calculation only increased the sensitivity of CTA to 52%. Given this data and the positives and negatives of these modalities, it would seem prudent to utilize CTA for initial screening studies in the acute phase of care, but to have a high clinical suspicion and low threshold to pursue confirmatory conventional angiography to confirm a diagnosis. Magnetic resonance angiography (MRA) is an attractive modality due to its lack of radiation and lower risk of contrast-induced nephropathy; however, it is not widely available and requires relatively long periods of time in a closed scanner, which is not ideal in multiple and severely injured patients. Regardless of imaging modality used, repeat imaging should be carried out 7–10 days after initial diagnosis to assess for progression of the injury.

To assist in clinical decision making and prognosis, as well as to aid in consistent communication among providers, Biffl et al. [6] created a grading system based on the degree of injury to the vessel wall.

- Grade I: Dissection with <25% luminal narrowing
- Grade II: Dissection with >25% luminal narrowing, intraluminal thrombus, or raised intimal flap
- Grade III: Pseudoaneurysm
- Grade IV: Vessel occlusion
- Grade V: Vessel transection

The Denver group also showed that these injuries are by no means static and can worsen over time with 66% of grade II injuries progressing to grade III or IV [6]. Furthermore, the Memphis group showed a stroke rate of 64% in untreated patients, while the Denver group has shown a 54% stroke rate in those untreated [9, 13]. These data make a compelling argument for liberal screening and the need for accurate and sensitive diagnosis, and stress the need for effective and safe treatment.

3.4 Medical Treatment

The main goal of therapy should be to decrease the risk of cerebral ischemic events. While it remains unclear exactly which agents have the best outcomes while minimizing complications, it is clear that antithrombotic therapy with either antiplatelet or anticoagulation agents significantly decreases the rates of neurologic events.

Burlew et al. at the Denver Health Medical Center reviewed their experience with BCVI and found that after January 2005, when antithrombotics became the mainstay of treatment, no patients suffered a stroke out of 109 grade II/III BCVI injuries when treated with antithrombotics [14]. This data was despite the fact that endovascular stenting had almost completely stopped at their institution due to high rates of complications in a previous study [11]. In one large study of 307 asymptomatic BCVI patients, the authors reported a stroke rate of only 0.3% and in another study the stroke rate was 2.5% with antithrombotic therapy. This is compared to historic rates of 54–64% in those untreated [9]. This shows conclusively that antithrombotic therapy does reduce neurologic morbidity in patients with these injuries.

It is unclear whether anticoagulation is superior to antiplatelet medications. There has been no literature to date to show that anticoagulation reduces stroke rates compared to antiplatelet medications. Like most difficult decisions in medicine, the choice of antithrombotics should be made based on weighing the risks versus benefits of each therapy. However, the risks of bleeding complications associated with concomitant injury, grade of injury, associated risk of neurologic sequelae, and likely future medication compliance should weigh heavily in the decision. Patients with grade I injury have approximately 3% risk of stroke without treatment and 63% resolve with heparin therapy alone [6]. Due to the lower stroke risk of these injuries, bleeding risk due to concomitant injuries should be weighed accordingly when selecting optimal medical therapy. In stark contrast, 70% of grade II injuries progressed to grade III and carry an 11% risk of stroke in grade II and 33% risk of stroke with grade III without treatment. Combine this with a mortality rate as high

as 50% in some studies and the risk of stroke and subsequent mortality compared to the risk of bleeding becomes much more significant. Previously considered "absolute contraindications" should be reconsidered in light of these concerning statistics in regard to these injuries. Grade IV and V injuries carry such high rates of stroke and mortality early in the course of treatment that, while antithrombotics are certainly still indicated, it is frequently not possible to treat them prophylactically before a significant neurologic event occurs.

3.5 Endovascular Treatment

The second goal of treatment for BCVI is to minimize and halt the progression of vessel wall injury in order to avoid further progression of dissection, true lumen stenosis, pseudoaneurysm enlargement/rupture, and increasing risk of embolism. It should be noted that Biffl et al. advocate open surgical repair of grade II–V injuries in surgically accessible areas of the neck, primarily Zone II. While this is an invasive approach, it is the only treatment that precludes the need for long-term antithrombotics of some sort. That being said, due to the mechanisms of blunt cerebrovascular injury, many of these injuries occur in surgically difficult locations and are associated with cervical spine, mandibular, and skull base fractures as well as intracranial traumatic brain injury (TBI), which can make general anesthesia, surgical positioning, and subsequent exposure very difficult. For these reasons, endovascular treatment has become increasingly attractive as the primary modality of intervention.

It has been advocated that after initial diagnosis and grading of vessel injury in surgically inaccessible areas, repeat imaging be carried out in 7–10 days to assess for injury progression [14]. As mentioned earlier in this chapter, a significant percentage of grade II and III injuries worsen over time. Therefore, intervention should be reserved for those injuries that continue to progress with increasing vessel stenosis in grade II and III lesions. Other authors have advocated embolizing grade IV lesions to avoid the risk of stroke via recanalization through an acutely thrombosed vessel.

Timing of intervention is ill-defined and no large series or studies has been undertaken to ascertain this data. Given that most endovascular procedures are utilized only in injury progression or failure of medical management, most intervention is delayed for at least a week in the case of blunt injury. This is favorable due to the theoretical friability and hypercoagulable state of the acutely injured vessel; however, one could theorize that this state is likely present for much longer than 7 days. Future data may well show that delayed endovascular intervention improves outcomes and further explains some of the higher rates of stent occlusion and perioperative complications seen in studies where earlier interventions are performed.

While most surgeons would advocate treatment for injury progression and pseudoaneurysm enlargement, the exact definition of pseudoaneurysm enlargement and progressive stenosis remains unclear. There are no defined size criteria for pseudoaneurysm repair and risk of rupture is unknown. Likewise, the degree of stenosis at

which repair is indicated has also not been defined. Seth et al. examined 53 blunt traumatic carotid injuries over a 10-year period at the University of Maryland. They suggested a modified grading system that subdivided grades II and III into grade IIa/IIIa as <70% stenosis and grade IIb/IIIb as >70% stenosis. They utilized this modification to limit treatment to those with grade IIb or IIIb lesions, progressive pseudoaneurysm growth, and continued neurologic events despite appropriate medical therapy. They utilized stent-assisted coil embolization which is a combination of uncovered stents with coiling of the pseudoaneurysms via the interstices of the stent. Three patients suffered transient complications (two weakness and one amaurosis) related to the procedures but all recovered without deficits. One patient was found to have an asymptomatic occlusion of his stent and was shown to be noncompliant with the prescribed antiplatelet therapy. The overall complication rate in this paper was 6.4% [3]. While this complication rate is consistent with other series of endovascular treatments, it did not improve overall outcomes compared with other studies.

While exact indications and thresholds for endovascular treatment remain unclear, it is also unclear as to what is the best technique for endovascular treatment, and most data in regard to technique come from small case series. Some of the techniques which have been utilized include embolization of the carotid with detachable balloons, coil, or glue embolization with balloon test occlusion, as well as uncovered stents with and without coil embolization of the pseudoaneurysms, and covered stent grafts. The former embolization techniques are often reserved for intracranial injuries due to the tortuosity of the carotid as it traverses the skull base making stenting difficult [15].

Stenting of the artery maintains normal anatomic/antegrade flow while also acting as a filter by trapping thrombus within a pseudoaneurysm via the interstices of the stent. Endothelial cell growth into the interstices also helps decrease flow into a pseudoaneurysm. Due to the mobility of the neck, flexible self-expanding uncovered stents have historically been chosen in comparison to stiffer balloon expandable or covered stents. Additionally, large pseudoaneurysms can be coiled through the interstices of uncovered stents which can prevent the coils from non-target embolization into the distal cerebral circulation. Furthermore, uncovered stents allow for improved laminar flow through the true lumen of the artery, decreasing turbulent flow into the dissection plane or pseudoaneurysm thereby theoretically decreasing the risk of embolization [5]. Overall, outcomes related to stenting have been favorable. Edwards et al. treated 18 patients with stents and followed 14 of these patients for a 30-month mean follow-up time. They showed no long-term stent occlusions and concluded that endovascular stenting was safe and effective [16]. Cohen et al. also treated ten patients with stenting without stent-related complications for a mean follow-up of 28 months [17].

Covered stent grafts seem very attractive given that they exclude the false lumen and pseudoaneurysm altogether, while restoring normal anatomic flow. Currently, there are no covered stent grafts which are FDA approved for use in the carotid, and there are no commercially available tapered covered stents which are often necessary when the repair involves both the internal and common carotid arteries. These

considerations not withstanding several series have shown them to be effective [5]. Assadian et al. showed no complications out to 6 months while Maras et al. showed a 15% occlusion rate, all of which were asymptomatic and were felt to be due to "complicated injuries" [18, 19]. While most covered stents have been used for penetrating trauma, there are no glaringly obvious reasons as to why they could not be considered in the case of pseudoaneurysms in blunt trauma.

Cerebral protection devices have also not been widely described in the trauma literature. This is likely due to the distal nature in Zone III in many of these injuries making distal protection devices difficult to place in the petrous portion of the carotid. Schultz et al. used embolic protection devices (EPD) in five of seven dissection patients with good results.

Another major factor to be considered in the use of stents, whether covered or not, is the use of postoperative antiplatelet medications. While it has become standard of care that some form of antiplatelet medications be used postoperatively, it is unclear as to the duration of treatment. Many authors advocate dual antiplatelet therapy with aspirin and clopidogrel for at least 3 months and some form of antiplatelet therapy for life. Furthermore, it is imperative to have long-term follow-up with imaging to evaluate for restenosis due to intimal hyperplasia and atherosclerosis in the long term. Duplex ultrasound seems like the obvious choice; however, it should be noted that there is no well-established velocity criteria for in-stent restenosis after endovascular therapy. CTA is probably a more reliable imaging modality for the initial short-term follow-up, with Duplex ultrasonography used as an alternative for long-term follow-up once several stable data points have been established.

While many uncertainties remain and future studies are needed to establish best practices, endovascular treatment is becoming increasingly utilized for blunt carotid and vertebral artery injuries. As technology and techniques improve, this minimally invasive treatment promises to be an important tool in the management of these difficult cases.

3.6 Penetrating Cervical Vascular Injuries

As reported in the 2013 National Trauma Data Bank annual report, penetrating cervical trauma contributed to less than 2% of all reported injuries [20]. These injuries occur predominately in adults secondary to assault from firearms and stab injuries. Other less frequent etiologies include falls or motor vehicle accidents. Despite being infrequent, these injuries are associated with a mortality rate as high as 6% and the majority of deaths are secondary to ischemic stroke with the remainder due to exsanguination [21]. Carotid artery injuries account for approximately 20% of all cervical vascular injuries and are seen predominantly in the common carotid and, to a lesser degree, in the internal carotid artery [22]. Vertebral artery injuries tend to have a much lower incidence and, unlike carotid injuries, rarely produce exsanguination, airway collapse, or stroke [23].

Penetrating trauma to the carotid and vertebral arteries can result in similar injuries to those seen in blunt cerebrovascular injuries, such as dissections or

pseudoaneurysms, and treatments are likewise similar. However, unlike blunt trauma, penetrating cervical vascular injuries can also result in arteriovenous fistulas (AVF), transections, expanding hematomas, and exsanguinating hemorrhage. Due to the often difficult exposure in this anatomic region, endovascular treatment is an attractive and often lifesaving therapy.

When discussing penetrating cervical trauma, it is best to start with the zones of the neck. Zone I extends from the clavicles to the cricoid cartilage; Zone II, from the cricoid cartilage to the angle of the mandible; and Zone III, from the angle of the mandible to the base of the skull (see Fig. 3.1). The vertebral arteries are not well represented in this classification system and are best described by location. V1 extends from the origin to the C6 transverse process, V2 extends through the cervical transverse processes of C6–C2, V3 is the segment between C2 and the skull

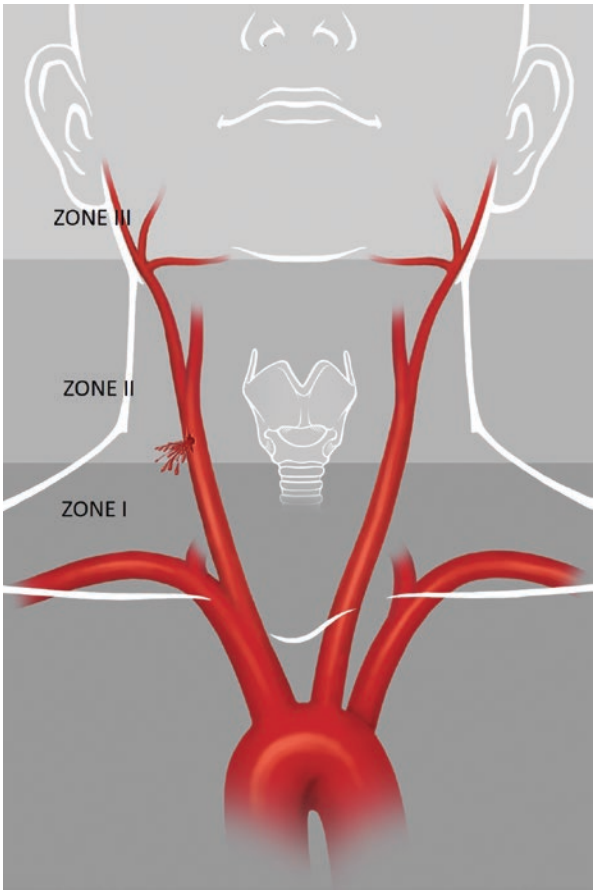

Fig. 3.1 Cervical trauma zones of the neck. Zone I extending from the clavicles to the cricoid cartilage. Zone II extending from the cricoid cartilage to the angle of the mandible. Zone III extending from the angle of the mandible to the base of the skull

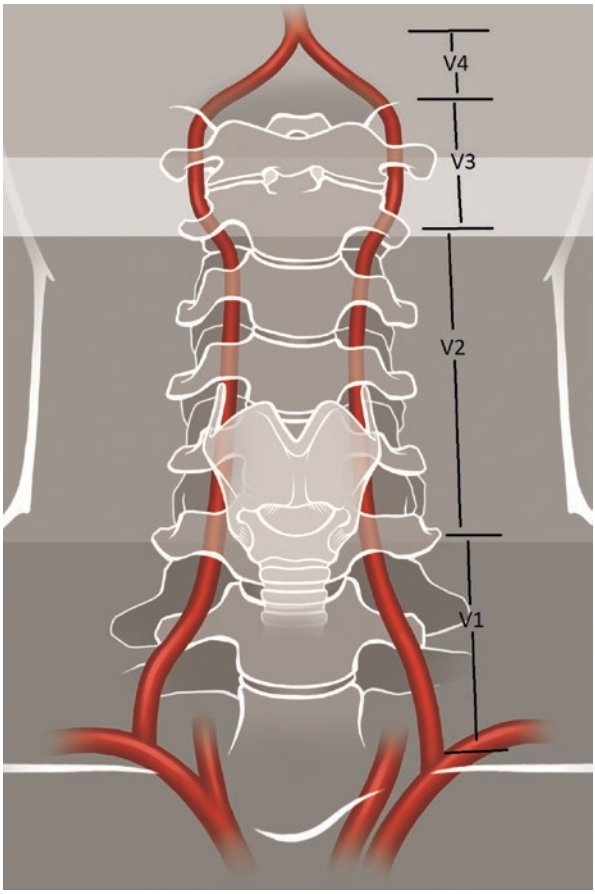

Fig. 3.2 Segments of the vertebral arteries. V1 extending from the origin to the C6 transverse process. V2 extending through the cervical transverse processes of C6–C2. V3 extending from C2 to the skull base. V4 intracranial segment from skull base to the confluence of the basilar artery

base, and V4 is an intracranial segment from the skull base to the confluence of the basilar artery (see Fig. 3.2). Direct surgical exposure and repair of injuries to the vertebral artery, as well as the common carotid artery in Zone I and the distal internal carotid artery in Zone III, can be extremely difficult and are beyond the intent of this chapter.

Based on several older studies involving penetrating neck trauma, physical examination tended to be the best initial guide in determining whether or not further diagnostic testing or operative intervention was needed [24–26]. When hard signs of vascular injury such as active pulsatile bleeding, expanding hematoma, bruit, or evolving stroke (distal ischemia) are present, quick operative exploration is the standard rather than delaying surgery for imaging studies. In patients with soft signs of vascular injury who are stable, data now supports CTA as the imaging modality of

choice. It has been shown to have a sensitivity of 90% and a specificity of 100% in diagnosing arterial injuries caused by penetrating neck trauma. Moreover, CTA can accurately diagnose associated injures to the spine, aerodigestive tract, chest, or head which are often present in this patient population [27]. In the recent PROOVIT registry, DuBose et al. reported that CTA was the most commonly used modality to identify vascular injury in 39.6% of patients. This was followed by operative exploration and traditional angiography in 29.7% and 11.4% of patients, respectively [28].

While surgical repair still remains the most common management technique in all zones of the neck for penetrating injuries, there has been an increasing trend over the years in the application of endovascular techniques [28–30]. This is especially true for Zones I and III of the neck. However, despite the growing use of endovascular therapy, open surgical treatment of penetrating Zone II injuries to the carotid artery via a vertical anterior neck incision is still advocated by the majority of surgeons [21]. This exposure is neither morbid to the patient nor as technically challenging to the surgeon.

Generally speaking, if patency is not an issue, the vessel can be embolized with coils such as in penetrating injuries to the external carotid artery and any of its branches. When patency is preferable, such as in the case of the internal carotid, inaccessible penetrating carotid artery injuries can be treated with covered stents. However, it should be stated that even internal carotid arteries can be ligated or embolized in lifesaving circumstances such as exsanguination. DuToit et al. reported their experience in treating 19 penetrating carotid artery injury patients using a variety of covered stents. Proximal common carotid injuries were seen in 14 patients, and 5 patients had distal internal carotid injuries as diagnosed by aortic arch and four-vessel arteriography. Injuries included 10 pseudoaneurysms and 9 traumatic arteriovenous fistulas. They reported 100% technical success with only one early stroke and one non-stent graft-related procedural death. Mean follow-up of 4 years was obtained in 14 patients, of which no stent-graft related deaths, stroke, or other complications were reported. Of note, embolic protection devices were not used during their interventions [22]. Yevich and colleagues advocate acute endovascular treatment of gunshot injuries to the face and neck in order to achieve hemodynamic stability and prevent or minimize neurological sequelae from thromboembolic events. They report on successful emergency endovascular treatment of two vertebral artery transections treated with embolization using coils and liquid embolic agents, eight external carotid artery branches also occluded with liquid embolic agents, and one severe dissection of the internal carotid artery treated with stenting. All except one patient survived these injuries with minor or no residual neurologic deficits [31].

Due to the difficult exposure of the vertebral artery regardless of its anatomic zone, endovascular treatment is an attractive option here too. In the rare case of exsanguinating hemorrhage, the practical endovascular intervention is to embolize the artery in order to stop the bleeding. Several authors have published small series and case reports of patients with reasonable outcomes. Cohen et al. presented a case report of a patient with exsanguinating hemorrhage due to a right VA transection from a gunshot wound to the face. In this case, the patient required additional embolization of the distal VA

from the contralateral vertebral artery in a retrograde manner in order to attain hemostasis. This case demonstrates the challenging technique of contralateral VA selection with navigation of a microcatheter through the distal left VA, the vertebrobasilar junction, and then in a retrograde fashion through the distal right VA to the injury site [32]. In the case of traumatic AVF, the optimal treatment is a little less clear. Herrera et al. treated 18 vertebral AVF with occlusion/embolization without any significant neurologic complications when performed with balloon test occlusion [33]. However, Greer et al. advocated stenting the vertebral artery due to the ability to maintain antegrade flow after they evaluated four penetrating combat vertebral injuries with pseudoaneurysms treated with a combination of coil embolization and covered stent placement with no short-term complications [34]. While stenting does offer the ability to maintain antegrade flow, this technique may not be possible in the case of hemorrhage or concomitant injury due to the need for long-term antiplatelet therapy to maintain stent patency in the carotid or vertebral arteries.

Starnes and Arthurs describe using endovascular techniques as an adjunct to standard open repair for penetrating Zone I injuries with hard signs that require immediate operative intervention. For instance, an occlusion balloon from the groin can provide endoluminal control proximally and allow for a more controlled surgical exposure as well as potentially avoiding a sternotomy and/or thoracotomy. This technique additionally allows time to perform an angiogram in order to locate and subsequently repair the injury [35]. Similarly, endoluminal balloon control of a Zone III internal carotid artery injury, where surgical exposure and distal control is complicated by the need for an extensive dissection, styloid resection, or mandible subluxation to gain exposure, might be best obtained this way [36].

Endovascular procedures are best done in an angiography suite with full operative capabilities or an operating room with fixed imaging or high-quality portable imaging with a vascular operating table. Furthermore, the vascular surgeon, interventional radiologist, or interventional neuroradiologist must be readily available and have sufficient experience with multiple endovascular techniques in order to achieve the best results. Lastly, for emergency endovascular treatment to be successful, one must have the appropriate supplies and equipment as well as ancillary staff who are knowledgeable and well trained. The desire to proceed with endovascular management must also be tempered by the potential need for anticoagulation and antiplatelet therapy [37, 38]. Of course these patients need to be carefully selected because stent placement in the carotid or vertebral arteries requires dual antiplatelet therapy for several months followed by aspirin indefinitely.

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Endovascular Management of Thoracic and Abdominal Trauma

4

Ravi R. Rajani and Christopher Ramos

4.1 Introduction

Traumatic injury imposes the highest burden on the global population for life years lost prior to the age of 65 years. Control of hemorrhage is the key to improving survival, since this is the second leading cause of death following central nervous system injury [1]. Unlike central nervous system injury, which is at times irreversible, hemorrhage can be intervened upon through direct measures such as compression, surgical repair, and more recently endovascular approaches. Major advances have been made in the rapid control of compressible hemorrhage through the use of tourniquets for extremity hemorrhage, yet initial management of non-compressible torso hemorrhage (NCTH) still presents a significant challenge.

This chapter outlines the contemporary utilization of endovascular techniques in the setting of NCTH as an adjunct to surgery for control and definitive repair. Developed and refined approaches for hemorrhage associated with axillosubclavian injuries, blunt thoracic aortic injuries, visceral injuries, aortic injuries, and pelvic injuries will be described.

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4.2 Initial Evaluation

Patient presentation and vital signs will determine the diagnostic pathway in all cases. Advanced Trauma Life Support (ATLS) guidelines should be followed during the initial survey of all trauma patients. If there is concern for a torso injury, a chest and pelvic X-ray and a focused assessment with sonography for trauma (FAST) will aid in the initial assessment to evaluate for a vascular injury in hemodynamically unstable patients and can suggest the localization of the bleeding. On chest X-ray, apical capping, hemothorax, and a widened mediastinum suggest a vascular injury that may require intervention or immediate chest tube placement if indicated. A displaced pelvic fracture may contribute to ongoing blood loss, and this can be stabilized with a pelvic binder. Despite stabilization, pelvic fractures may have ongoing venous and arterial bleeding that may require intervention in unstable patients. In victims of blunt trauma, the FAST may reveal free fluid in the abdomen consistent with hemoperitoneum or hollow organ injury. FAST, CXR, and pelvic X-ray can suggest the localization of the bleeding or other causes of circulatory distress and guide one to the correct body cavity in the correct order [2].

In patients in extremis or with unstable vital signs, the initial evaluation of a trauma patient is typically performed using a multidisciplinary approach, and actions are performed in parallel. During this evaluation, a common femoral arterial (CFA) line can be placed under ultrasound guidance if performed in a timely manner. Ultrasound guidance is recommended to ensure that the arterial puncture site is above the bifurcation of the CFA but below the circumflex iliac artery and on the anterior wall of the artery. Common femoral arterial access can then be used to help guide resuscitation, but in the event of clinical deterioration, this can be readily upsized to a larger sheath for additional diagnostic imaging and intervention [3].

4.3 Line Placement Considerations

CFA access should not delay any additional diagnostic or therapeutic interventions in the trauma bay. Previous algorithms have been proposed for the management of exsanguinating torso trauma [4]. Patients who arrive to the trauma bay receiving cardiopulmonary resuscitation (CPR) should undergo a resuscitative thoracotomy (RT) in the ED, as long as the duration of CPR does not exceed 15 min for penetrating thoracic trauma, 10 min for blunt trauma, or 5 min for non-torso-penetrating trauma. Patients in hemorrhagic shock after penetrating or blunt thoracic trauma will generally require additional emergent interventions based on ATLS guidelines [4]. In these patients, lifesaving interventions should not be delayed for the placement of an arterial line.

Prior to line placement, the area should be prepared using an antiseptic such as chlorhexidine or Betadine. Following placement, a sterile occlusive dressing should be placed, in the event this access will be used for additional imaging/interventions. If

there is concern for laterality of the injury (diminished femoral pulse or groin hematoma), then the common femoral line should be placed on the contralateral side [3].

It is important to note the inner diameter of the arterial line catheter that is placed so that the appropriate wire can be used to replace the catheter in an over-the-wire technique. If a patient's clinical status deteriorates, this access can rapidly be used to perform additional diagnostic angiography, therapeutic interventions, and resuscitative endovascular balloon occlusion of the aorta (REBOA) after exchanging the arterial line catheter for a sheath of an appropriate size [3].

4.4 Angiography for Diagnosis and Treatment of Hemorrhage

Computed tomography angiography (CTA) has evolved as the modality of choice in diagnosing vascular injuries for the majority of stable trauma patients. Although rapidly obtained and available at most centers, CTA images do require time that may not be afforded in patients in extremis due to NCTH. Once the mainstay of vascular imaging, traditional digital subtraction angiography (DSA) has now largely been replaced by CTA. In stable patients who have undergone a CTA which reveals extravasation or a blush, DSA can be used to localize and exclude the injured vessel. In specific instances, DSA can prove to be more sensitive in detecting a vascular injury, particularly when foreign metal objects are in proximity to vascular structures which result in scatter artifacts that obscure CTA images.

The utilization of DSA and embolization for the diagnosis and treatment of traumatic hemorrhage has increased significantly since being first published in the 1970s. These reports demonstrated that endovascular therapy could effectively be utilized to treat hemorrhage from pelvic, renal, and subsequently intercostal arteries [5–7]. These early successes have led to an increased adoption of algorithms that have incorporated endovascular therapies as routine elements of hemorrhage control for patients with both pelvic and solid organ injuries. These techniques have become well established and now play a major role in the management of NCTH [8–13]. This adjunct has proven most valuable during attempts in non-operative management in patients without a hollow viscous injury, who are not in extremis and do not need immediate operative intervention. Patients in extremis with unstable vital signs must be taken to the operating room for open exploration.

With the increased prevalence of angiography with embolization of splenic, hepatic, pelvic, and intercostal artery injuries, there have been significant advancements in the technology used for hemorrhage control with endovascular modalities. Microwires and microcatheters have been developed for higher selectivity of bleeding vessels. Additionally, a wide variety of hemostatic agents can be delivered in a precise manner directly at the site of injury. These include endovascular coils and plug devices as well as simple gelfoam to promote thrombosis in areas of ongoing hemorrhage.

Angiography with embolization can be used as an adjunct to open surgical intervention in a hybrid approach to decrease the loss of blood, although selection criteria for trauma patients remain a point of contention. It is more commonly used in patients that are stable enough to undergo axial imaging, with attempts for non-operative management. A significant hematoma and active contrast extravasation or "blush" on CTA guides the employment of this modality. Patient physiology (including those that are transient responders or with an ongoing transfusion requirement) are usual indications for embolization at most centers. The importance of these imaging and physiologic findings in guiding optimal patient selection for endovascular intervention remain controversial [14]. Despite four decades of experience with this therapy, it is difficult to develop protocols for a truly randomized controlled study to develop ideal selection criteria for endovascular embolization, and therefore this topic continues to be actively investigated. Additionally, the optimal thrombogenic agents used for embolization have not been identified and this too remains under investigation. With the available data for angioembolization, the American Association for the Surgery of Trauma (AAST), the Eastern Association for the Surgery of Trauma (EAST), and the Western Trauma Association (WTA) have developed algorithms for the non-operative management of penetrating and blunt trauma to solid organs and pelvic arteries.

There is consensus that treatment at the specific site of hemorrhage is the most ideal, leading to less risk of ischemia to tissue with exclusion of more distal branches off of named arteries rather than the origin of larger arteries. Achieving this pinpoint hemostasis of small bleeding vessel branches requires a significant amount of time and may be technically challenging. The time spent doing a more "selective" embolization must be weighed against other pressing needs in a multi-injured trauma patient. This has led to an area of controversy regarding the delivery of endovascular hemostatic agents at more distal "selective" or "superselective" sites. Defining the optimal approach has proven challenging, as multiple variables must be considered including patient physiology and multisystem trauma. This has led to ongoing investigation with regard to patient selection, type of hemostatic adjunct used, and the level of the area treated.

Extensive collateral circulation can provide distal circulation to areas of vascular injuries resulting in continuous bleeding. This is seen in the liver and the pelvis. In order to avoid distal reconstitution of the injured vessels, distal and proximal embolization (the sandwich technique) is recommended. This technique requires crossing the area of injury, which is feasible when dealing with a pseudoaneurysm, but may not be possible with a vessel transection. After crossing the vessel injury, coils are placed distal and proximal to the site of vessel injury. Due to the small size of many of the vessels in solid organs, distal embolization with particles or gelfoam followed by proximal embolization with coils is an effective option.

Some organs, such as the spleen and liver, can tolerate proximal embolization as collateral circulation will preserve the organ parenchyma. End arterial organs like the kidney have poor collateral circulation and embolization will result in parenchymal loss. In end arterial organs, superselective embolization is indicated.

4.5 Embolization Agents

Embolization agents are classified as temporary or permanent. Permanent embolization agents include particles and metallic coils. Gelfoam is a temporary agent. Particles and gelfoam can be used to obtain distal target embolization followed by proximal embolization with coils.

4.6 Gelfoam

Gelfoam is derived from a biologic substance made of purified skin gelatin that has been used for many years as the primary embolization agent. Gelfoam has a highly porous structure without intrinsic hemostatic actions but induces thrombosis by acting as a scaffold for platelet aggregation. The most commonly used form is the sheet or block of gelfoam that is cut with scissors in small 1–2-mm cubes that are then mixed with contrast medium in a 3–5-mL syringe using a three-way stopcock until a slurry is created. Advantages of this agent include that it is inexpensive and provides temporal embolization. In most clinical instances, vessel recanalization after gelfoam is seen within 2 weeks but may take from 3 weeks to 4 months. The main disadvantages are that the sizes of the particles are not uniform and that disruption of the clot with rebleeding is possible [15].

4.7 Particles

Particles create a permanent occlusion by adherence to the vessel wall, creating a mechanical occlusion and inflammatory reaction. Particles include polyvinyl alcohol (PVA), tris-acryl gelatin microspheres (TAGM), and hydrogel particles, among others. The particles can be reconstituted in saline and contrast in order to be injected under fluoroscopic guidance. The advantage of particles is the ease of reconstitution. The disadvantage of these particles is a higher cost and particle aggregation leading to occlusion of delivery catheters [15].

4.8 Metallic Coils

A coil is basically a piece of wire that is looped in different shapes and sizes. Coils provide a platform for clot formation and some have the addition of fibers to increase thrombogenicity. For trauma embolization, the main types of coils used are the macrocoils in 0.038- and 0.035-in. sizes and available in diameters from 3 to 15 mm. Microcoils are inserted through microcatheters usually with a 0.021-in. lumen and available in sizes from 1 to 20 mm. In general, coils should be sized to about the size of the vessel. A coil that is too small for the vessel may migrate distally. A coil that is too large may push the delivery catheter back and cause unintentional proximal embolization. A larger short coil can be placed first followed by smaller softer coils

for dense packing (scaffold technique). Pushable coils are deployed by pushing them with a wire or a special wire pusher; these are harder to control but less expensive. Detachable coils have some mechanism with controlled deployment that allows reposition before final release of the coil.

4.9 Amplatzer Vascular Plugs

Amplatzer vascular plugs (AVP) consist of uncovered nitinol mesh with a three-disk configuration and range in size from 3 to 22 mm using 4- to 7-Fr sheaths. The device is more expensive than pushable coils, but usually only a single device is required. This saves valuable time in a trauma patient and the cost of multiple coils. The plug is deployed by unsheathing it through a guiding catheter or sheath at the target position. The device can be resheathed and repositioned until it is at a satisfactory location. The AVP is released by rotating the delivery wire counterclockwise. The main disadvantage of AVP is that the device is relatively stiff compared with regular coils, and placing the guiding catheter or sheath inside tortuous vessels can be very difficult. AVP are primarily used for the occlusion of large vessels and for traumatic AVF where coils have the potential to embolize.

4.10 Liver Endovascular Embolization

Most parenchymal liver injuries involve small or medium branches, and collateralization from distal branches after proximal embolization is not uncommon. If possible, superselective embolization with microcoils proximal and distal to the lesion is the most ideal therapy. Otherwise particle or gelfoam embolization to achieve distal control followed by proximal coil embolization is recommended. Particle embolization should be performed distal to the cystic artery to help prevent gallbladder infarction. Embolization in the liver is usually well tolerated due to the dual supply of the liver. In high-grade liver injuries, major hepatic necrosis and biliary and abscess complications have been reported. Biliary injuries with bile leakage may contribute to delayed hemorrhage that can present with hemobilia or arterio-portal fistulae [11].

4.11 Spleen Endovascular Embolization

Proximal versus distal embolization of splenic injuries remains a highly controversial issue. A shattered spleen with multiple areas of contrast extravasation is best treated with proximal embolization of the splenic artery. Collateral circulation from the pancreatic and short gastric vessels maintains distal splenic perfusion. Parenchymal injuries can be treated with selective distal coil or particle embolization. Partial splenic infarction, fever, and pleural effusion are not uncommon. Complete splenic infarction and atrophy, and less frequently pancreatitis and splenic abscess, are also reported complications [13].

4.12 Kidney Endovascular Embolization

The renal arteries are true end arteries therefore renal parenchyma distal to the level of embolization will infarct. Therefore, the main renal artery is treated by surgical repair or placement of a stent graft. Superselective embolization of peripheral lesions, usually with microcoils, is recommended. For very distal injuries, the use of gelfoam or particles is also a viable alternative.

4.13 Pelvic Endovascular Embolization

NCTH after pelvic fractures is difficult to control with surgery. Upon arrival to the trauma bay, these patients are temporarily managed with external pelvic fixation using sheets, pelvic binders, and pelvic C-clamps. Pelvic fixation can successfully stop venous bleeding as well as bleeding from bony surfaces. Some centers have adopted pre-peritoneal pelvic packing at the time of pelvic fixation for control of venous bleeding. Once coagulopathy is corrected, if there is an ongoing transfusion requirement without other sources of bleeding, then embolization is used to control arterial bleeding. Other centers proceed directly to angiography with embolization following pelvic fixation. Selective arteriography of each hypogastric artery is performed with superselective embolization, if possible. There is a high potential for distal bleeding from collateral circulation. In patients with several areas of uncontrolled bleeding who become hemodynamically unstable, nonselective proximal embolization of the anterior or posterior divisions of the hypogastric arteries can be a lifesaving procedure. Unfortunately, nonselective hypogastric embolization has been shown to have a higher risk of complications including pelvic organ necrosis, buttock ischemia, and impotence [9].

4.14 Endovascular Stent Grafts

Unlike embolization agents, covered stents can provide hemostasis while maintaining vessel patency. Covered stents can be used to exclude pseudoaneurysms, arteriovenous fistulas, and other injuries in the renal, iliac, subclavian, and axillary arteries and other nonexpendable vessels in NCTH. Adequate sizing of stent grafts is key for exclusion of an injured vessel. This can be performed with axial imaging prior to angiogram or intravascular ultrasound. Some fluoroscopy software has the capability of measuring distances in real time. Oversizing of stent grafts may lead to kinking and invaginations and subsequent occlusion, whereas undersizing may result in an endoleak due to inadequate apposition against a vessel wall. Major drawbacks of stent grafts include cost and the need for larger introducer sheaths. Additionally, stent grafts will cover vessel branches, which may be of importance. For example, stent graft placement in the proximal left subclavian may lead to coverage of the left internal mammary artery which could

lead to acute myocardial infarction in patients that have had a coronary bypass using this conduit. Similarly, coverage of the vertebral artery may lead to vertebrobasilar insufficiency.

4.15 Axillosubclavian Injuries

Axillosubclavian injuries continue to carry high morbidity and mortality in contemporary studies, and traditional open exposure and repair of these vessels frequently require thoracotomy or sternotomy in addition to clavicular exposure in up to 50% of patients [16]. These approaches pose a risk of collateral damage to surrounding neurovascular structures in the thoracic outlet. Therefore, endovascular therapy in axillosubclavian injuries has been embraced and experience in this topic continues to grow.

When outcomes were compared between matched patients with axillosubclavian arterial injuries who underwent endovascular and open procedures, patients undergoing endovascular procedures had significantly lower in-hospital mortality (12.9% vs. 22.4%, $p < 0.001$) and decreased rates of sepsis after intervention (7.5% vs. 5.4%, $p = 0.025$) [16]. The largest multi-institutional review to date by the Endovascular Skills and Resuscitative Surgery Working Group revealed that in 150 axillosubclavian injuries, 96.9% of patients had initial successful stent placement, with up to 84.4% patency and no mortalities related to the endovascular therapy [17]. Table 4.1 summarizes outcomes from the more contemporary reports analyzing endovascular management of axillosubclavian injuries [16–20]. Despite a high rate of successful therapy and patency, experience with this modality and data on late follow-up remain limited and require ongoing investigation.

When treating pseudoaneurysm or vessel transections of the axillosubclavian segment, both antegrade femoral access and retrograde brachial access can help cross the injured vessel. A "body flossing" technique can be performed by snaring a wire in the hematoma and obtaining through-and-through access. The stent graft can then be deployed to treat the vessel injury (Fig. 4.1).

Table 4.1 Summary of contemporary reviews of outcomes of axillosubclavian injuries following endovascular management

Outcomes of endovascular management of axillo-subclavian injuries							
Study	Reference	Cases reviewed	Pentrating/ blunt	Therapy success	Mortality (%)	Mean follow up (months, range)	Patency
Branco et al.	[16]	92	92/0	95.60%	5.40	13.2 (3–48)	88.10%
Dubose et al.	[17]	150	90/32	96.90%	0	Up to 70	84.40%
Branco et al.	[18]	18	11/7	94.40%	5.60	8 months (1–30)	90.90%
Chopra et al.	[19]	76	31/45	–	9	–	–
Matsagkas et al.	[20]	7	0/7	100%	0	27 (6–44)	86%

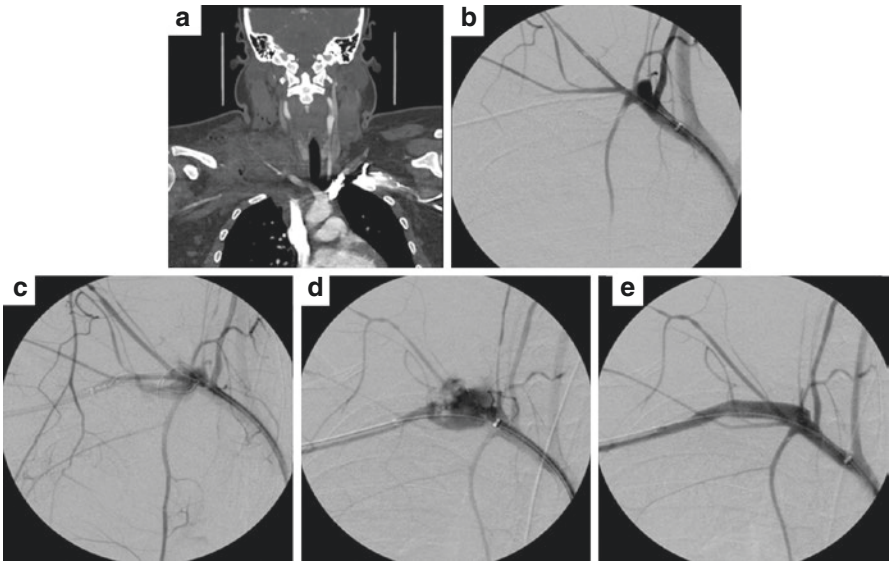

Fig. 4.1 GSW to R clavicle found to have pulseless R upper extremity. (**a**) CTA reveals injury to R SCA with associated hematoma. (**b**) Angiogram reveals occlusion of R SCA just past the internal mammary artery. (**c**) Snaring of wire in hematoma through retrograde brachial access. (**d**) Through-and-through access using "body floss" technique. (**e**) Completion angiogram following stent graft deployment

4.16 Thoracic Endovascular Aortic Repair

A key application of endovascular stent grafts in trauma is their use in the treatment of blunt thoracic aortic injury (BTAI). The advent of thoracic endovascular aortic repair (TEVAR) has resulted in both improved morbidity and mortality among patients who survive to reach care after severe BTAI. Although appropriate patient selection remains paramount to success, the proven track record TEVAR has provided has dramatically altered the standard of care for BTAI [21].

Azizzadeh et al. were among the first to describe a functional grading system for BTAI, designing the current system utilized by the Society of Vascular Surgery (SVS) for description of these injuries [22]. This grading system has been used to describe the SVS clinical practice guidelines currently followed for BTAI management at many trauma centers. Grade I injuries are an intimal tear with a normal external contour of the aorta, and these can be managed medically and non-operatively. Grade II injuries have an intramural hematoma and can be managed medically or with TEVAR. Grade III injuries have a pseudoaneurysm. Patients with grade III injuries with high-risk findings including a large pseudoaneurysm, a large mediastinal hematoma, or a large hemothorax should undergo emergent TEVAR (Fig. 4.2). Grade III injuries without high-risk findings should undergo urgent TEVAR within 24 h. Grade IV injuries have a pseudoaneurysm with rupture and have a substantial risk of decompensation and death and should undergo emergent

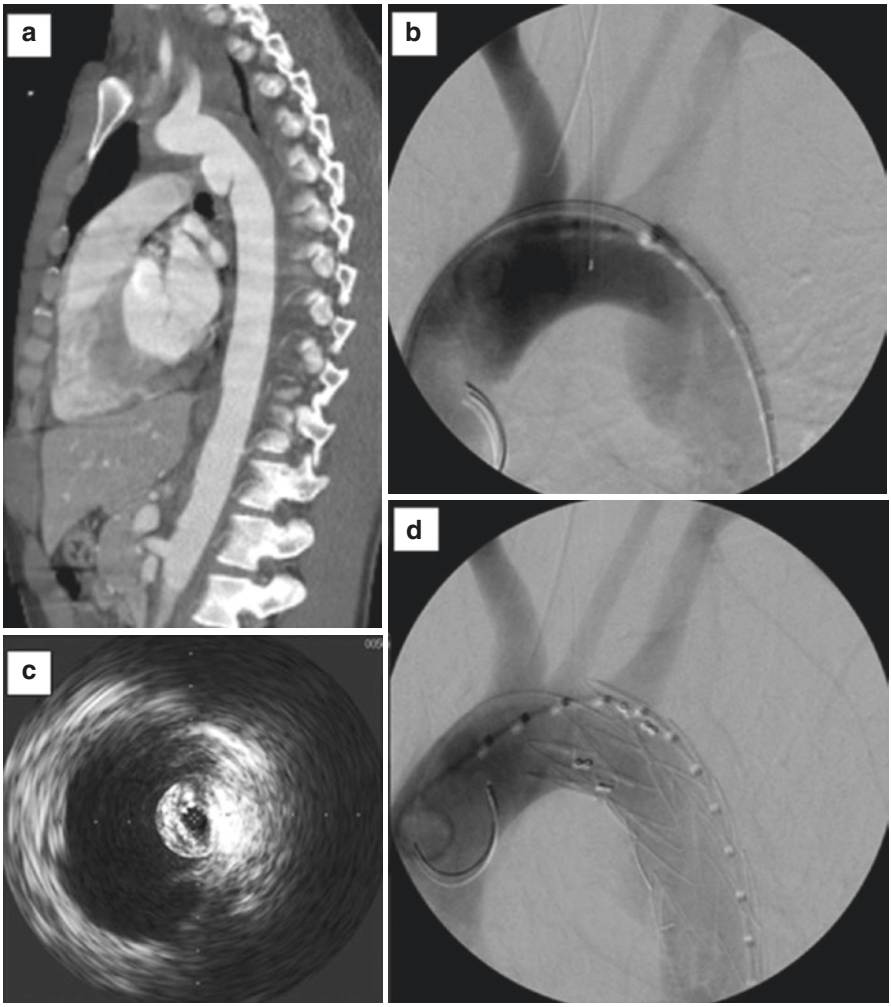

Fig. 4.2 MVC with polytrauma found to have a (**a**) traumatic pseudoaneurysm of the proximal descending aorta at the level of the ligamentum arteriosum measuring 3.0 × 2.5 cm with associated hemomediastinum, (**b**) initial angiogram revealing pseudoaneurysm and associated (**c**) intravascular ultrasound. (**d**) Exclusion of pseudoaneurysm following stent graft deployment

TEVAR [22–24]. The SVS guidelines suggest that the majority of grade I BTAI patients can be managed non-operatively. In a large contemporary multicenter study by DuBose et al., 76.6% of patients with grade I injury were treated non-operatively with only one patient requiring salvage TEVAR. Conversely, the majority of grade II, III, and IV injuries are treated via either TEVAR or open repair (72.1%, 87.0%, and 75% respectively). In this cohort, all patients with grade II injuries initially managed non-operatively with impulse control did not require salvage therapy. On the contrary, patients with grade III and IV injuries had high

aortic-related mortality occurring before the opportunity for repair, 90% and 69%, respectively [21]. Early reports of TEVAR were prone to higher rates of complications and mortality [25], but with the development of newer devices and increased experience, the complication rates have decreased. Stent graft-related complications include endoleaks, stent migration, and access complications. When compared to open repair following BTAI, many contemporary studies reveal a significantly reduced rate of mortality, with comparable rates of spinal cord ischemia and strokes (Table 4.2) [25–28].

Any patient with suspicious findings on CXR (i.e., widened mediastinum, loss of aortic knob, hemothorax, etc.), or those injured by significant deceleration or acceleration mechanisms, should undergo additional imaging with CTA, if hemodynamics allow. The sensitivity of CT of the chest is comparable to aortography. Once the diagnosis is confirmed, aggressive beta-blockade is highly recommended in the absence of contraindications. Although there is no consensus on goal SBP or MAP following BTAI, one busy trauma center sets their therapeutic targets at a SBP <120, MAP <80, and pulse <120. With SBP >120 or pulse >120, then a bolus of esmolol 500 μg/kg is given over 30 s, and if SBP remains >120, a repeat bolus is administered and an esmolol infusion at 50 μg/kg/min is then titrated to achieve target SBP. It is very important to avoid hypotension (SBP <80 or MAP <60), particularly in patients with a possible brain injury [29].

The decision regarding endovascular versus open repair is made largely on the position of the lesion relative to arch vessels. Fortunately, the descending thoracic aorta near the level of the ligamentum arteriosum is most commonly affected. Traditionally, a proximal landing zone of 2 cm was considered acceptable, but newer devices have been used successfully with shorter landing zones. Aortic injuries are usually shorter than lesions due to aortic disease, negating the need for extensive coverage of the distal thoracic aorta, and the need for a preoperative spinal drain to mitigate the risk of subsequent paralysis associated with extensive coverage of the thoracic aorta with a stent graft.

The left subclavian artery (LSCA) is commonly covered to provide effective coverage of the injured descending thoracic aorta. Coverage of the LSCA can add up to 2 cm of a seal zone. Recent experience has revealed that coverage of LSCA by TEVAR can be performed routinely with minimal associated morbidity. Symptoms of subclavian steal or arm ischemia may develop, although both are rare occurrences in the trauma setting. Closely monitoring for symptoms of effort-induced ischemia and cerebellar hypoperfusion with associated retrograde flow in the left vertebral artery will help determine if a carotid-subclavian bypass may be required. There are specific situations that require carotid-subclavian bypass prior to LSCA coverage with TEVAR. Of highest importance is the patient who has previously undergone coronary artery bypass graft using the left internal mammary artery. Coverage of the LSCA in these patients will lead to coronary malperfusion leading to cardiac complications and arrest. It is also important to note the patency of the left vertebral artery and its role in cerebellar perfusion. Left vertebral artery dominance compared to the right may suggest that cerebral perfusion may be compromised following coverage of the LSCA.

Table 4.2 Outcomes comparing endovascular versus open management in the last decade in chronological order

Outcomes of endovascular vs. open management of blunt thoracic aortic injuries											
			Endovascular					Open			
Year	Study	Reference	*N*	Mortality (%)	Stroke (%)	Paraplegia (%)	Stent related complications	*N*	Mortality (%)	Stroke (%)	Paraplegia (%)
2009	Demetriades et al.	[25]	125	7.2	0	0.8	20%	68	23.5	0.00	2.9
2011	Murad et al.	[26]	1538	9	0.3	3.0	5.4%	1215	19.0	0.30	9.0
2013	Azizzadeh et al.	[27]	50	4.0	2.0	0	–	56	8.9	4	0
2015	Dubose et al.	[21]	198	2.5	1.0	0.5	5.5%	61	13.1	0	0
2017	Shackford et al.	[28]	176	5.7	2.8	2.8	9%	28	10.7	4	7.1

4.17 Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA)

Resuscitative endovascular balloon occlusion of the aorta (REBOA) is becoming a more commonly used adjunct to the management of patients in profound shock following trauma. The use of an intra-aortic occlusive balloon was first described for controlling major hemorrhage in the Korean War [30]. Balloon occlusion of the aorta has been shown to be a lifesaving measure after significant hemorrhage from a variety of causes, including for control of bleeding during pelvic surgery, hepatobiliary surgery, orthopedic surgery, postpartum hemorrhage, and repair of ruptured abdominal aortic aneurysms. Reports of this lifesaving adjunct have led to a resurgence of REBOA research in the current era. With the growing interest in the use of REBOA in trauma patients, there has been translational research supporting its potential following hemorrhage. Recently, in one such report in a porcine model of hemorrhagic shock, REBOA showed an improvement in physiologic parameters such as serum lactate, pH, pCO_2, and central, cerebral and coronary perfusion when compared to aortic clamping [31]. A contemporary multi-institutional evaluation of the AAST Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) registry also revealed a trend toward improved survival in patients that underwent REBOA compared to open occlusion of the aorta [32].

Although Level 1 data for the use of REBOA does not exist, there have been a number of retrospective publications reporting at least equivalent outcomes with regard to mortality when comparing REBOA to emergency department thoracotomy (EDT) with open occlusion of the descending thoracic aorta. This has led to the development of indications for REBOA based on expert opinion and case reports in both the military and civilian sectors. Various groups have developed management algorithms for the role of REBOA in control of NCTH. These state that patients with pre-hospital arrest or thoracic hemorrhage should not undergo REBOA and should instead undergo EDT. In the setting of thoracic hemorrhage, the use of REBOA may be potentially dangerous because it could exacerbate hemorrhage from thoracic great vessels. In patients with SBP <80 found to have abdominal hemorrhage, the use of REBOA in Zone 1, which extends from the origin of the left subclavian artery to the celiac artery, with rapid transport to the OR for emergency laparotomy may be as beneficial and potentially less morbid than an EDT. Patients with a SBP >80 mmHg should proceed to the OR for direct control of hemorrhage without attempts to further increase the blood pressure. It seems that REBOA deployed in Zone III, infra-renal aorta to aortic bifurcation, may prove to be the optimal means of immediate hemorrhage control in the patient with pelvic fractures in hemorrhagic shock with a SBP <80. This appears to be the most fitting use for this technology. It is in these patients that, initially, femoral arterial access may be obtained in the trauma bay while primary and secondary assessment is being carried out. The arterial line catheter can then be upsized to the appropriate size sheath for the REBOA balloon. Additionally, this arterial access may be used to perform an angiogram and angioembolization in the operating room if the patient continues to show hemodynamic instability following pelvic packing and external fixation. This

can all be done in the operating room since the transfer of patients to an interventional radiology suite for angioembolization may be disastrous in the setting of ongoing uncontrolled hemorrhage [3].

Japan and the UK have access to smaller-diameter REBOA devices, which may improve the safety profile of this adjunct. Until recently, a 32- or 40-mm CODA balloon (Cook Incorporated, Bloomington, IN) was primarily used for REBOA. These balloons have good conformability but require large sheath access, 10 and 14 Fr, respectively. In the USA, FDA-approved devices were traditionally not well suited for the trauma population. More recently, the ER-REBOA has been FDA approved for trauma use (Prytime Incorporated, Boerne, TX). This device is 7 Fr with a maximal balloon diameter of 32 mm and does not require to be delivered over a wire. Ongoing research is required to determine the applicability of this balloon as an adjunct to trauma resuscitation in the current era.

Although there is no clear consensus on the duration of aortic occlusion, it is obvious that definitive hemostasis should occur as rapidly as possible. At present, we recommend Zone 1 occlusion times of less than 30 min and Zone III of less than 60 min until better evidence can be obtained. Following REBOA placement, the highest priority is to facilitate the shortest possible occlusion time by transferring the patient to an environment where definitive hemorrhage control can be achieved either through an open approach or with angioembolization.

Conclusion

Endovascular methods to achieve torso hemorrhage control continue to evolve. Early results suggest that endovascular hemostasis is associated with fewer systemic complications when compared with open repair for many vascular beds. Technical improvements in the devices available have made endovascular control first-line therapy for aortic transection, life-threatening pelvic bleeding, and axillo-subclavian disruption. Additionally, endovascular adjuncts are seeing increased use as tools to facilitate open repair, such as with REBOA or selective balloon occlusion prior to an incision. Long-term outcome data remains a work in progress, but thankfully, several large national databases are beginning to demonstrate the superiority of endovascular methods compared to standard open surgical hemorrhage control.

Expert's Comments by Yoram Kluger

This chapter by Ravi R. Rajani, MD, FACS, and Christopher Ramos, MD, outlines the various angiographic diagnostic and therapeutic tools available for the management of injuries presenting with non-compressible bleeding.

Correctly indicated endovascular methods to achieve torso hemorrhage control continue to advance. The endovascular approach is associated with fewer unwarranted complications than traditional open techniques. Specifically, this chapter describes endovascular approaches associated with axillo-subclavian, blunt thoracic aortic, visceral (liver, spleen, kidney), aortic, and pelvic injuries. Approaching these life-threating injuries with an endovascular technique has revolutionized trauma

management and resulted in saving the lives of many patients who would previously have succumbed to their injuries or to complicated surgery in the operating theater.

The proper selection of patients, based on their mechanism of injury, injury pattern, and hemodynamic status, is of utmost importance in the utilization of endovascular techniques to arrest bleeding. The timely availability of expert personnel to carry out diagnostic and therapeutic angiographic maneuvers, of a designated operating room (hybrid operating theater) that will allow management of other injuries, and a coordinated team approach to the injured will result in better outcomes due to early and prompt control of the bleeding vessels or organs. Thereafter, the trauma surgeon will continue with surgery to manage hollow viscus injuries or other injuries as indicated.

The authors of this chapter wish to highlight current knowledge on resuscitative endovascular balloon occlusion of the aorta (REBOA). This approach to resuscitation is becoming more frequently used as an adjunct to the management of patients in profound shock following trauma. However, even with the increasing attention paid to REBOA as a temporary tool to arrest bleeding in trauma patients, Level-1 data is currently lacking. The present guidelines are based on expert opinions and a limited number of case reports only.

In a recent publication [33] on REBOA in selected patients with hemorrhage and shock, Brenner and colleagues indicated that REBOA has a survival advantage over emergency room thoracotomy, predominantly in patients not requiring CPR (REBOA = 44% survived to discharged vs. EDT = 0%, $p = 0.008$). This cohort is a subset of the American Association for the Surgery of Trauma (AAST) Aortic Occlusion in Resuscitation for Trauma and Acute Care Surgery (AORTA) study initiative that did not show any difference in survival between patients who received REBOA and those who underwent emergency room thoracotomy. The authors [33] also conclude that *considerable* additional study is needed to further recommend this resuscitative approach in the management of subsets of trauma patients.

In this chapter, the authors quote systolic blood pressure of <80 mmHg as a potential indicator for proceeding with resuscitation using REBOA. Obviously, REBOA should not be applied to hemorrhaging injuries in the thorax. It is obvious that intra-aortic balloon occlusion has a place in the armamentarium of the trauma surgeon while dealing with an exsanguinating patient. We should carefully scrutinize the available data and conduct prospective randomized well-controlled trials to define REBOA's place in resuscitation.

Proper use of REBOA versus abuse is currently a major concern.

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Endovascular Surgery for Extremity Trauma

5

Paul W. White and Erin Koelling

5.1 Introduction

Open surgery has long been the treatment of choice for traumatic extremity vascular injuries. In the early days of endovascular intervention, treatment options were limited and equipment was expensive, unwieldy, and not readily available. Now that vascular surgery has undergone an endovascular revolution, treating trauma patients with endovascular methods is often an option [1]. The decision about whether to use open or endovascular techniques in a trauma case can be difficult. Each surgeon needs to consider the patient, including other injuries and hemodynamic stability; the logistical challenges of each approach, including equipment and staffing; and their own experience level. Other factors, such as the need for and duration of evacuation or transfer to a higher level of care, the ability of the patient to comply with postoperative surveillance and medical therapy, and durability of repair given the patient's age, should be considered.

Literature comparing open and endovascular approaches to extremity trauma is sparse, as most endovascular data focuses on atherosclerotic or aneurysmal disease. How well this data about endovascular therapy can be extrapolated to trauma situations remains unclear. Outcomes such as patency, limb salvage, and complications may not correlate well in a different patient population with different pathophysiology.

When making these decisions, surgeons should keep in mind the possible need for fasciotomy. As with some abdominal vascular pathology, one may be able to treat the vascular pathology with purely endovascular techniques, only to require subsequent open surgery in order to treat compartment syndrome. Does this tilt the cost-benefit ratio towards open surgery in some patients?

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5.2 Endovascular Damage Control

Traumatic vascular injuries are often associated with other pathology according to the mechanism of injury. While a focal, penetrating injury like a stab wound may injure only a vessel, high velocity, blunt, or blast injuries are more likely to have concomitant orthopedic, neurologic, or soft tissue injury. In order to prioritize treatment effectively, a team approach is often required for patients with multiple injuries. Adherence to trauma principles with a "big picture" view of the patient should always be kept in mind. Any change in clinical status should prompt reevaluation and reassessment of the operative approach and goals.

Some polytrauma may raise questions of operative timing—for example, if a patient needs both an exploratory laparotomy for abdominal injuries and revascularization of a vascular extremity injury, open vascular repair may allow both operations to proceed simultaneously. The question of timing of vascular intervention is also encountered when patients have both orthopedic and vascular traumas. Patients with extremity arterial injuries have a 10–70% rate of associated skeletal trauma. Combined arterial and orthopedic injuries have higher amputation rates and rates of graft failure than isolated injuries [2]. Prioritizing the management of these injuries is key in such cases. In the past, repair of the orthopedic injury was generally advised first, since it was thought that manipulating bony structures after vascular repair would cause disruption. Current recommendations are for prompt revascularization, whether by definitive repair or shunting if severe limb length discrepancy exists. Endovascular techniques can be used to temporarily restore blood flow to a limb with definitive open repair delayed to stabilize the patient. Additionally, an endovascularly deployed balloon can provide rapid proximal vascular control if employed by a skilled operator [3, 4]. Intracranial or solid organ injury may hinder the ability to systemically anticoagulate a patient. This may affect the choice of open or endovascular repair, depending on the anticipated length and difficulty of the procedure.

5.3 Lower Extremity Vascular Injuries

Lower extremity arterial trauma has long been recognized as a significant threat to life and limb. In the civilian trauma population, even isolated lower extremity arterial injury has a 10% rate of mortality or limb loss [5]. Most trauma guidelines dictate that patients with "hard signs" of vascular trauma (active hemorrhage, expanding hematoma, absent pulses, or thrill/bruit) should be taken immediately for open surgical exploration. The role of endovascular intervention in patients with lower extremity arterial trauma has not been well delineated. Indeed, the Eastern Association for the Surgery of Trauma (EAST) guidelines for penetrating lower extremity arterial trauma state that "There are no data to support the routine use of endovascular therapies following infrainguinal trauma (Level 3)," although the authors go on to mention endovascular embolization as a treatment for branch

vessel hemorrhage [6]. Treatment of vascular injuries with stent grafts has long been described [7], but routine endovascular intervention remains controversial, with no clear guidelines. Despite this, endovascular management of vascular trauma is becoming more frequent [8]. As with trauma in other locations, trauma to the lower extremity arterial system can cause hemorrhage or ischemia. Proximal injuries (to the common femoral artery and proximal superficial femoral artery) are associated with higher mortality from hemorrhage [5], while injuries to the popliteal and tibial arteries have a higher risk of amputation. The ability to treat both problems is essential to saving life and limb, and endovascular interventions can provide the tools to do so.

5.3.1 Common Femoral Artery

The most immediate goal in treating trauma of the common femoral artery is control of hemorrhage. In one review, half of the mortality in patients with isolated lower extremity arterial injuries was due to injury of the common femoral artery (CFA) [5] and 80% of deaths were due to CFA or superficial femoral artery (SFA) injury. Therefore, rapid control of hemorrhage is essential in this location. Balloon occlusion, from an open ipsilateral approach or contralateral endovascular approach, provides a fast and efficient method of hemorrhage control.

Open surgical access to the CFA has several advantages over endovascular treatment once hemorrhage is under control. It is one of the most commonly performed exposures by vascular surgeons, and many general surgeons are quite experienced in this exposure as well. This site is rarely treated with endovascular therapy in the elective setting due to mechanical forces of the joint and inguinal ligament and proximity to the critical femoral bifurcation. For these reasons, there are limited data on endovascular interventions in the common femoral artery.

As with most locations traditionally treated with open surgery, there is increasing curiosity about the feasibility and durability of endovascular interventions in the common femoral artery [9]. This is due to the availability of technologies such as atherectomy, drug-eluting balloons, and bioabsorbable stents. Endovascular interventions in the CFA tend to have good technical success and low procedural complication rates (especially infection), but have lower patency rates and require more secondary intervention. Additionally, there is concern about using the common femoral artery as an access site or inflow after an endovascular intervention. Currently, endarterectomy remains the gold standard for treatment of atherosclerotic disease. Similarly, open surgery is generally recommended for definitive reconstruction after trauma to the common femoral artery. Any endovascular intervention beyond balloon occlusion for hemorrhage control should be considered only on a case-by-case basis. An exception can be made for use of covered stents as a temporizing measure. Their use in patients with femoral pseudoaneurysm has been described as a bridge to definitive therapy [3].

5.3.2 Profunda Femoris

The profunda femoris artery is not commonly intervened upon for atherosclerotic disease, in part due to its early arborization. There are limited data on endovascular therapy in this location. Embolization of distal branches of the profunda have been described for some time [10], generally after penetrating trauma or iatrogenic injury from orthopedic surgery. Endovascular intervention has the advantage of easier access to the distal profunda branches, as opposed to open surgery which often requires extensive dissection in the musculature of the thigh. This dissection often requires sacrifice of collaterals. Bleeding from proximal branches of the profunda can be controlled with covered stents [11], although attention must be paid to coverage of other branch points. Injuries to the origin of the profunda are best treated with open surgery, so the origin of the SFA is not compromised.

5.3.3 Superficial Femoral Artery

The SFA is the most commonly injured artery in trauma patients. Proximal injuries can cause life-threatening hemorrhage, and ischemia of the leg is also a risk. Providers must be aware of both possibilities when treating this vessel.

Endovascular intervention has several advantages over open surgery in the SFA. Because of its relatively straight course, lack of branches, and the extensive experience with endovascular intervention, it is often chosen as the first-line treatment for atherosclerotic disease. The SFA, however, is a dynamic vessel prone to torsion, compression, and flexion/extension forces. Balloon angioplasty has given way to bare metal stents in this location in many atherosclerotic cases. Since bare metal stents are plagued with in-stent restenosis, drug-eluting stents, covered stents, drug-coated balloons, and atherectomy have become popular.

The choice of treatment for blunt, non-flow limiting dissections and intimal flaps in trauma has not been standardized. Medical treatment, angioplasty, or stenting are all possible treatment options. In the elective setting, stenting is generally done for residual stenosis after angioplasty only, or flow limiting dissection. The length of stent should be kept as short as possible.

Covered stents in the SFA have been studied extensively for atherosclerotic disease. Studies have shown covered stents to have some benefit in long lesions (>20 cm) [12] and to potentially reduce in-stent restenosis [11]. While primary use of covered stents in the SFA for atherosclerosis may be controversial, enough experience has accumulated so that they can be safely used in trauma scenarios.

5.3.4 Popliteal Artery

Injury to the popliteal artery is a grave problem. As the lone inflow to the lower leg, with a collateral supply that is delicate and prone to injury itself, any suspicion of

injury to the popliteal artery must be investigated. Historical studies show that ligation of the popliteal artery in military injuries resulted in a 72.5% amputation rate, with a significant morbidity even in those whose limbs were salvaged [13]. Repair resulted in much better limb salvage rates. Risk factors for amputation include delay in revascularization, blunt injury, and other injuries [14]. Thus, restoration of flow in the popliteal artery in a timely manner is critical.

In the elective setting, stenting the popliteal artery has been controversial. Stent fracture rates of up to 65% have been found in the femoropopliteal segment in the past [15]. As stent technology advances, stenting of the popliteal artery for atherosclerotic disease has become more common [16]. One of the most widely reported non-trauma indications for covered stenting of the popliteal artery is for treatment of popliteal artery aneurysms. Some studies have shown similar rates of patency for endovascular treatment versus open repair [17, 18], while others have shown better results in open repair [19, 20], especially after 1 year [21]. Generally, patients are offered open repair unless they are a poor surgical candidate. Use of stents in the popliteal artery should be done on a case-by-case basis, taking into consideration the injury, the patient's age, concurrent injuries, and hemodynamic stability.

Blunt popliteal or tibial artery injury is twice as likely to result in amputation than penetrating injury. These patients are more likely to have concomitant injuries, including disruption of the soft tissues around the knee [22]. Endovascular intervention for these patients avoids surgical dissection through these injured soft tissues. Interestingly, one series reports placement of two layers of bare metal stents for all popliteal trauma endovascular interventions, even arterial transection, with no contrast extravasation, is reported [23].

5.3.5 Infrapopliteal Arteries

Traditionally, revascularization of tibial vessels for trauma was done only selectively, as one vessel outflow to the foot was deemed adequate. Some question this method, since one study showed amputation rates of 75% in patients with revascularization of only one tibial vessel after injury to all three [24]. Open surgery on traumatically injured tibial vessels can be difficult due to hematoma and vasospasm, thus endovascular intervention may be promising in the infrapopliteal vessels. Data on tibial interventions in trauma are scarce. However, endovascular management of blunt arterial injury at the level of the ankle with cardiac stents has been described [25]. Coverage of traumatic tibial artery pseudoaneurysms with covered cardiac stents has also been described [26]. Due to their relative difficulty to access in an open fashion, the effect of vasospasm in a generally younger population, and increasing experience with endovascular treatment of tibial vessels in an elective fashion, one could predict an increase in the number of endovascular interventions carried out for trauma.

5.4 Venous Injuries

Management of venous injuries is controversial in trauma literature, but it is generally accepted that when possible, venous injuries should be repaired [27]. Although many repairs eventually thrombose, patients who undergo vein repair have lower blood loss, acute edema, and amputation rates than those who undergo ligation. Venous access to the lower extremity via the groin can be difficult to navigate because of valves. Since venous injuries are associated with arterial, nerve, or soft tissue injury, open repair is generally recommended.

5.5 Traumatic Arteriovenous Fistula and Pseudoaneurysm

Open surgical treatment of pseudoaneurysms consists of vessel control and exposure, with either ligation or repair of the vessel directly, with a patch, or with an interposition graft. As with open surgery, endovascular treatment depends on whether the vessel in question is expendable. If so, embolization via coils [28], glue, microspheres, or thrombin (via direct injection) can be performed. Ultrasound-guided compression is also an option if the location of the pseudoaneurysm is amenable to compression. If the vessel must be preserved and is relatively straight with a large diameter, covered stent placement will exclude the pseudoaneurysm.

Traditional repair of traumatic fistulas included ligation and primary repair. Because of a pressurized venous system, this can be difficult to perform in an open manner, so endovascular intervention has therefore become more popular. Endovascular treatment of traumatic arteriovenous fistulas has been described, both by placement of a covered stent across the artery [29, 30] or by embolization if the fistula arises from an expendable artery [31, 32].

5.6 Upper Extremity Vascular Injuries

Upper extremity vascular injuries are less common than lower extremity vascular injuries, but still constitute a significant portion of peripheral vascular injuries [33]. The brachial artery is the most commonly injured upper extremity artery [34]. Compared to the lower extremity, upper extremity injuries have a lower mortality rate and risk of amputation [35]. However, there is a higher incidence of concomitant nerve injuries due to the proximity of the brachial plexus to the axillo-subclavian arteries and the median nerve to the brachial artery [36].

The management of upper extremity trauma remains predominantly open, with endovascular techniques used to treat less than 5% of upper extremity arterial injuries [1, 37]. As in other locations, the number of upper extremity vascular injuries repaired with endovascular techniques has increased over time [1, 8]. Endovascular treatments may also be used more frequently for lower extremity injuries, but the axillo-subclavian artery is the single most frequently treated artery [38, 39]. Covered stents, bare metal stents, balloon occlusion for proximal control, balloon

angioplasty, thrombin injection, and coil embolization have all been used to treat arteries of the upper extremity [33, 37, 40–43].

The goals of both endovascular and open surgical therapy remain stopping hemorrhage and restoring arterial flow to prevent ischemia. The upper extremity contains some of the most and least suitable arteries for endovascular interventions. The subclavian and axillary arteries, with their high flow, large diameter, and static anatomic position, are well suited for covered stent placement. Moreover, these arteries are difficult to expose with open surgery and are intimately associated with the brachial plexus. With concomitant hematomas and tissue destruction so commonly seen in traumatic injuries, the attractiveness of endovascular approaches to injuries to these arteries is clear. Less well suited to endovascular intervention are the distal vessels of the arm, with their smaller size and dynamic conformation. In addition, these arteries are also easily accessible with open incisions, making open surgery a more attractive option.

5.6.1 Axillo-subclavian Arteries

Multiple mechanisms of injury have been described for axillo-subclavian arterial injuries, including iatrogenic injuries from central line placement, gunshot wounds, stabs, fragments from blasts, clavicular fractures, and shoulder dislocations. Subclavian and axillary artery injuries are more commonly treated endovascularly than other peripheral arterial injuries [39]. As mentioned previously, the large caliber and relatively stable conformation of these arteries is favorable to covered stent placement. The treatment of subclavian stenosis due to atherosclerosis with endovascular techniques has been well established, but much of the literature on endovascular treatment of axillo-subclavian trauma consists of case reports or small case series.

DuBose and colleagues in the Endovascular Skills for Trauma and Resuscitative Surgery (ESTARS) working group conducted a review of the literature on the endovascular treatment of axillo-subclavian artery trauma from 1990 to 2012. They described reports of 160 injuries in 160 patients. Approximately 60% of injuries were the result of penetrating mechanisms, 20% were the result of blunt mechanisms, and about 20% were the result of iatrogenic injuries. Over 90% of the injuries were initially successfully treated endovascularly. When long-term follow-up was available, patency was about 85% [44].

Another large review of axillo-subclavian injuries was presented at the Western Trauma Association meeting in 2017. This was a multicenter retrospective review of patients treated for subclavian or axillary injuries from 2004 through 2014 with 239 axillo-subclavian artery injuries identified. Open operations were performed for 61% of these injuries. Treated with an endovascular modality were 17% of patients. Interestingly the use of endovascular techniques did not significantly increase over the time period of the study. In three patients, temporary proximal vascular control was obtained with a balloon catheter. Definitive surgery was then performed with an open repair. Of the 47 patients treated with a stent, thrombosis occurred in three

(6%). One (2%) patient developed a stent infection. Two (5%) patients treated with a stent required amputation. Endovascular modalities were also used more frequently for pseudoaneurysms, whereas open procedures were more frequently used for more severe injuries such as transection or lacerations involving more than 50% of the circumference of the vessel [45].

Branco et al. conducted a retrospective review of patients with axillo-subclavian arterial injuries treated at two trauma centers comparing outcomes between open and endovascular surgery. Of 234 patients with axillo-subclavian injuries, 153 met inclusion criteria. Of these, 12% underwent endovascular repair and 88% underwent open repair. The use of endovascular techniques did increase from 5% to 22% over the study period from 2003 to 2013. To compare outcomes, 72 patients (1:3 ratio endovascular to open) were selected after propensity score matching. In matched patients, those who underwent endovascular repair had a statistically lower mortality. There was also a trend toward lower complication rates and surgical site infections in particular [46].

Chopra et al., in a review of the endovascular treatment of axilla subclavian artery injuries in their institution combined with a review of the national trauma databank from 2010 to 2012, found a stent occlusion rate of 30% within 4 months. They also described a significant lost to follow-up, which impairs our ability to determine long-term outcomes [47]. Perhaps the most extensive review of the existing literature was performed by Sinha et al. who reviewed 74 studies on the open and endovascular management of thoracic outlet vascular injuries. Because of the differences in patient characteristics, they felt comparison between open and endovascular management was possible in three studies. There was no difference in mortality, but endovascular management was associated with a shorter operating time. The incidence of stent graft-related complications varied between 14% and 23% [48]. These reviews commented on the lack of high-quality data to clearly define the benefits of endovascular surgery.

Multiple techniques have been described for treating axillo-subclavian injuries. The most common is the placement of a covered stent or stent graft. Either a transfemoral antegrade approach or a trans-brachial retrograde approach can be used for the placement of a covered stent [49]. Drs. Shalhub, Starnes, and Tran have described the technique to accomplish endovascular repair in complete transections of the axillary or subclavian artery. After passing one wire retrograde from the brachial artery, it is snared with a device from the groin. Once through-and-through access has been obtained, the larger catheter carrying the appropriately sized covered stent is passed retrograde from the brachial artery so as to avoid neurologic complications potentially caused by passing the larger device through the aortic arch [50]. Rohlffs et al. described a similar “body floss” technique with the addition of proximal balloon control in order to control hemorrhage as soon as possible. Several days after placement of covered stents in the artery, the patient was taken back to the operating room for an open repair of the clavicle and brachial plexus. At that time, the stent grafts were replaced with a saphenous vein graft [41].

An endovascular approach to these complex injuries offers an appealing adjunct to open surgery [51]. Balloon occlusion can quickly control life-threatening

hemorrhage in an anatomic area where open proximal vascular control can be difficult to achieve. Covered stents can be used as a temporary shunt or, in suitable patients, definitive repair.

5.6.2 Brachial Artery and Forearm Arteries

The endovascular experience with brachial and forearm arterial injuries is exceedingly small. The literature has a few case reports on these injuries. Many of the injuries described are a result of iatrogenic trauma. In the PROspective Observational Vascular Injury Treatment (PROOVIT) registry, brachial, radial, and ulnar arteries accounted for only 7.7%, 4.6%, and 4.6%, respectively, of the vascular injuries recorded. Only one of 42 brachial artery injuries and no forearm artery injuries were treated with endovascular surgery [39]. In their review of upper extremity arterial injuries over 5 years at a Level I Trauma Center, Franz et al. described no attempts to manage brachial or forearm artery injuries with endovascular techniques, despite the fact that they accounted for over 90% of the 159 injuries sustained in their series [37].

Maynar et al. reported two cases of brachial artery transection treated with covered stents. One of these patients had an early thrombosis of the stent requiring a second endovascular procedure with a second stent placement. Both injuries were the result of blunt trauma. One required a combined femoral-brachial approach similar to the technique described for axillo-subclavian injuries [52]. Lonn et al. also reported two cases of brachial artery injury. Both injuries were dissections from blunt trauma. Both patients had significant decrease in the radial pulse, as well as symptoms of pain and paresthesias. Both dissections were treated with balloon angioplasty, and both brachial arteries were patent at follow-up, one at 10 months and one at 4 years [42]. Of 11 patients with upper extremity arterial injuries who underwent endovascular treatment, Carrafiello et al. reported two brachial artery injuries. They reported a primary patency rate for all 11 injuries of 92.3% and an assisted primary patency rate of 100% at a mean follow-up of 47 months [33]. Lastly, Temizkan et al. reported a case of a brachial artery pseudoaneurysm treated with a covered stent. This procedure was complicated by a broken catheter which had to be removed with a snare [53].

Most of the reports of endovascular treatment of the forearm arteries involve iatrogenic injury to the radial artery. Nough et al. reported a case of right ulnar and right radial artery injuries in the same patient after a gunshot wound. Coronary balloon expandable stent grafts were placed in each artery. Patient follow-up at 6 months revealed normal radial and ulnar pulses without signs of ischemia [54]. Summaria et al. also used a covered coronary stent to repair a pseudoaneurysm caused by a radial approach for cardiac catheterization [55]. Others have described treating pseudoaneurysms with prolonged angioplasty or placement of a second radial artery sheath for a prolonged period of time. Both techniques successfully addressed the pseudoaneurysms by occluding the neck of the pseudoaneurysm [56, 57].

5.7 Postoperative Care

In the immediate postoperative period, the distal vascular examination should be monitored as in all arterial repairs. The patient should be assessed for compartment syndrome and reperfusion injury, and attention should be paid to urine output and renal function in order to avoid or temporize contrast-induced nephropathy.

Medical therapy will depend on the intervention performed and coexisting injuries. Accepted medical treatment after endovascular therapy is generally taken from the literature on atherosclerotic disease, where prevention of restenosis is key. If tolerated, patients should be placed on an antiplatelet agent for life and probably dual antiplatelet (DAPT) for the first month postoperatively. DAPT is thought to prevent stent thrombosis, but this data is extrapolated from coronary literature. It may not have the same risk reduction benefit in a young, healthy, trauma patient, but does have a relatively low-risk profile. Although statin therapy is recommended for all patients with atherosclerotic disease who can tolerate it, there are no current recommendations on routine statins in patients with traumatic vascular injuries [58].

Postoperative surveillance of endovascular repairs is mostly extrapolated from endovascular interventions for atherosclerotic disease, and trauma patients may not have the same risks factors for recurrent atherosclerosis as peripheral arterial disease patients. Providers must tailor their surveillance to the patient and the specific repair performed. A strategy of arterial Duplex with ankle brachial indices (ABIs) prior to discharge, with scheduled Duplex following discharge at intervals determined by the surgeon, is a conservative approach.

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Principles of REBOA

6

Anna Romagnoli and Megan Brenner

6.1 Introduction

Hemorrhage is responsible for 30–40% of civilian trauma mortality [1] and 80% of combat mortality occurring in patients with potentially survivable injuries [2]. Decreased time to hemorrhage control is associated with less morbidity and improved outcomes [1].

Resuscitative thoracotomy is the procedure of last resort for obtaining proximal vascular control, initially described in the 1800s [3], with primary objectives of releasing tamponade, controlling cardiac hemorrhage and intrathoracic bleeding, performing open cardiac massage and providing temporary occlusion of the descending thoracic aorta [4]. Resuscitative thoracotomy is associated with an overall survival rate of 7%, with a 9% survival rate for penetrating injuries and a less than 2% survival rate for blunt trauma [5]. Resuscitative thoracotomy in the setting of penetrating thoracic injury is associated with an almost 20% survival rate [5] and serves the dual purpose of directing circulating blood to the myocardium and brain [6] while also permitting access to injury, allowing an opportunity for temporization and treatment. In the setting of abdominal injury, resuscitative thoracotomy with aortic cross-clamping does stem blood loss [7] but does not allow direct access to the area of injury, thereby requiring additional interventions before obtaining definitive hemorrhage control. The thoracotomy is wrought with significant morbidity to patient and exposure risk to provider and, with a less than 5% survival rate [5] in the setting of abdominal trauma, may not be the intervention of choice [8].

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Resuscitative endovascular balloon occlusion of the aorta (REBOA) is an alternative, less invasive, means of obtaining proximal aortic control. It has been shown to be feasible in comparison to resuscitative thoracotomy with aortic cross-clamping [9] and has been demonstrated in animal studies to support proximal pressure and minimize hemorrhage in an equivalent manner [10, 11].

In addition to its use as an alternative to emergency department thoracotomy, REBOA is also a resuscitative tool to be utilized for prevention of hemodynamic collapse. In hemodynamically unstable trauma patients, REBOA can be used as a temporizing measure to maintain coronary and cerebral perfusion proximally, and decrease hemorrhage distally, while awaiting definitive surgical or angiographic intervention. Mature Level-1 and Level-2 trauma centers are generally able to intervene on an unstable patient in expeditious fashion. Patients who present in low resource settings where delay to hemostasis is routine may potentially benefit from aortic occlusion with REBOA [12].

While the majority of hemodynamically significant bleeds associated with unstable pelvic fractures are secondary to venous plexus disruption, transient inflow occlusion with REBOA in combination with reduction of pelvic volume with binder or external fixator anecdotally may facilitate intrinsic coagulation and hemostasis, as evidenced by subsequent negative pelvic angiograms [13]. Additionally, early placement of a common femoral artery catheter facilitates subsequent angiography in the operating room or interventional suite. The efficacy of inflow occlusion in the setting of abdominal venous injury has also been demonstrated in a porcine model [14].

6.2 History

The concept of endovascular hemorrhage control is not a new one; it was initially described in 1954 in a case series of soldiers in the Korean war [15]. Several early case series demonstrating a potential benefit appeared in the 1980s; Low et al. reported endovascular balloon occlusion of the aorta using the "Percluder" balloon in patients with life-threatening hemorrhage after trauma resulting in 13% survival [16]. Additional promising data were reported by Gupta et al. in 1989, who attempted endovascular aortic occlusion in 21 hemodynamically unstable penetrating trauma patients with a 35% survival rate [17]. During the 2000s, endovascular interventions gained traction in elective vascular surgery, and data began to support endovascular management of ruptured abdominal aortic aneurysms [18, 19]. REBOA in these cases were performed by interventionalists rather than in the resuscitation areas by acute care surgeons.

Endovascular balloon occlusion of the aorta has been described in many case reports for a variety of indications, including post-traumatic liver hemorrhage, obstetric and gynecologic hemorrhage, and complex pelvic oncologic procedures [20–24]. Initial reports of use in trauma patients for management of hemodynamic instability resulting from pelvic fractures were promising, but relied upon in-house interventionalists for definitive control [25]. Dependence on providers who are not in-house for management of traumatic injury has been shown to result in disparate standards of care and patient outcomes [26]. The first contemporary case series of REBOA performed at the bedside by acute care surgeons

was published in 2013 [27] after providers had completed the Basic Endovascular Skills for Trauma (BEST™) course [28].

Early clinical data demonstrated improved overall survival and improved survival out of the emergency department to definitive intervention [9]; the trend toward survival to definitive intervention has been re-demonstrated [29], as has the overall survival benefit [30]. Real-time videography has demonstrated that the rate-limiting step of REBOA is arterial access [31], and the procedure can be performed in an equivalent time frame to resuscitative thoracotomy with aortic cross-clamping [32].

6.3 Indications

Indications for use of REBOA are still under investigation and are based on location of aortic occlusion. Zone I is the descending thoracic aorta between the origin of the left subclavian and celiac arteries. Zone II is a zone of non-occlusion and is comprised of the paravisceral aorta between the celiac and lowest renal artery. Zone III is the infra-renal abdominal aorta, between the lowest renal artery and the aortic bifurcation [33]. Zone I occlusion is indicated for subdiaphragmatic bleeding, while Zone III is indicated for pelvic fractures and other bleeding below the aortic bifurcation (Fig. 6.1 [33], Algorithm 6.1 [28]).

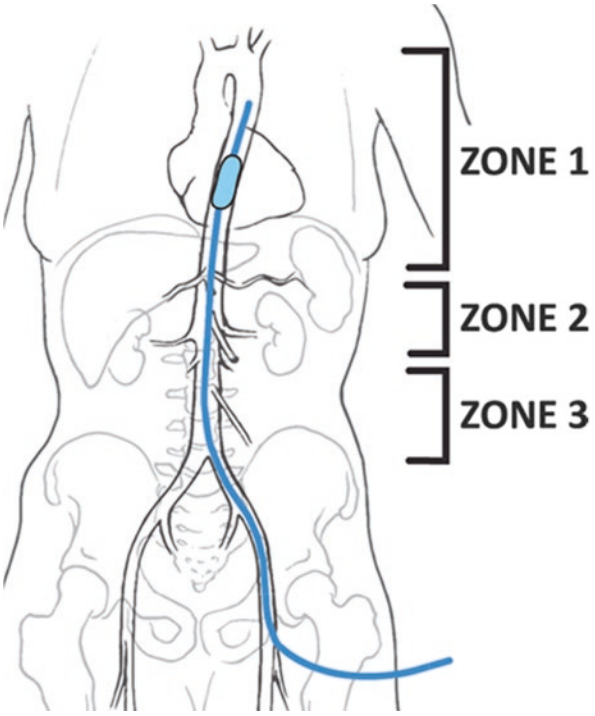
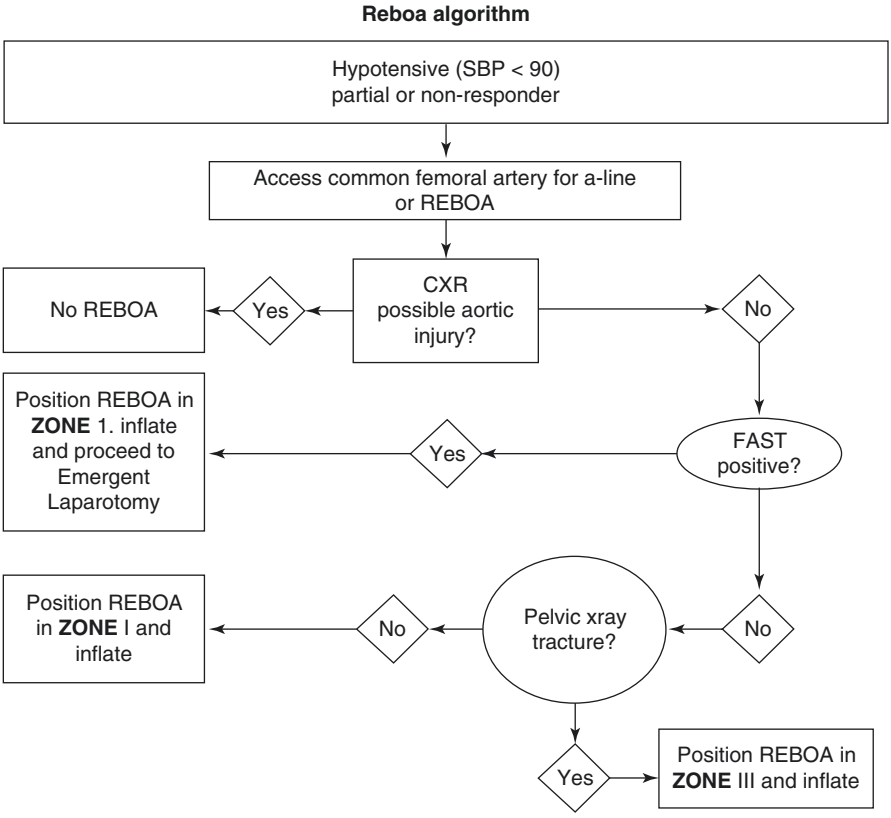


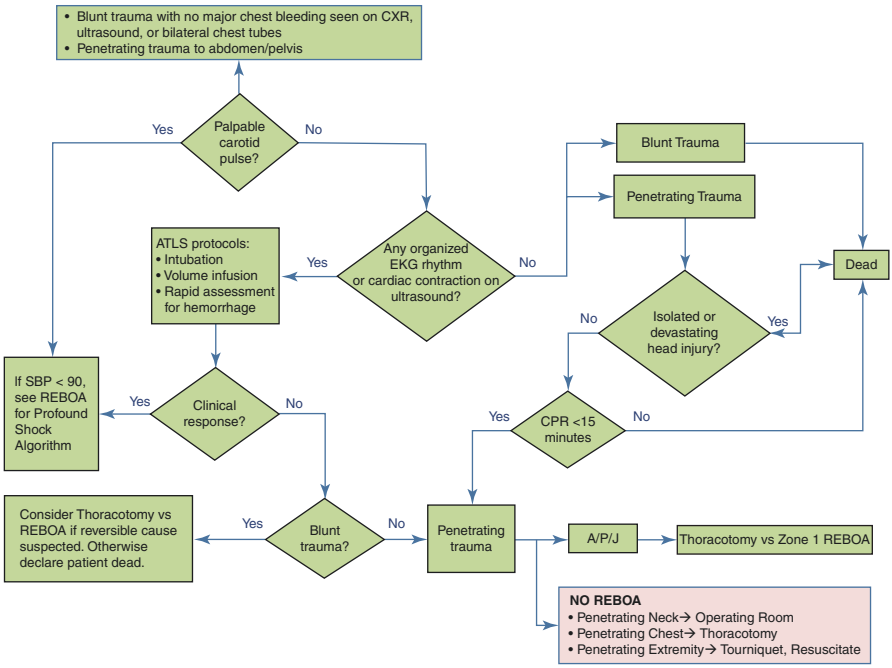
Fig. 6.1 Zones of occlusion



Algorithm 6.1 As published in J Trauma Acute Care Surg 2014

Penetrating thoracic injury in patients in arrest is an absolute contraindication for REBOA placement, as aortic occlusion at the level of the diaphragm or bifurcation without surgical control of hemorrhage will likely increase rate of hemorrhage. Patients in hemorrhagic arrest or extremis following penetrating thoracic injury should undergo emergent thoracotomy [34] for both diagnostic and therapeutic purposes. Using REBOA to occlude the aorta for resuscitation once hemorrhage control is achieved is a viable alternative to open cross-clamping in this setting. Unstable patients with penetrating abdominopelvic or junctional injuries can be considered for Zone 1 REBOA [35].

Blunt traumatic thoracic injury causing major thoracic bleeding detected on CXR, US, or by chest tube placement is an absolute contraindication for REBOA placement [35]. Widened mediastinum or other clinical concern for blunt aortic injury is a relative contraindication for REBOA placement; while these patients may benefit from endovascular management of their injury, intraluminal interventions should be performed under fluoroscopic guidance by trained vascular trauma specialists. Blind instrumentation of the injured aorta can result in disruption or embolization of clot, propagation of intimal injuries and false lumens, or even aortic rupture.



REBOA: resuscitative endovascular balloon occlusion of the aorta; CXR: chest X-ray; EFAST: extended focused assessment with sonography for trauma; ATLS: advanced trauma life support; EKG: electrocardiogram; SBP: systolic blood pressure; CPR: cardiopulmonary resuscitation; A/P/J: abdomen/pelvis/junctional lower extemity.

Algorithm 6.2 Algorithm for patients with cardiac arrest [35]

Patients undergoing prehospital cardiopulmonary resuscitation (CPR < 10 min for blunt trauma, CPR < 15 penetrating trauma) [34] following traumatic arrest were traditionally thought to be candidates for ED thoracotomy alone. However, recent data suggest that REBOA may be an appropriate alternative in patients in arrest from blunt thoracoabdominal injury or penetrating abdominal injury. When compared to ED thoracotomy with open cardiac massage, there is an improved cardiac compression fraction with REBOA [36], no difference in efficacy of compressions as measured by end-tidal CO_2 [37], and both procedures can be performed in an equivalent time frame [32]. A potential overall survival benefit has been demonstrated in patients without penetrating thoracic injuries who receive Zone 1 REBOA compared with ED thoracotomy with aortic cross clamping [30].

The US Military Joint Trauma System is the first organization to promulgate a dedicated REBOA-in-arrest algorithm (Algorithm 6.2) [35]; however several algorithms are in use.

After localization of site of hemorrhage with CXR, FAST, and PXR, other institutions recommend EDT for all traumatic arrests with CPR in progress and consideration of REBOA for patients with abdominal or pelvic hemorrhage with sustained SBP < 80 [12]. The World Society of Emergency Surgery has incorporated REBOA

into the algorithm of patients as an adjunct to be considered along with PPP, AE, and pelvic stabilization [38].

In addition to use in trauma, there are other potential applications for REBOA. Endovascular aortic occlusion is a routinely employed method of obtaining proximal vascular control in ruptured abdominal aortic aneurysms and shows promise as a bridge to hemorrhage control in non-traumatic bleeding from gastric ulcers, duodenal ulcers, visceral pseudoaneurysms [39], postpartum hemorrhage [40], uterine rupture [41], tumor resections [42], and retroperitoneal hemorrhage [43].

6.4 Procedure

6.4.1 Arterial Access

Arterial access is the first and most time-consuming step of REBOA [31]. The ideal location is the common femoral artery below the inguinal ligament. A distal puncture in the superficial femoral artery carries a risk of arterial thrombosis and vessel occlusion due to the smaller diameter of the sheath relative to the vessel. A proximal puncture can lead to injury to the external iliac artery, which can be difficult to compress, leading to uncontrolled retroperitoneal hemorrhage. Ultrasound-guided arterial access is the standard of care in elective vascular interventions, due to decreased incidence of access site complications, including hematoma [44, 45]. Inflicting minimal damage to the vessel during initial access decreases the likelihood of a subsequent access complication. While not always feasible, ultrasound-guided access should be strongly considered, even in the emergent setting. If percutaneous access cannot be obtained, the rapid decision to proceed to arterial cutdown must be made, or REBOA abandoned. Due to the time-consuming nature of this step of the procedure, the initial evaluation phase should include placement of a small micropuncture catheter or femoral arterial line in trauma patients with sustained systolic blood pressure <90 mmHg (Algorithm 6.1).

6.4.2 Special Considerations for Access

In the setting of hemodynamic instability in a patient with severe pelvic fracture, common femoral access can be challenging. When a pelvic binder is already in place, our institution recommends identifying the probable location of the common femoral artery by ultrasound or bony landmark. While manually maintaining pelvic stabilization, the initial pelvic binder should be shifted caudad, such that it is overlying the greater trochanter. A notch is then cut out of the binder overlying the common femoral artery, and a second binder can be placed cranial to the first, leaving an open window over the CFA. This allows for continued pelvic stabilization and access to the groin vessels.

In obese patients, especially in those with a large pannus, the importance of appropriate identification of anatomic landmarks cannot be overstated. The skinfold of the pannus generally does not overlie the inguinal ligament. Cranial retraction of the pannus by an assistant allows for easier palpation of the anterior superior iliac spine and pubic tubercle and appropriate identification of the inguinal ligament. In cases where the anatomy is unclear, ultrasound-guided access is strongly encouraged.

6.4.3 Sheath Placement

Once arterial access has been obtained and the decision has been made to perform REBOA, the arterial line must be upsized to the appropriate sheath. The ER-REBOA catheter can be delivered through a 7 Fr sheath, which is generally easily accommodated in the common femoral artery. If utilizing a large compliant balloon which must be delivered through a 12 Fr or 14 Fr sheath, one must be cognizant of the fact that this sheath may be occlusive in smaller patients (Fig. 6.2), and delivery of a large sheath through a calcified vessel may result in significant intimal injury, although this has not been described as a common complication. The rigid guidewire is placed through the micropuncture or arterial line catheter, and the sheath is upsized over the guidewire.

6.4.4 Balloon Position and Inflation

The length of insertion of the compliant balloon or ER-REBOA catheter is then determined based on injury pattern and external landmarks and the balloon is deployed in

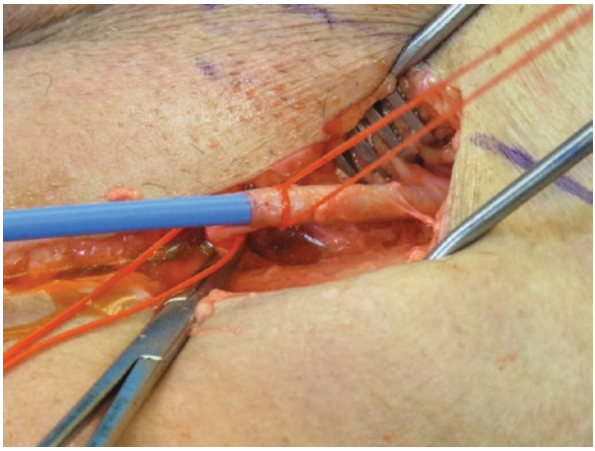


Fig. 6.2 The 12 Fr sheath is seen to be completely occlusive in the common femoral artery; thus antegrade flow is completely obstructed and the limb relies on collateral circulation during REBOA

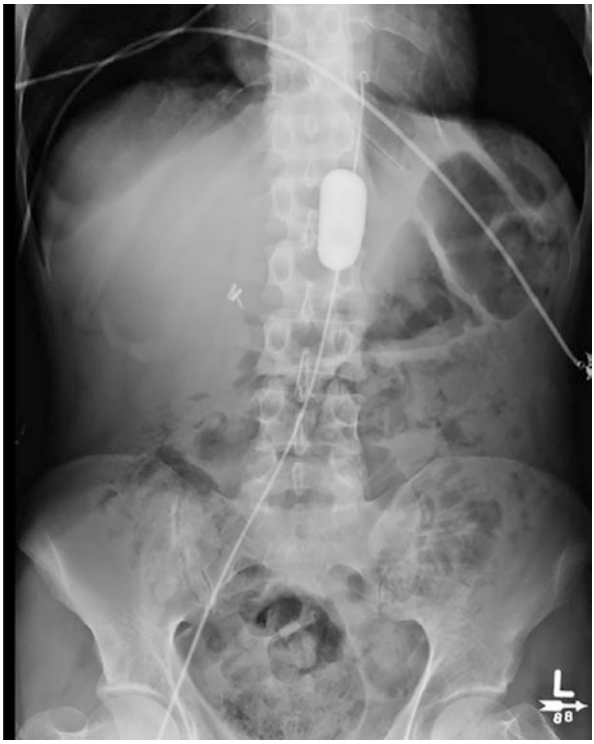


Fig. 6.3 Overinflation of the ER-REBOA balloon as demonstrated on fluoroscopy. The balloon is seen to have an irregular bulge at the 10 o'clock position (shown here), or 2 o'clock position, which is commonly the site of balloon rupture. This can be corrected by removal of 1–2cc of fluid depending on the degree of overinflation

either Zone I or Zone III. Recommendations for length of insertion and volume of inflation are patient dependent, and currently under active investigation [46].

The balloon is manually inflated until the aorta is occluded. This is evidenced by a change in tactile feedback of the balloon (less pronounced with the ER-REBOA), increase in systolic blood pressure measured from the ER-REBOA catheter, an upper extremity cuff or arterial line, and loss of pulsatile flow distal to the occlusion which may be appreciated by a loss of femoral pulse in the contralateral groin. Location of the catheter should be confirmed with X-ray *prior to* inflation of the balloon. Inflating the balloon with a contrast/saline mixture provides easier visualization. Imaging after inflation can rule out balloon over-distension by assessing the shape of the balloon in the aorta (Fig. 6.3).

6.4.5 Management While Occluded

Ischemic burden increases with longer balloon inflation times. Inflation times for Zone 1 should, ideally, not exceed 30 min, and for Zone III should not exceed 60 min [47], although patients have demonstrated tolerance to much longer occlusion times.

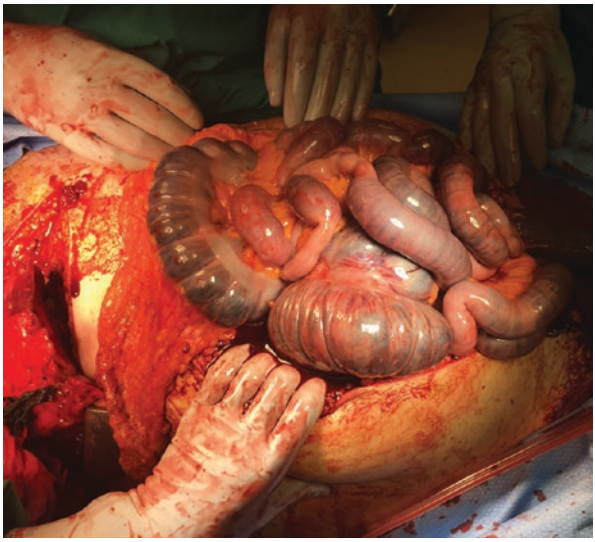


Fig. 6.4 Visceral ischemia after prolonged Zone 1 occlusion

One institution reported mean Zone 1 and 3 occlusion times of 48.6 min and 73.9 min, respectively [13]. In another study, a significant disparity between Zone 1 occlusion times was noted between survivors (52 min) and nonsurvivors (97 min) [39] (Fig. 6.4). Once aortic occlusion has occurred, especially at Zone 1, the maximal duration of occlusion is under active investigation and will likely be expanded with the use of partial REBOA. It has been our observation that the team breathes a collective sigh of relief after balloon inflation due to normotensive values displayed on the monitor. It is critical to remember that the patient continues to be hemodynamically unstable and still requires emergent intervention. Zone 1 REBOA should occur only in settings where emergent hemorrhage control is available, although hospital transfer has occurred successfully within a mature trauma system [48].

6.4.6 Balloon Deflation

Deflation of the balloon may result in an abrupt drop in afterload. This, in combination with exposure to liberated ischemic byproducts, can result in vasodilation and profound hypotension [47]. The current recommendation is slow, graded balloon deflation over a period of at least 5 min [28]; if this is not tolerated, slower deflation and further resuscitation may be required. If profound hypotension occurs after a series of deflation attempts with resuscitation, a careful inspection for further hemorrhage must occur, or a search for non-hemorrhagic causes of instability (cervical spine injury, cardiac dysfunction, etc.). Finally, some patients do not tolerate balloon deflation at all, having succumbed to extensive, irreversible physiologic devastation and cardiac stress. In these cases, the balloon can remain inflated and in position while the patient is moved to another area of the hospital.

6.4.7 Sheath Removal and Post-resuscitation Care

Both catheter and sheath should be removed as soon as possible. One of the attractive aspects of the ER-REBOA catheter is that the smaller 7 Fr sheath does not mandate an operative exploration and arteriotomy closure at sheath removal, unless complications have occurred. Japanese data suggest that fewer limb complications occur with smaller sheaths [49]; however sheath complications have been documented in a recent clinical series in the United States [50]. It is imperative that the operating surgeon is comfortable diagnosing and managing access site and limb complications, including hematoma, pseudoaneurysm, arteriovenous fistula, thrombosis, embolism, and compartment syndrome. A low threshold to consult with endovascular experts should be the rule rather than exception, as troubleshooting sheaths, catheters, and assessing distal ischemia can be a challenge for those who do not perform these tasks routinely.

ICU care should focus on prevention and identification of local and systemic complications. Femoral access complications include arterial disruption, dissection, pseudoaneurysm, hematoma, distal embolism, and distal ischemia [30, 47, 51]. There have been isolated reports of ischemia progressing to extremity amputation [29, 52, 53]. Hourly distal peripheral vascular checks should be performed for 24 h following the procedure, and regular assessment for development of bilateral lower extremity compartment syndrome should be performed. Distal angiography is recommended prior to removal of the sheath, or immediately after if concern exists for thromboembolism, to ensure adequate perfusion [51]. Ultrasound surveillance of the groin sites 24–72 h after sheath removal to assess for pseudoaneurysm formation or thrombus is recommended. Although in the setting of polytrauma it is difficult to attribute renal dysfunction to aortic occlusion alone, judicious monitoring of post-procedural renal function is critical, as acute kidney injury in varying severity is a well-reported systemic complication [52].

It has been hypothesized that supraphysiologic blood pressure and carotid flow generated by aortic occlusion may exacerbate concomitant traumatic brain injury, and this initially seemed to be substantiated by case reports [39, 54]. However, an animal study designed to specifically explore this demonstrated that, while REBOA increased carotid flow and mean arterial pressure, it was not associated with traumatic brain injury progression; in fact, this study suggested that rapid resuscitation showed the greatest correlation with TBI progression [55].

6.5 Current Research

Over the past 5 years, REBOA has experienced an exponential increase in use. It has been embraced by trauma and acute care surgeons in both civilian and military settings.

The AAST prospective Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) registry was initiated in 2013 with the purpose of prospectively recording modern use of aortic occlusion in the acute

resuscitation of trauma patients. AORTA1 reported no difference in time to successful aortic occlusion between RT or REBOA and concluded that REBOA is a viable alternative to open aortic occlusion in centers that have developed this capability [32]. A subsequent analysis of the registry (AORTA2) demonstrated a survival benefit in patients undergoing REBOA when compared to resuscitative thoracotomy [30].

As previously discussed, resuscitative thoracotomy for proximal control in the setting of abdominal injury has dismal outcomes. In addition to providing a less invasive approach to proximal vascular control, patients in traumatic cardiac arrest who receive REBOA as part of their resuscitation, as opposed to resuscitative thoracotomy, have a markedly higher cardiac compression fraction (fraction of time during resuscitation that high-quality chest compressions are being performed), which is associated with superior outcomes in medical arrest patients [36]. This data, in combination with the fact that open cardiac massage has been demonstrated to be no better than closed chest compressions in traumatic arrest as measured by end-tidal CO_2 [37], makes REBOA an attractive, less invasive option for trauma patients in arrest.

Because the majority of potentially survivable combat deaths are due to noncompressible torso hemorrhage and junctional hemorrhage [2], REBOA is of particular interest to the military, specifically on how to effectively move it forward in the deployed setting. Non-surgeon physicians and non-physician providers have been able to demonstrate proficiency on some of the same learning platforms as utilized in the BEST course [56, 57]. These studies fail to address the arterial access phase of the procedure, which is the most challenging aspect. Case reports and series have documented the successful use of REBOA in the forward setting by surgeons and non-surgeons [58]. REBOA is being utilized in a relative mass-casualty situation in the deployed setting; aortic occlusion was performed by an emergency medicine physician while the sole surgeon was operating on another more severely injured casualty [59]. While utilization as a surgeon extender is certainly attractive in this sort of setting, it is important to minimize the time that the aorta is occluded. Zone 1 REBOA is not recommended unless the definitive intervention is anticipated to be initiated within 15 min [51].

When REBOA is utilized in the far-forward setting, the bridge to definitive hemostasis it creates does not seem to be quite long enough. The major downfall of REBOA is the limited time the balloon can be inflated, especially at Zone I, without creating unrecoverable hemodynamic and metabolic derangements. This has resulted in much interest in exploring means by which balloon inflation time can be expanded. One method currently being explored, Partial REBOA (P-REBOA), aims to decrease distal ischemia by allowing titrated, controlled, low-volume flow distal to aortic occlusion while maintaining physiologic carotid flow [60]. Clinically, this can be accomplished by placing the REBOA catheter through an 8 Fr or 9 Fr sheath and transducing a pressure off the sheath during slow decrements in balloon inflation, until a minimal arterial waveform can be observed [61]. While this approach does have the potential to mitigate some of the risks associated with prolonged aortic occlusion, it is resource intensive and requires the ongoing attention of a

physician provider. One animal study confirmed the presence of physiology closer to baseline in partial REBOA animals [55]; however a larger volume and continued blood loss is associated with utilizing REBOA in this fashion [60]. Intermittent REBOA is an alternative approach whereby the REBOA is deflated for short periods of time at planned intervals. This method has been shown in animal studies to support intermediate systolic blood pressure compared with complete REBOA and no REBOA groups [62].

Conclusion

Resuscitative endovascular balloon occlusion of the aorta is being increasingly used for proximal control of hemorrhage in both trauma and non-trauma patients. While it offers a feasible and viable alternative to resuscitative thoracotomy with aortic cross-clamping for aortic occlusion, it can be associated with significant metabolic derangements and ischemia reperfusion injury. Further research is necessary to maximize the potential of this device, especially if it is to be utilized in the pre-hospital setting.

Expert's Comments by Catherine Arvieux

The concept of endovascular hemorrhage control is not a new one; it was initially described in 1954 [15]. A recent technique, the resuscitative endovascular balloon occlusion of the aorta (REBOA), is being increasingly used as a noninvasive clamp of the aorta to stabilize patients' hemodynamics until definitive hemostasis is achieved [38]. Depending on the location of hemorrhage, the aortic balloon can be inflated in two different aortic zones, namely, Zone 1 or III. It has become a salvage therapy in patients with both post-traumatic and non-trauma life-threatening hemorrhage [38]. As shown in this exhaustive documented chapter, REBOA is a swift and effective method for treating circulatory failure in patients, not only those with hemorrhagic shock from intra-abdominal or pelvic injuries and post-traumatic liver hemorrhage but also obstetric and gynecologic hemorrhage and complex pelvic oncologic procedures [38]. In hemodynamically unstable trauma patients, REBOA can be used as a temporizing measure to maintain coronary and cerebral perfusion proximally, and decrease hemorrhage distally, while awaiting definitive surgical or angiographic intervention, especially in the case of angiographics resources not being located within the site of admission. The main concern about the REBOA procedure is safety [38]. Several authors reported complications after REBOA such as groin access complications, lower limb ischemia, limb amputation, acute kidney failure, or rhabdomyolysis [63]. However, the incidence of REBOA-related complications appeared to be acceptable in the hands of experienced radio-interventional radiologists [64]. As shown in this chapter, ultrasound guidance and using a small-size sheath (7 Fr) has been proved to be associated with less vascular complications than larger diameter [38]. It has been described good results with REBOA performed at the bedside by trained acute care surgeons or intensivists, which may be very useful in the pre-hospital

setting [58]. In the future, Partial-REBOA aims to decrease distal ischemia by allowing titrated, controlled, low-volume flow distal to aortic occlusion while maintaining physiologic carotid flow [60].

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Partial REBOA

7

Anders J. Davidson and Timothy K. Williams

7.1 Introduction

Resuscitative endovascular balloon occlusion of the aorta (REBOA) has emerged as a feasible technique for modern hemorrhage control and trauma resuscitation [1, 2]. REBOA results in decreased bleeding below the level of complete occlusion and augmentation of blood pressure and blood flow to the heart, lungs, and brain [3]. While initially advocated for trauma patients in extremis as an alternative to emergency thoracotomy, the indications for REBOA have continued to expand [4]. Its use has been described as a prophylactic hemorrhage control adjunct in major elective surgery, for the management of postpartum hemorrhage, and in nontraumatic cardiac arrest [5–10].

Despite its increasing utilization and broadening applications, REBOA carries several negative physiologic consequences primarily related to the profound distal ischemia created by complete aortic occlusion. Additionally, REBOA can produce severe supraphysiologic proximal hypertension and cardiac afterload, which may have detrimental effects [11, 12]. One proposed alternative to complete aortic occlusion is a technique of partial REBOA (P-REBOA) [13]. The application of partial aortic occlusion allows a *limited amount* of blood flow beyond the occlusion balloon. This technique maintains the benefits of increased perfusion created above the level of occlusion, while simultaneously allowing some blood flow to areas distal to the level of occlusion. The purpose of P-REBOA is to minimize distal ischemia and limit proximal hypertension, while simultaneously limiting downstream bleeding. This may serve to extend the duration of intervention,

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allowing prolonged application in scenarios where hemorrhage control will be delayed beyond the ischemia threshold of complete REBOA (Figs. 7.1, 7.2, 7.3, 7.4, 7.5, and 7.6, Table 7.1).

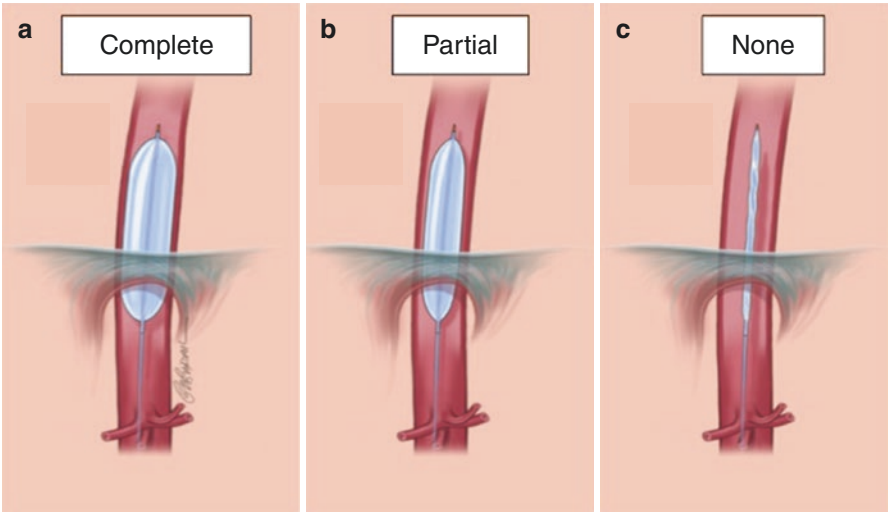

Fig. 7.1 (**a–c**) P-REBOA is partial aortic balloon occlusion and can occur anywhere between 0% and 100% occlusion. This makes P-REBOA dynamic and able to respond to physiologic changes, but makes comparison of studies difficult

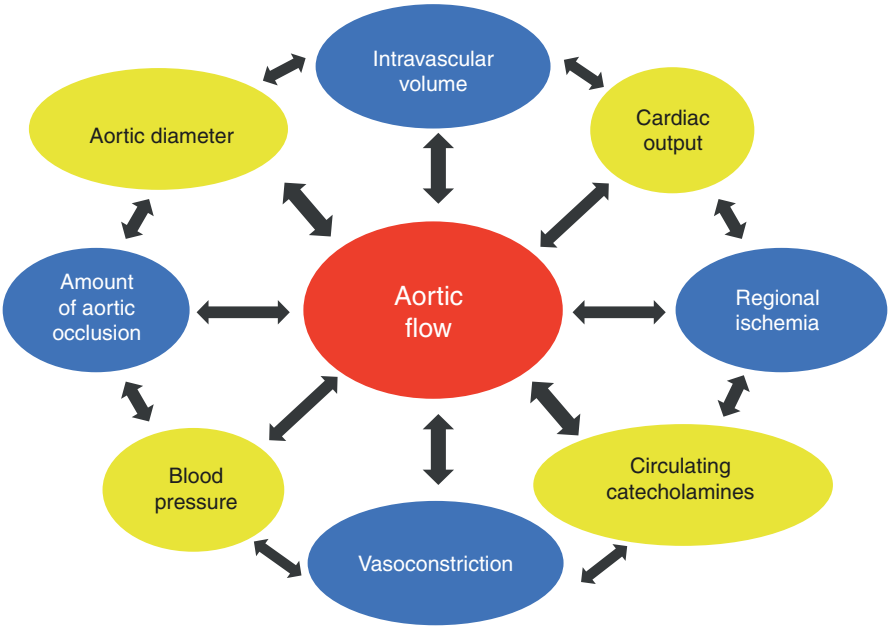

Fig. 7.2 Determinants of aortic flow. Reliably predicting aortic flow at a given degree of occlusion is difficult given complex interactions between physiologic, mechanical, and metabolic factors

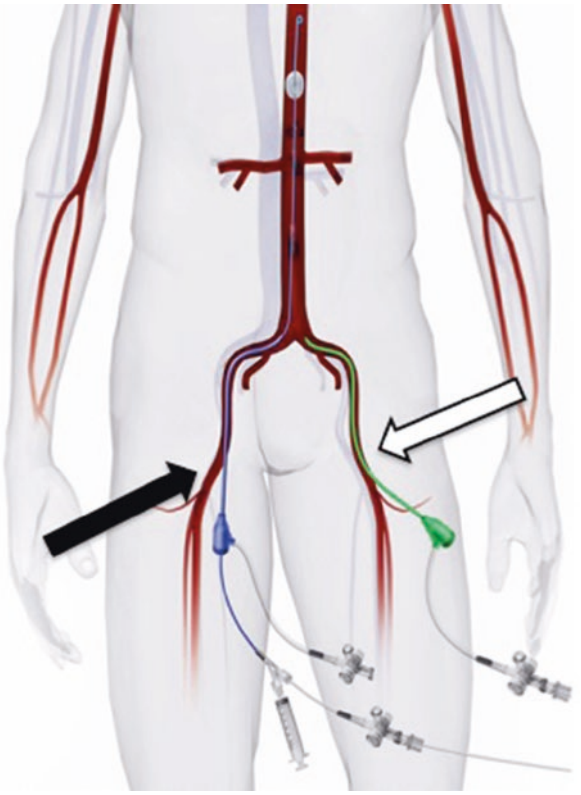

Fig. 7.3 Establishing arterial access is key for P-REBOA. Distal pressure can be transduced through the femoral sheath through which a REBOA catheter is placed, or though the contralateral femoral artery. Proximal pressure can be transduced through a radial arterial line or directly from more modern occlusion catheters such as the ER-REBOA™. The black arrow denotes arterial sheath with REBOA (note integrated arterial pressure port). The white arrow denotes contralateral femoral access

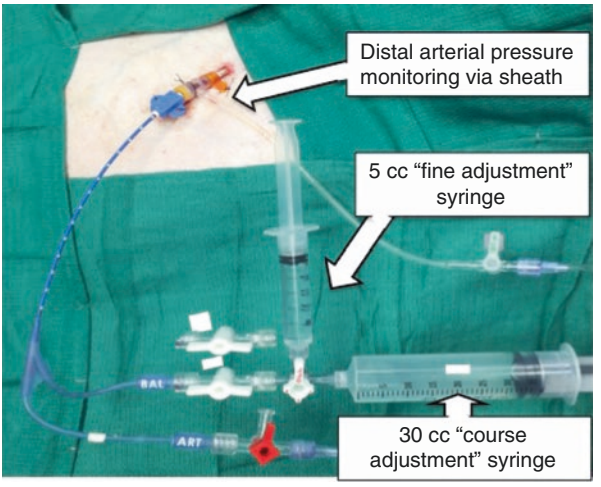

Fig. 7.4 Our preferred setup for REBOA. Note "course inflation" syringe, "fine adjustment" syringe, and distal arterial pressure monitoring through arterial sheath. This example utilizes an ER-REBOA™ catheter, which can also transduce proximal arterial pressure

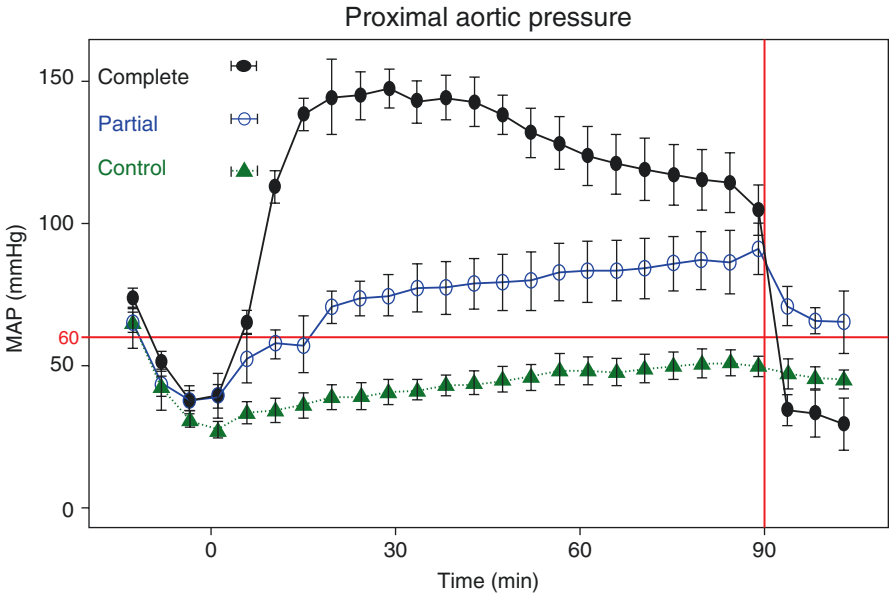

Fig. 7.5 Effects of REBOA, P-REBOA, and no occlusion on proximal blood pressure during intervention in a translational animal model of trauma. Note supraphysiologic pressures created by REBOA with more physiologic blood pressures in the P-REBOA group. The vertical red line at 90 min indicates balloon deflation. The horizontal red line indicates mean arterial pressure of 60

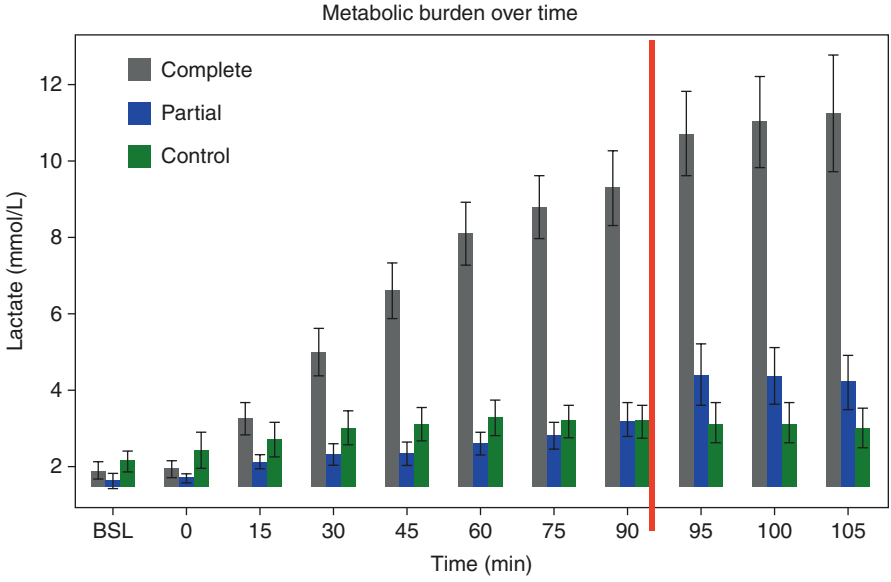

Fig. 7.6 Effects of REBOA, P-REBOA, and no occlusion on circulating lactic acid over time. The red line at 90 min indicates balloon deflation

Table 7.1 Comparison of REBOA and P-REBOA

	REBOA	P-REBOA
Proximal blood pressure	Supraphysiologic	More physiologic
Distal ischemia	Near complete	Relative ischemia
Metabolite washout	Immediate with return of distal blood flow	More protracted
Degree of aortic occlusion	Static: Only complete	Dynamic 0–99%
Potential for ongoing bleeding	Minimal	Considerable
Ease of use	Simpler: Single provider	Difficult: multiple providers
Tolerable duration of use	Shorter	Longer

This chapter will discuss the technique of P-REBOA including the physiology of partial aortic occlusion, translational and early clinical data of P-REBOA, as well as future considerations for continued refinement of the technique.

7.2 Physiology

7.2.1 The Effects of Complete Aortic Occlusion

Occlusion of the descending aorta is associated with a complex hemodynamic response with several intended and unintended physiologic consequences.

It creates a relative arterial hypertension proximal to the level of occlusion with a redistribution of blood flow in order to preserve perfusion to vital proximal organs [14]. Although some scant collateral arterial blood flow remains, this is insufficient to maintain organ viability over prolonged periods [15]. Therefore, aortic occlusion creates an "on the clock" phenomenon, with progressive ischemia as a function of the duration of occlusion [16]. Ultimately, this can result in irreversible ischemia once a critical time threshold has been passed [17]. Additionally, once aortic blood flow is restored, these distal tissue beds experience a reperfusion injury with a wash-out of ischemic metabolites such as potassium and lactic acid. This ischemia-reperfusion injury is quite dramatic and is the primary reason that aortic occlusion is a time-sensitive modality [18]. Notably, patients experience worse outcomes the longer aortic occlusion is maintained due to this phenomenon [19].

The primary intended consequence of aortic occlusion is a near instantaneous increase in blood pressure proximal to the level of occlusion with a resultant increase in blood flow to organs cranial to the level of occlusion. In the shock state, this has the ability to promote and maintain perfusion to critical organs such as the heart, lungs, and brain [20]. The development of arterial hypertension is the most consistent and dramatic finding that occurs during aortic occlusion. This increase in blood flow has the desired effect of maintenance of perfusion; however, often this dramatic increase in pressure can create an additional burden on the heart and may exacerbate injuries such as traumatic brain injury or pulmonary contusions [21, 22].

The two primary physiologic limitations of aortic occlusion are ischemia and reperfusion. This pathologic condition is characterized by an initial restriction of blood supply followed by subsequent restoration of perfusion and oxygenation. The ischemic period is associated with impaired endothelial cell barrier function with a concomitant increase in blood vessel permeability and leakage. In the short term, this causes a cellular transition to anaerobic metabolism in the affected tissues with inhibition of key enzymes that require oxygen as a cofactor. This is associated with alterations to transcription and gene expression. As the duration of ischemia is increased, activation of cell death (apoptosis) occurs. This in turn causes a release of proteases, lysosomes, and key intracellular electrolytes (i.e., potassium) into the extracellular compartment. These ischemic metabolites will continue to collect as the duration of ischemia increases. Eventually, an organ reaches an ischemic threshold of irreversibility beyond which recovery cannot occur [23]. Reperfusion then reintroduces blood flow into the area. This creates an abrupt "washout" of these ischemic metabolites to the systemic circulation. If the duration of ischemia is short, this may be of limited physiologic consequence. However, if the duration is longer, there may be severe consequences such as cardiac arrest or multiorgan failure. Resistance to ischemic injury is dependent on the organ type and its metabolic requirements for oxygen (i.e., skeletal muscle is more resistant and kidneys are less resistant) [24].

7.2.2 The Effects of Partial REBOA

The physiologic rationale for P-REBOA is to decrease distal ischemia by allowing limited blood flow beyond the level of occlusion, while simultaneously reducing proximal hypertension and cardiac afterload. This limited downstream blood flow created by P-REBOA generates a "relative" ischemia as opposed to "complete" ischemia created by REBOA, which serves to extend the duration of intervention and limit the reperfusion injury that occurs at the time of full balloon deflation. Furthermore, P-REBOA may mitigate the "washout" of ischemic metabolites experienced during reperfusion by continuously clearing some metabolites through continued low volume distal flow. Additionally, P-REBOA may lessen the potentially detrimental effects of proximal arterial hypertension and increased afterload associated with complete aortic occlusion. In theory, this will decrease the strain on the heart, and may reduce the potential for pulmonary or cerebral edema.

In the context of uncontrolled injury, P-REBOA does create the potential for ongoing bleeding by perpetuating blood flow to injured vascular beds. This is inherently unpredictable and influenced by factors such as the extent and location of injury, tamponade and thrombus formation at the injury site, and overall coagulation status. It is conceivable that hemorrhage may ensue, particularly from injuries involving large blood vessels such as the aorta and its primary branches. However, this bleeding may occur at tolerable levels that can be met by ongoing resuscitation efforts. This concept is supported by the notion of permissive hypotension after traumatic injury [25]. The theory is that low arterial blood pressures may support

some coagulation and clot formation, which is not easily dislodged by low flow and low arterial pressures. Therefore, P-REBOA may carry a benefit over other REBOA alternatives such as intermittent REBOA that periodically restores high-pressure arterial blood flow.

7.3 Development of the Technique

The complications of ischemia-reperfusion caused by aortic occlusion prompted practitioners to find alternative endovascular solutions to REBOA. One technique considered was intermittent balloon deflation that was extrapolated from other techniques in trauma such as the Pringle maneuver or intermittent aortic cross-clamping. The theory was that intermittently providing blood flow to distal organs could extend the duration of tolerable ischemia. This technique is essentially an "all-or-none" approach of complete occlusion alternating with brief periods of no occlusion. An alternative to the binary nature of intermittent occlusion was to provide continuous, low volume, distal perfusion through partial inflation of an occlusion balloon catheter. By simply changing the volume of fluid in the balloon, varying degrees of arterial occlusion and thus downstream blood flow can be achieved. However, the term P-REBOA is not ubiquitous and can imply any degree of aortic occlusion. This simple fact makes comparison of scientific studies challenging and makes discussion about P-REBOA problematic. The fact that this process is dynamic is a source of strength and also a disadvantage. The inherent advantage of P-REBOA is that the degree of occlusion can be proportionate to the patient's physiology at a given time point. At times complete occlusion may be appropriate, whereas at others no occlusion may be required. However, the physiologic processes that determine aortic blood flow are complex. Determining and maintaining a consistent degree of aortic occlusion is difficult due to the interaction of multiple physiologic, mechanical, and metabolic factors. Therefore, the technique of P-REBOA is somewhat variable from patient to patient and user to user. However, we use the following strategies as guidelines when utilizing a technique of P-REBOA [13].

The first step for P-REBOA is a brief period of complete occlusion. This brief period allows for clot development and hemostasis and provides a brief period for initial volume resuscitation to occur. Next, we establish proximal and distal arterial pressure lines to measure the arterial pressure gradient that will occur across the balloon. During this time, we also use a three-way stopcock on the REBOA balloon with a 30-cm^3 "coarse" balloon syringe for initial balloon inflation and a 5-cm^3 "fine" adjustment syringe to enable precise balloon deflation. Once proximal hemodynamics are in the acceptable range, distal reintroduction of flow is considered. We typically aim for a 7–10 mmHg increase of distal pressure above the baseline distal pressure measurement with the balloon at full occlusion. In other words, if the distal pressure is 10 mmHg at full occlusion, we would target a pressure of 17–20 mmHg. Alternatively, we aim for the beginning of the return to a pulsatile waveform. Ideally, this should look like a dampened arterial pressure waveform with minimal

pulsatility. If the pressure spikes become too high, there is a risk of clot destabilization or hemodynamic collapse. If the patient decompensates, the balloon can rapidly be reinflated to allow for resuscitation to catch up. Additional attempts at P-REBOA can always be re-established when improved hemodynamics are achieved. Once hemostasis has been achieved, the degree of P-REBOA support can be progressively decreased to allow for even more distal perfusion. However, practitioners should be aware that if hemostasis is not ongoing or has not been achieved, there is a risk of disruption of a clot that may have formed with the consequence of resuming hemorrhage. In our experience, the range of desired distal flow occurs over a very narrow range of balloon volume manipulation and requires vigilance and frequent balloon volume titrations. Therefore, when using the technique of P-REBOA a dedicated provider should be available whose sole focus is the balloon occlusion catheter.

7.4 Preclinical and Translational Studies of P-REBOA

Early large animal studies attempted to determine if P-REBOA offered an advantage over complete aortic occlusion. One of the first large animal studies to evaluate the effects of partial aortic occlusion compared REBOA, P-REBOA, and control groups in swine who had undergone a controlled hemorrhage over a 90-min intervention period. P-REBOA was defined as a 50% proximal to distal pressure gradient in this initial work. This study demonstrated feasibility of P-REBOA, demonstrating lower markers of ischemia and less rebound hypotension at the time of balloon deflation compared to complete REBOA. Furthermore, P-REBOA resulted in a more modest blood pressure augmentation, avoiding the severe hypertension seen in the complete REBOA cohort [26].

A similar follow-up study compared complete occlusion to partial occlusion in a severe uncontrolled liver hemorrhage model using similar methodology. However, in this study, partial REBOA was defined as a 60–70% proximal to distal arterial pressure gradient. Complete occlusion again demonstrated supraphysiologic proximal arterial blood pressures, whereas partial REBOA restored near physiologic pressures. However, study animals in the complete occlusion group had a longer mean survival time and experienced less blood loss. Notably, in this study the authors noted difficulty in maintaining a consistent pressure gradient across the balloon. This required frequent balloon volume titrations and resulted in significant fluctuations in blood flow beyond the balloon. This study highlighted the difficulty in maintaining consistent low-volume blood flow beyond the level of balloon occlusion [27].

In another study comparing the effects of REBOA vs. P-REBOA on the progression of traumatic brain injury in swine, the investigators noted that P-REBOA followed a similar pattern of more physiologic proximal hemodynamics and smaller increases in intracranial pressure compared to REBOA [28]. Additional animal studies have focused on the hemodynamic changes that occur during occlusion balloon volume titration. These studies have found that there is a point during

P-REBOA at which there are large fluctuations in aortic blood flow despite very small changes in balloon volume [29]. One study noted that absolute arterial pressure distal to the level of balloon occlusion appeared to have a linear relationship with distal blood flow during early restoration of flow. This relationship was preserved at varying degrees of blood loss, suggesting that absolute distal arterial pressure may be the best surrogate for low-volume aortic flow [30]. Another study in sheep noted that, during balloon inflation, there appeared to be a linear relationship with balloon volume, proximal blood pressure, and distal blood pressure, but the authors did not comment on changes observed during deflation or after an ischemic period [31].

Alternative partial flow strategies have been investigated using unconventional experimental models [32]. In a novel experiment, an extracorporeal flow circuit and automation was used to precisely regulate aortic flow to low level in an uncontrolled hemorrhage model with a 90-min intervention period. This study was the first to utilize a flow-based strategy, termed Variable Aortic Control (VAC), where direct flow measurements were utilized to guide intervention. Unique to this study was a period of 20 min of complete occlusion to allow for some initial hemostasis, followed by distal flow rates of 100–300 mL/min in the VAC group based on preset proximal blood pressure ranges. In this experiment, survival was 90% in the VAC group and only 50% in the complete occlusion group. Additionally, the study again found that complete occlusion caused supraphysiologic arterial blood pressures, whereas VAC was able to maintain more physiologic pressures. VAC animals also experienced less rebound hypotension once complete aortic flow was restored and had faster lactate clearance and higher urine output despite requiring approximately half the volume of crystalloids for resuscitation during a critical care period [33]. The authors went on to develop an automated endovascular platform using conventional balloons, termed Endovascular Variable Aortic Control (EVAC), which was compared to REBOA in a 45-min controlled hemorrhage large animal study. Even at this shorter occlusion interval, EVAC resulted in similar physiologic benefits seen in prior studies, with less ischemia and lower resuscitation requirements during critical care.

Overall, animal studies have demonstrated that P-REBOA is feasible and creates more physiologic proximal arterial pressures compared to that of REBOA. P-REBOA is associated with more blood loss compared to REBOA. It is also difficult to achieve with manual balloon volume titration alone and this fluctuation has shown a higher mortality due to ongoing blood loss in large animal models. Nonetheless, these experimental models have not entirely recapitulated the nuances of an active resuscitation, where ready access to blood products may allow for continued hemorrhage seen with P-REBOA in favor of the progressive ischemic penalty incurred by prolonged complete REBOA. In the future, novel techniques such as EVAC, where automation is used to tightly regulate continuous low-volume flow, may overcome the challenges that exist currently with P-REBOA, striking a delicate balance between ischemic injury and ongoing hemorrhage and enabling prolonged interventions without the need for large volume blood product administration.

7.5 Clinical Evidence and Case Reports

Early clinical reports describing the use of P-REBOA have been generally positive. An early case report describing the use of P-REBOA in the United States noted a positive outcome, but also described the difficulty maintaining a consistent degree of aortic blood flow. The surgeon noted not only wide fluctuations in blood pressure during titration but also minimal blood loss distal to the balloon with rapid resolution of acidosis [34]. P-REBOA has been utilized successfully in cases of hemorrhage from ectopic pregnancy and *placenta accreta* [7, 35]. In these cases, REBOA was able to provide initial hemostasis and then intra-operatively provided some distal blood flow while definitive hemostasis efforts were ongoing. The authors noted that hemostasis was able to proceed at a much more methodical pace given that the degree of ongoing blood loss was minimal with P-REBOA as an adjunct.

P-REBOA has been noted to be the preferred method of REBOA in several centers in Japan [36]. A population-based study reported better hemodynamic responses and longer occlusion duration with P-REBOA compared to REBOA in 78 cases of P-REBOA vs. 63 cases of REBOA. However, there was no noted difference in 24-h or 30-day survival [37].

7.6 Feasibility

Due to the complex interplay of physiologic and mechanical factors, determining and maintaining the degree of P-REBOA is challenging. The benefits of regional hypoperfusion are extrapolated from the positive effects observed from permissive hypotension after traumatic injury. Translational research has shown that use of P-REBOA is effective as a treatment for noncompressible torso hemorrhage and carries advantages over REBOA for mitigation of ischemia-reperfusion.

P-REBOA is not ubiquitous and is difficult to reliably and reproducibly perform with current balloon catheter technology. However, with appropriate resources and a dedicated provider, P-REBOA has been successfully utilized with favorable outcomes. In the event of distal injury, P-REBOA may be associated with ongoing blood loss and a balance needs to be struck between minimizing ongoing hemorrhage and reducing distal ischemia.

7.7 Future Directions

Current use of P-REBOA is through proximal and distal pressure gradients across the balloon. However, it has been demonstrated that maintaining a consistent and reliable blood *flow* rate is difficult at best. Without a direct understanding of blood flow, it is almost impossible to determine the amount or rate of oxygen delivery or organ perfusion. This makes translational and preclinical studies extremely difficult to reproduce and compare to one another. In the future,

balloon catheters will be designed that are able to either measure blood flow directly or dictate the exact amount of blood flow that is allowed past the balloon. Once we understand the amount of blood flow that is delivered the tissues, we can begin to understand how much blood flow is "enough" to maintain tissue viability and delay or prevent cell death. The ischemia threshold after hemorrhage appears to be much earlier than that described for patients with peripheral arterial disease. However, the relationship between minimum blood flow, ischemia, reperfusion, and cell death is not yet known in trauma. This relationship will help inform blood flow titration strategies which during P-REBOA or EVAC allow for comparisons between patients and studies. P-REBOA may also allow for CT scanning with contrast. Translational studies have shown that CT angiography is feasible in the setting of P-REBOA, which may allow for more accurate diagnosis of distal injuries with an occlusion catheter in place [38]. However, its utility for injury diagnosis is unclear at this point.

We envision that P-REBOA will be a feasible alternative to REBOA across multiple and variable applications. Already we have seen it utilized for high-risk pregnancy deliveries and high-risk oncologic resections. We also envision that P-REBOA may develop expanded indications such as a resuscitation adjunct. Practical applications for P-REBOA are likely to expand as balloon catheter technology develops and our understanding of the physiology of P-REBOA continues to grow.

Conclusion

P-REBOA is an alternative strategy for aortic occlusion which allows for some blood flow across the area of occlusion in the hope of minimizing ischemia and reperfusion injury. P-REBOA appears to mitigate supraphysiologic arterial blood pressures that can be observed with complete aortic occlusion. Future catheter designs aimed at improving the ability to perform manual control of P-REBOA are ongoing. Next-generation automated techniques such as EVAC, which build upon the concept of P-REBOA, have shown a survival benefit by carefully regulating low-volume continuous flow in the face of uncontrolled hemorrhage. Benefits of this strategy include reduced cognitive burden on the provider and early detection of hemodynamic deterioration. Future studies will focus on the amount of blood flow required to maintain tissue viability yet prevent ongoing hemorrhage.

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REBOA in Traumatic Brain Injuries

8

Carl A. Beyer and M. Austin Johnson

8.1 Introduction

Traumatic brain injuries (TBIs) are a considerable burden on the healthcare system and society. The Centers for Disease Control and Prevention (CDC) in the United States estimates that TBI is responsible for approximately 2.5 million Emergency Department (ED) visits per year and over 50,000 deaths per year, either as a single injury or as a part of multiple traumatic injuries [1]. Despite a substantial research effort from government and private entities, there has been limited success establishing effectiveness for brain trauma interventions. The cornerstone of TBI management remains the optimization of systemic hemodynamics to ensure the continued perfusion of the injured brain and to minimize secondary injury [2]. However, the concept of permissive hypotension with minimal fluid resuscitation has emerged for patients with noncompressible torso hemorrhage (NCTH) at risk for ongoing bleeding [3, 4]. Thus, optimal hemodynamic goals have become contradictory for multiply injured trauma patients with both TBI and NCTH.

Resuscitative endovascular balloon occlusion of the aorta (REBOA) has emerged as a viable alternative to resuscitative thoracotomy for NCTH by restoring perfusion to proximal vascular beds while arresting downstream hemorrhage [5, 6]. While adoption of REBOA is increasing, appropriate patient selection remains problematic because no consensus clinical guidelines exist [7, 8]. The capability for REBOA to reverse hypotension and promote cerebral perfusion is a potential benefit to the patient with a TBI. However, the secondary side effects of complete aortic occlusion

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may be detrimental to patients with NCTH and concomitant TBI [9, 10]. REBOA can result in supraphysiologic blood pressure proximal to the point of occlusion and increased carotid blood flow which could contribute to secondary injury after TBI by worsening cerebral edema, increasing intracranial pressure, or exacerbating intracranial hemorrhage.

Due to these concerns, alternative techniques of achieving partial aortic occlusion have been developed to off-load proximal pressure by permitting persistent low-volume distal blood flow through partial-REBOA (P-REBOA) or Endovascular Variable Aortic Control (EVAC) [11]. Animal studies demonstrate that P-REBOA can mitigate the hypertension and excessive carotid flow observed with complete aortic occlusion while simultaneously minimizing ischemia-reperfusion injury and subsequent hemodynamic instability upon balloon deflation [12]. To date, there is limited clinical or animal data to fully understand the effects of endovascular aortic occlusive technologies on TBI.

8.2 Traumatic Brain Injury

8.2.1 Epidemiology

TBIs are a global health problem common in both military and civilian populations and the incidence of TBI is rising. Estimates suggest that 50–60 million new TBIs occur every year, the majority of which are minor TBIs [13]. In the European Union, there were 1.5 million TBI-related hospital discharges and 57,000 TBI-related deaths in 2012 [14]. The most recent reports in the United States estimate 2.5 million ED visits per year and 56,000 deaths per year due to TBI [1]. The percentage of all injury-related mortality caused by or associated with TBI is staggering: 30.5% in the United States and 37% in the European Union [13].

A TBI can result from blunt trauma, penetrating injury, or acceleration-deceleration forces [15]. The most common mechanisms for fatal TBI in the United States are motor vehicle collisions, suicides, and falls [16]. In the military, TBI is now considered the "signature injury" of recent conflicts in Iraq and Afghanistan due to blast injuries from improvised explosive devices. Over 70% of battlefield casualties from 2004 to 2013 were caused by explosions and 31% of wounded military personnel suffered a head or neck injury [17].

TBIs are especially pernicious because they can cause deficits in emotional, behavioral, cognitive, and physical domains. TBI is increasingly being recognized as a long-term process and not just an isolated event [18]. Even if patients survive the initial insult, the chronic disease following TBI contributes to increased morbidity and mortality months to years later. Indeed, patients with a TBI have shortened life expectancies compared to matched cohorts even after rehabilitation [19]. Additionally, the financial costs of TBI are significant and growing [20]. The economic impact is a combination of direct medical costs, caregiver costs, and costs due to lost productivity. The cost estimates for TBI are often much higher than for

other "high-cost" diseases due to the prevalence of TBI and the sustained increase in costs over the lifetime of often young victims [21].

8.2.2 Normal Brain Physiology

In an uninjured brain, cerebral blood flow is maintained at a constant rate despite fluctuations in systemic blood pressure to maintain normal cerebral perfusion [22]. This autoregulation is achieved primarily by changes in the caliber of small resistance arteries and functions well across a wide range of systemic blood pressures [23]. The result of cerebral autoregulation is consistent cerebral perfusion irrespective of systemic blood pressure. Autoregulation can maintain optimal cerebral perfusion across most physiologic blood pressures; however, this mechanism begins to fail at the extremes of systemic hemodynamics [24]. Under normal circumstances, cerebral blood flow will not decrease until mean arterial pressure drops below approximately 60 mmHg. Once systemic blood pressure reaches these extremes, decreased cerebral blood flow can result in confusion, dimming of vision, and eventually loss of consciousness and brain death if prolonged. Alternatively, as mean arterial pressure rises above approximately 150 mmHg, cerebral blood flow increases and can lead to headache, encephalopathy, and hypertensive hemorrhagic events. Over time, chronic hypertension leads to changes in the cerebral vasculature which shift the cerebral autoregulation curve [25].

8.2.3 Pathophysiology After Traumatic Brain Injury

Extensive evidence has demonstrated that cerebral autoregulation is impaired after TBI. The usual cubic relationship between systemic blood pressure and cerebral blood flow is replaced by a more linear relationship [26, 27]. Under these circumstances, even mild systemic hypertension or hypotension can cause changes in cerebral blood flow and perfusion. Hypotension with subsequent impaired cerebral blood flow results in ischemia. In the setting of damaged neurons, even short periods of hypoperfusion result in increased neuronal death, increased byproducts of inflammation, and worse outcomes. The duration of hypoperfusion resulting in worse outcomes is short, with multiple clinical studies demonstrating that even 2 min of hypoperfusion results in significant reductions in functional outcomes at discharge [28, 29]. Although less well characterized, episodes of hypertension following TBI with resultant increased cerebral blood flow have been hypothesized to cause clot disruption, further hemorrhage, worsening edema, and increased intracranial pressure. This is further supported by clinical literature that describes a U-shaped relationship between early systemic blood pressure and mortality in patients with moderate-to-severe traumatic brain injuries with worse outcomes for patients who present with either hypotension or hypertension [30, 31]. Current clinical guidelines recommend maintaining systolic blood pressure above 100 mmHg

and targeting a cerebral perfusion pressure between 60 and 70 mmHg in order to stay within the middle of the cerebral perfusion autoregulatory curve [2].

8.3 Aortic Occlusion in Patients with Traumatic Brain Injury

8.3.1 Complete REBOA, Partial REBOA, and Existing Technology

The use of an endovascular balloon to occlude the aorta at the level of the diaphragm to limit distal hemorrhage in patients with thoraco-abdominal trauma was first described during the Korean Conflict [32]. Although one of the patients in this seminal work did have normalization of his blood pressure after balloon inflation, both patients eventually died from their injuries. Despite the promise of a new therapy to salvage patients on the brink of hemodynamic collapse, there were few follow-up studies to this pioneering work until the 1980s, when Gupta et al. described the use of intra-aortic balloon occlusion in 21 consecutive trauma patients suffering from penetrating abdominal trauma [33]. Although hemorrhage control was obtained in 11 patients with seven survivors, thoracotomy with aortic cross-clamping became the preferred method for distal hemorrhage control for the following 30 years, as existing technology for continued advancements in intra-aortic balloon occlusion was limited.

Continued advancement of endovascular technologies and procedures to treat vascular injuries over the past 30 years has resulted in the re-emergence of REBOA as an option to treat thoraco-abdominal trauma. Porcine models of hemorrhagic truncal trauma with delayed intervention and resuscitation have validated the interest in this technology in several studies [34–36]. These landmark translational research studies were followed by the first clinical case series of REBOA for penetrating trauma in 25 years published from two main trauma centers in Baltimore and Texas [5]. This demonstrated the feasibility of REBOA as a salvage therapy in exsanguinating trauma patients. Since then, several additional publications have demonstrated that REBOA is capable of the rapid reversal of hypotension proximal to the level of the balloon while limiting ongoing hemorrhage distal to the point of occlusion.

In the multiply injured trauma patient with a TBI and noncompressible torso injuries in hemorrhagic shock, REBOA offers a theoretical benefit by overcoming hypotension and increasing perfusion to the brain. However, the empirical evidence is not clear and significant data demonstrates that during periods of complete aortic occlusion, blood pressure proximal to the balloon can become supraphysiologic. Large animal studies have demonstrated mean arterial blood pressures approaching 150 mmHg in conjunction with tripling of carotid blood flow [37]. Furthermore, registry data and case reports have reported proximal systolic blood pressures reaching 154 and 180 mmHg during REBOA [38, 39]. In a patient with TBI and subsequent impaired cerebral autoregulation, it has been hypothesized that these elevated blood pressures may result in increased bleeding, clot disruption, and increased intracranial pressure. An additional risk in the use of REBOA in a patient with TBI is the vasodilatory shock state induced by the ischemia-reperfusion injury with ensuing

episodes of hypotension that can occur after balloon deflation. The severity of this shock state depends on the required duration of occlusion and can necessitate aggressive resuscitation once definitive hemorrhage control has been obtained, resulting in nonoptimized cerebral perfusion. These potential complications of REBOA in patients with TBIs have resulted in recommendations that REBOA be employed cautiously or not used at all in this complicated patient population [39, 40].

Currently, there is limited data to support any conclusions. Perhaps the most widely cited publication is a recent case report of massive intracranial hemorrhage following REBOA. In this case, an 86-year-old woman was a pedestrian hit by a car who had a small cerebral contusion with subarachnoid hemorrhage on her initial imaging. The patient decompensated due to hemorrhage from pelvic injuries following her initial imaging and a REBOA was placed with post-placement systolic blood pressures above 180 mmHg. A follow-up CT scan revealed massive intracranial hemorrhage and she ultimately died due to brain herniation [39]. In a separate Japanese study of propensity matched cohorts of trauma patients, patients with TBI were more likely to die after REBOA [41]. Another case series showed a higher mortality rate (67%) in brain-injured trauma patients receiving REBOA compared to the entire cohort (52%) [42].

There is also an argument that elevated blood pressure in patients with TBI may not be as detrimental as initially hypothesized. In a large retrospective study, after controlling for severity of injury as well as other patient demographics, the U-shaped curve of mortality and arrival blood pressure lost significance for patients arriving with hypertension, suggesting that the hypertension was associated with the severity of injury, and not an independent predictor of mortality [43]. Hypertension is also a potential therapeutic adjunct for patients with severe TBIs. In patients with elevated intracranial pressure that is refractory to other interventions, maintenance of cerebral perfusion pressure with elevated systemic blood pressure may minimize cerebral ischemia and secondary injury [44]. While it has now become routine to lower blood pressure in patients with spontaneous intracerebral hemorrhage, most large clinical trials have failed to demonstrate smaller hemorrhage volumes or decreased hemorrhage progression by actively lowering systemic blood pressure [45].

While there has been a tremendous amount of translational clinical data published related to REBOA, there has only been one study directly addressing the effects of REBOA on TBI. In a cortical contusion model of traumatic brain injury, 60 min of complete aortic occlusion did not result in a significant increase in the size of contusion despite a significant increase in proximal systolic blood pressure, a doubling of carotid flow from baseline, and an increase in intracranial pressure during the period of occlusion [11]. This is suggestive that REBOA may not be as detrimental as initially hypothesized; the clinical results may be secondary to the increased morbidity in TBI patients and the difficulty adjusting for this increase with statistical techniques. It is important to note that in this translational model, the duration of hypertension proximal to the balloon was not sustained for the entire occlusion period, suggesting the TBI had a significant effect on the ability of the cardiovascular system to generate the often supraphysiologic blood pressures seen in similar models without a TBI. Further translational work is needed to continue

investigating both the effects of aortic occlusion and REBOA on TBIs, but also the effect that a TBI can have on the normal cardiovascular response to REBOA.

8.4 Future Directions

Alternative techniques and technologies to attempt to maximize benefits from aortic occlusion while minimizing the detrimental effects of proximal hypertension and distal ischemia have been developed and explored by multiple groups. As these new technologies are developed, minimizing distal ischemia will likely have the greatest effect on prolonging occlusion times. The ability of some of these techniques to simultaneously decrease the proximal hypertension that is common with complete aortic occlusion may also prove beneficial if REBOA does truly exacerbate TBIs. Partial-REBOA and EVAC [46] are both techniques that permit small amounts of blood flow distal to the balloon, which has the effect of decreasing the overall ischemic burden as well as decreasing proximal hypertension. These techniques may prove most beneficial in the multiply injured patient with injuries above the level of occlusion in conjunction with NCTH requiring REBOA as an initial intervention.

In the same translational study of complete aortic occlusion with TBI, EVAC was also tested in the setting of TBI and hemorrhagic shock. Partial flow past the point of occlusion provided a more physiologic level of proximal blood pressure support and carotid blood flows were close to baseline. However, there was an increase in intracranial pressure when compared to baseline [11]. The animals that underwent EVAC experienced larger increases in intracranial pressure during resuscitation with shed blood at the end of the occlusion period compared to animals in the REBOA group. This may be explained by the early failure of the cardiovascular system in the REBOA group due to complete aortic occlusion in the setting of a TBI, which may have been partially mitigated by EVAC.

The pace of development related to endovascular aortic occlusion technologies for the trauma patient has been significant. The use of REBOA or any other occlusive technology in the patient with a TBI represents one of the most difficult patient populations to treat. Continued translational research is needed to help guide early clinical use and to further elucidate the complex neuro-cardiac interactions that occur during aortic occlusion in the setting of TBI. As new technologies are developed that attempt to minimize the physiologic side effects of REBOA, it is imperative that these are tested in poly-trauma models that include TBIs. Current REBOA registries should also specifically track REBOA use in patients with injuries proximal to the level of occlusion. In the future, novel aortic occlusion technologies may provide the optimal early intervention for multiply injured trauma patients with TBIs and NCTH.

Expert's Comments by Edoardo Picetti

Traumatic brain injury (TBI) is a leading cause of morbidity and mortality worldwide [47]. The presence of extra-cranial hemorrhagic lesions further worsens the outcome for brain injured patients [48]. Resuscitative Endovascular Balloon

Occlusion of the Aorta (REBOA) is a valuable adjunct for the control of massive subdiaphragmatic post-traumatic hemorrhage [49]. Providing an early aortic occlusion, REBOA improves blood pressure and transiently stabilizes patients awaiting definitive hemorrhage control [49]. In this regard, the temporary occlusion of the aorta would seem to be useful in exsanguinating TBI patients with non-compressible torso injuries. However, as has been thoroughly explained in this well-written chapter, the utilization of REBOA in TBI patients presents several concerns, mainly related to arterial blood pressure (ABP) variations during balloon inflation (ABP ↑) and deflation (ABP ↓) phases [11, 39, 50]. New emerging techniques (e.g., partial REBOA), associated with less ABP variations, seem to be promising [11, 51]. More laboratory and clinical studies are needed to better define the role of temporary occlusion techniques in TBI patients with hemorrhagic shock.

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REBOA-Induced Ischemia-Reperfusion Injury

9

Jigarkumar A. Patel and Joseph M. White

9.1 Introduction

In the critically injured trauma patient, restoration of flow following vascular injury repair with significant or prolonged distal ischemia results in ischemia-reperfusion injury (IRI). IRI is a complex pathophysiologic process involving dysfunction of intracellular and extracellular components responsible for metabolic, thrombotic, and inflammatory signaling and cellular function. Re-establishing blood flow is critical with respect to salvaging ischemic tissues; however, reperfusion paradoxically causes further cellular damage to vulnerable ischemic tissues resulting in threatened function and viability of the end-organs.

IRI in the trauma patient results as a direct consequence of significant, uncontrolled hemorrhage. Hemorrhage has been implicated as the principal physiologic insult responsible for 40% of civilian trauma-related deaths and more than 90% of combat-related military deaths from potentially survivable injuries [1]. Specifically, intracavitary hemorrhage from injury to central vascular structures, solid organs, and pelvic fractures represents the anatomic distribution of vascular injury in 90% of prehospital fatalities [2]. Uncontrolled exsanguination, dependent on the severity and duration of bleeding, leads to cardiovascular collapse, failure of tissue oxygenation, and end-organ ischemia. Furthermore, the incidence of wartime vascular injury has demonstrated a significant increase with respect to historical comparisons [3–9]. As a result, the subsequent management of IRI, in the context of a greater burden of traumatic vascular injury, requires additional investigation to understand the complex relationship between ischemia and reperfusion, as well as novel strategies and therapies to mitigate IRI when encountered.

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Resuscitative endovascular balloon occlusion of the aorta (REBOA) generates limited distal blood flow and perfusion when deployed. This strategy allows for proximal vascular control while the injury (i.e., central vascular injury, solid organ injury, pelvic fracture) is definitively managed. The anatomic location of aortic occlusion and duration of REBOA are critical factors that contribute to IRI during the trauma management process. At present, there is limited clinical data on the incidence of IRI following REBOA deployment. The current literature regarding IRI as a consequence of REBOA is limited to small cohorts and predominantly from animal studies. Given this limitation, this chapter aims to review IRI as a result of REBOA and discuss the current literature on REBOA-associated IRI mitigation strategies.

9.2 Pathophysiology of IRI

The ischemic phase of IRI results from tissue hypoxia and microcirculation stasis (Fig. 9.1). At the molecular level, it involves the interplay between adenosine triphosphate (ATP) stores, intracellular calcium (Ca^{2+}), and reactive oxygen species (ROS) on the mitochondrial membrane permeability transition pore (MPTP). The MPTP is responsible for converting the mitochondria function from an energy producer to a promoter of cell death [10].

With ischemia, there is a relative deficiency of oxygen to stimulate ATP production by oxidative phosphorylation, which in turn decreases the intracellular pH from

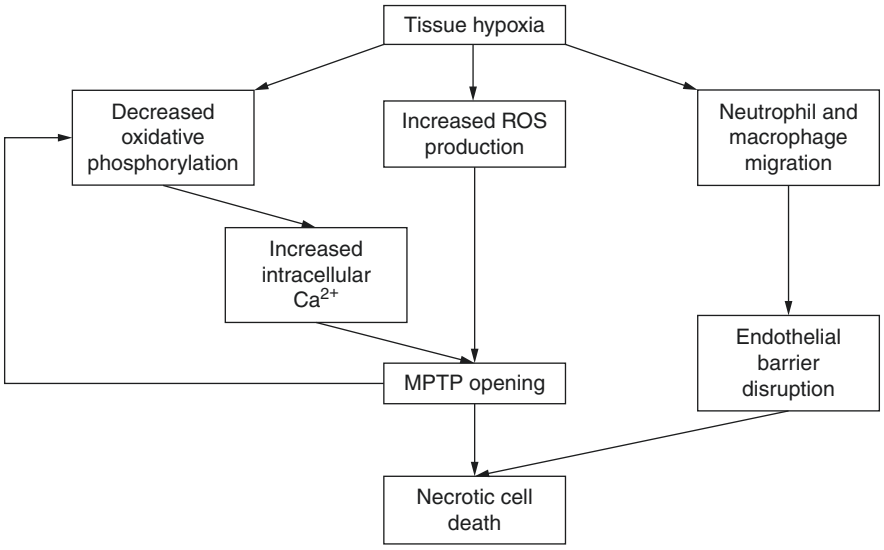

Fig. 9.1 Pathways involved in cell death secondary to tissue hypoxia. *ROS* reactive oxygen species, *MPTP* mitochondrial permeability transition pore, *Ca^{2+}* calcium ion

the accumulation of lactic acid. Glycolysis is typically stimulated; however, this process remains insufficient to meet the metabolic demands of the cell. Through a series of cell membrane transporters, the Na+/H+ antiporter attempts to raise the pH by pumping out H+ ions and raising the intracellular Na+ content. However, the Na+/K+ ATPase cannot remove the Na+ ion due to the lack of ATP. This rise in intracellular Na+ reduces the electrochemical gradient to drive the Na+/Ca+ antiporter, thereby increasing the intracellular Ca^{2+} concentration, triggering MPTP opening [11–14].

Regarding immunomodulation, neutrophils and macrophages migrate to areas of inflammation, inducing cytoskeletal rearrangement, gap formation, and increased permeability [15–17]. At the same time, activated neutrophils also release mediators such as glutamate and adenine nucleotides, which are converted to adenosine, which attenuates the inflammatory response as a feedback mechanism. Adenosine has been shown to stabilize the endothelial barrier, blocking the transmigration of neutrophils [18–20].

During reperfusion, there is a complex relationship between metabolic, inflammatory, and thrombotic pathways. The opening of MPTP is a key contributor, allowing free passage of water and solutes that cause alterations in the electrical potentials and pH gradients, thereby inhibiting oxidative phosphorylation [10, 21]. The innate immunity is also triggered by the amplification of Toll-like receptors (TLR) that induce the NF-kB that stimulate a host of cytokines and immunoglobulin-M antibodies which activates the complement system [22, 23].

9.3 Clinical Consequences of IRI

In patients in hemorrhagic shock secondary to trauma and ischemia-reperfusion, dysfunction at a cellular level leads to a host of clinical consequences. Most commonly, the lower extremities are at risk for acute compartment syndrome, especially with concomitant crush injury or combined arterial and venous injury. On reperfusion, the release of inflammatory cytokines may cause significant fluid shifts and edema to compromise blood flow necessitating fasciotomies.

Renal IRI is well-known in cardiovascular surgery with an interplay between mechanisms generating radical oxygen species, activating complement, and stimulating inflammation to cause acute tubular necrosis and renal dysregulation. Furthermore, with reperfusion of the lower extremities, skeletal muscle breakdown from prolonged ischemia may induce severe rhabdomyolysis, further worsening acute kidney injury.

Pulmonary IRI results secondary to adhesion and sequestration of activated leukocytes, and is the most common organ injured in multiple-organ failure. Pulmonary IRI may also be exacerbated by acute kidney injury causing fluid sequestration, alongside acute lung injury and acute respiratory distress syndrome [24].

In clinical practice, the incidence of organ-specific IRI varies due to many confounding variables and mechanisms. In the Aortic Occlusion for Resuscitation in Trauma and Acute Care Surgery (AORTA) registry from the American Association for the Surgery of Trauma (AAST) AORTA Study Group comparing REBOA with open aortic occlusion, there were no reports of extremity ischemia or spinal cord ischemia in either group. However, acute kidney injury requiring dialysis was 4.3% in the REBOA group versus 2.9% in the open aortic occlusion group, and acute lung injury or acute respiratory distress syndrome occurred in 0% in the REBOA group versus 4.4% in the open aortic occlusion group [25].

9.4 Mitigation Strategies

REBOA generates effective proximal or inflow vascular occlusion. In the context of a complex trauma patient in variable hemorrhage shock and associated end-organ ischemia, the risk of REBOA-mediated IRI is often a necessary repercussion. Considerations to reduce or mitigate the metabolic and physiologic effects of IRI require preprocedure planning, execution and postprocedure management. Preprocedure considerations include patient-specific variables such as the anatomic location of injury and degree of physiologic insult and hemorrhagic shock. Additionally, procedure-specific variables for preprocedural considerations include zone of placement, available resources, and access options. Execution considerations for REBOA comprise duration of occlusion, consideration of partial REBOA or intermittent REBOA strategies for prolonged occlusion times, and hemodynamic maintenance. Postprocedure considerations include management of IRI with respect to continued resuscitation, pharmacologic modalities, and hypothermia. The remainder of this chapter will review the current literature to mitigate IRI as a consequence of REBOA (Table 9.1).

Table 9.1 Mitigation strategies to reduce ischemia-reperfusion injury

Adjunct	Mechanism	Selected reference
Surgical interventions		
Restoration of perfusion	Reduction in ischemia time	Markov et al. [29]
REBOA[a]		
Zone of placement	Reduction in ischemic burden	Standard et al. [26]
Duration of REBOA	Reduction in ischemia time	Reva et al. [28]
Partial REBOA	Reduction in ischemia time	Russo et al. [34]
Hypothermia	Reduction of radial oxygen species	Ward et al. [57]
Conditioning	Reduction of radial oxygen species	Kharbanda et al. [66]
Pharmacologic interventions		
Nitric oxide inhibitors	Reduction in inflammatory response	Li et al. [40]
Valproic acid	Reduction in inflammatory response	Causey et al. [47]
Adenosine	Reduction in inflammatory response	Ross et al. [53]
Heme oxygenase	Reduction of radial oxygen species	Ryter et al. [55]
Statins	Reduction in inflammatory response	Cowled et al. [59]

[a]Resuscitative endovascular balloon occlusion of the aorta (REBOA)

9.4.1 Zone of Placement

When positioning a REBOA device, the appropriate aortic zone for deployment must be determined. Figure 9.2 depicts the standard aortic zones for deployment related to REBOA positioning. Zone 1 is located at the intrathoracic descending aorta from the left subclavian artery to the celiac axis. Zone II is located at the visceral segment of the aorta from the celiac axis to the renal arteries. Zone III is located at the infrarenal abdominal aorta. Zone 1 deployment is associated with a higher risk of IRI compared to Zone III, as the visceral aorta would be perfused with Zone III aortic occlusion. Infrarenal aorta cross-clamping or Zone III balloon placement allows the cardiac output to distribute into the splanchnic circulation, perfusing the abdominal viscera and reducing the risk for ischemia in the abdomen. Suprarenal aortic clamping during abdominal aortic surgery is associated with a

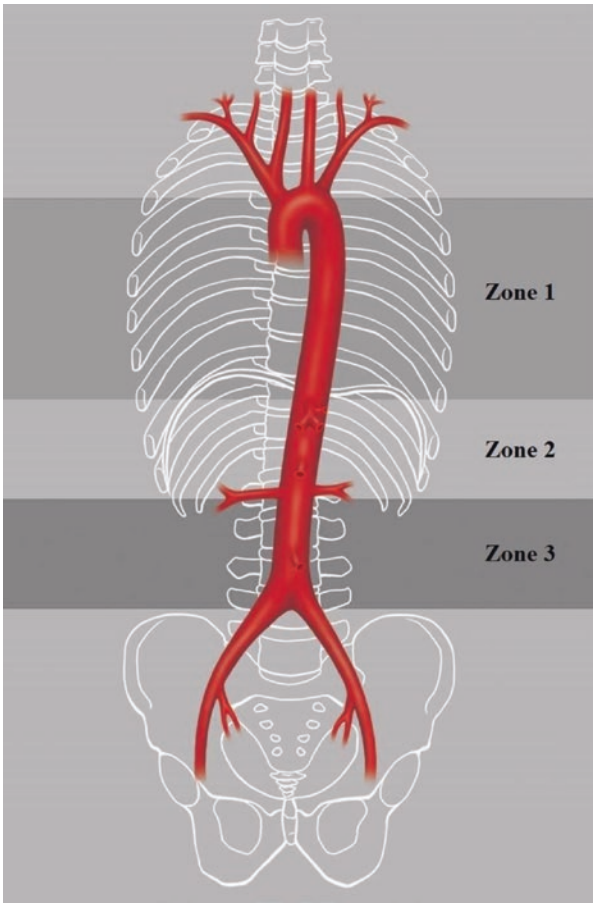

Fig. 9.2 Zones of aortic occlusion for resuscitative endovascular balloon occlusion of the aorta (REBOA)

higher risk of acute kidney injury [26, 27]. Precise placement of the REBOA catheter and balloon based on the clinical scenario should be cautiously judged to avoid unnecessary occlusion and thus creating a larger extent of ischemic tissue. However, comparative models of different zones of occlusion on the degree of IRI have yet to be studied.

9.4.2 Balloon Occlusion Time

Prolonged aortic occlusion significantly contributes to the development of IRI and mortality. In multiple animal models, longer occlusion times produce higher serum lactates, higher levels of circulating IL-6, and TNF-alpha, and are associated with a higher incidence of renal dysfunction, liver necrosis and acute respiratory distress syndrome [28–30]. Not surprisingly in these comparative models, 30–40 min of occlusion was associated with a superior metabolic profile compared to occlusion times between 60 and 90 min [31]. However, no large animal study comparing endovascular balloon occlusion times has demonstrated increased mortality [28–30, 32]. Despite previous studies demonstrating no significant impact on mortality, Martinelli et al. showed that in patients with severe pelvic fracture-associated bleeding who underwent Zone III aortic balloon occlusion, the mean occlusion time statistically correlated with survival rate. A mean aortic occlusion time of 91 min was associated with lower survival compared to a mean of 46 min in this cohort [33].

9.4.3 Partial REBOA

It is recognized that complete aortic occlusion causes abrupt changes in aortic flow, marked elevations in the proximal mean arterial pressure (MAP), and significant risk of inducing IRI. Partial REBOA (PREBOA) strategies have offered promising results in animal models to potentially reduce distal and visceral ischemia and reperfusion. PREBOA allows for continuous, low-volume, distal perfusion while delaying exsanguination and extending survival in multiple animal models [34–36]. PREBOA establishes permissive regional hypoperfusion or regional perfusion optimization distal to the balloon creating a balance between injury hemostasis and the metabolic demands of the downstream tissues. Preserving distal perfusion while controlling hemorrhage has been shown to prolong survival in swine animal models sustaining a highly lethal injury pattern with delayed exsanguination, but results in greater overall blood loss as a consequence [34]. However, additional studies need to be performed in order to identify the optimal targeted distal flow to achieve regional perfusion optimization necessary to minimize IRI injury while controlling hemorrhage.

Russo et al. conducted comparative analyses of complete REBOA and PREBOA in swine injury models with informative results. Compared to complete REBOA (CREBOA), PREBOA provided distal and visceral MAPs similar to the control hemorrhage swine models allowing for reduced acidosis, lower and more

stable lactate concentrations, and reduced leukopenia [35]. In visceral ischemia, the PREBOA cohort demonstrated a significant reduction in duodenal necrosis and no histologic evidence of renal ischemia or necrosis compared to CREBOA and control groups. The authors hypothesized that this effect was observed as a result of the preservation of distal perfusion and continuous washout of toxic metabolites [35, 36].

9.4.4 Pharmacologic Interventions

Aside from Zone III occlusion when clinically feasible and reducing balloon occlusion time with REBOA to reduce the risk of IRI, modulating metabolic and inflammatory targets potentially offers strategies to limit the magnitude and severity of IRI. Many of the current pharmacologic therapies have come from coronary and transplantation interventions, and no studies exist to date on pharmacologic interventions to reduce IRI specifically following REBOA deployment and implementation.

9.4.5 Nitric Oxide Inhibitors

Nitric oxide (NO) regulates vascular tone by relaxing vascular smooth muscle cells that decreases vascular resistance and subsequently increases tissue perfusion. During ischemia, a lack of oxygen reduces NO availability and upon reperfusion acts as a free radical that can form cytotoxic peroxynitrite reactive nitrogen species [37, 38]. Targeting NO production and peroxynitrite has shown protective results in reducing the IRI effects. Metalloporphyrins have been demonstrated to stabilize peroxynitrite molecules into less toxic derivatives that limit reperfusion injury [39].

In addition to forming radial nitrogen species, excess NO can cause systemic hypotension which can become extremely deleterious in the setting of hemorrhagic shock. NO inhibitors, such as N(G)-nitro-L-arginine methyl ester (L-NAME), reduced cerebral infarct volumes, attenuated IRI injury on histology, and reduced free radical species in multiple small animal models [40–42]. However, Li et al. demonstrated a dose-dependent exacerbation of IRI with higher concentrations of L-NAME, implicating the need for additional studies to determine effective and safe dosing [40].

9.4.6 Valproic Acid

Efforts have been made to identify approaches to reduce cellular metabolism to better tolerate ischemia. Valproic acid (VPA), a histone deacetylase inhibitor, has been shown to reduce inflammatory markers, decrease cellular metabolism, and provide protective effects on acute lung injury and acute kidney injury as a result of IRI [43, 44]. On a molecular level, VPA conferred a protective benefit in

multiple hemorrhagic shock animal models by reducing apoptosis through heat shock proteins and antiapoptotic Bcl-2 and downregulating NF-kB, TNF-alpha, and interleukin-6 [45–47]. Shults et al. found prolonged survival with VPA in post-hemorrhagic shock administration, even in the absence of fluid resuscitation [48]. However, in a randomized trial by Nelson et al., no survival or resuscitation benefit was noted, demonstrating that additional studies need to be done to further elucidate dosing, timing, and development of other therapeutic targets [49].

9.4.7 Adenosine

The most widely studied drug in clinical practice is the use of adenosine during acute myocardial infarctions. Adenosine acts to protect endothelium and preserve microvascular flow through anti-inflammatory and anti-ischemic properties [50]. It reduces free oxygen radicals, reduces leukocyte infiltration, and replenishes the depleted phosphate stores during ischemia [51]. In the AMISTAD-I and AMISTAD-II trials, adenosine served as an adjunct to thrombolysis to reduce myocardial infarct size by 50%, but the overall beneficial effect remains to be found [52, 53]. Currently, studies aimed at timing of administration and its effect on IRI resistance are ongoing.

9.4.8 Heme Oxygenase

Heme oxygenase (HO) is upregulated in IRI and provides a strong protective effect on free oxygen radials through multiple pathways [54]. Heme oxygenase is an enzyme that catalyzes the degradation of heme, producing biliverdin, carbon monoxide (CO), and iron byproducts [55]. Each of these byproducts takes part in IRI pathways. Heme serves as a catalyst for free oxygen radical formation, and CO is a vasodilator on the cellular level, and inhibits apoptosis and inflammation through TNF-alpha and IL-6 suppression at a molecular level [55, 56]. Ward et al. demonstrated a protective effect with HO administration in localized ischemia models [57].

9.4.9 Statins

Statins or HMG-CoA reductase (hydroxy-methylglutaryl-coenzyme A reductase) inhibitors function as ubiquitous lipid-lowering medications prescribed for hyperlipidemia. Additionally, statins have been shown to improve endothelial function, increase elevating nitric oxide synthase (eNOS) activity, and inhibit expression of cytokines, adhesion molecules, and superoxides [58]. Cowled et al. administered statins in a rat model of hind limb ischemia and reperfusion. This study demonstrated that rats treated with statins, IRI-mediated neutrophil infiltration, and

sequestration in reperfused skeletal muscle tissues were markedly attenuated [59]. Additionally, these findings support the study performed by Dillon and colleagues which demonstrated a significant reduction in tissue oxidative damage and edema following tourniquet-induced IRI in a rat hind limb model [60].

9.4.10 Hypothermia

Hypothermia may reduce ischemic damage by decreasing oxygen demand and cellular metabolism. In open thoracoabdominal aortic aneurysm repairs, hypothermia has been shown to provide a protective effect on spinal cord ischemia [61, 62]. In skeletal muscle, local hypothermia protects muscle contractility and microvascular permeability after IRI [57, 63, 64]. With respect to free oxygen radicals, hypothermia reduces the concentration of free oxygen radicals [65]. In addition, Ward et al. made an interesting observation that animal models that had hypothermia induced and received heme oxygenase or nitric oxide had an increased microvascular permeability compared to using any of these therapies alone, suggesting a complex interplay between IRI pathways [57]. More studies need to be performed to find the balance between coagulopathic effects of hypothermia, the optimal temperature, and the duration of hypothermia to reduce IRI injury. The clinical feasibility of temperature modulation during the management of a critically injured trauma patient remains to be established.

9.4.11 Preconditioning and Postconditioning

Ischemic preconditioning has been explored as a mitigation strategy in cardiovascular surgery to protect from IRI. Repetitive short periods of ischemia and reperfusion before sustained ischemia may increase ischemia resistance within organs. In a cohort of patients with acute ST-elevation myocardial infarction, prehospital 5-min blood pressure cuff inflation was demonstrated to reduce infarct size [66]. In preconditioning, it is thought that there is an upregulation of the anti-inflammatory pathways that may allow circulation of IRI modulators to reduce IRI, such as NO and calcium homeostasis for MPTP stabilization [66].

In the setting of PREBOA or intermittent REBOA, preconditioning is practiced by allowing partial ischemia with limited distal perfusion. However, in a large meta-analysis review, remote ischemic preconditioning by blood pressure cuff inflation did not demonstrate a significant benefit in acute kidney injury with mixed results in clinical practice, and additional studies focusing on trauma and REBOA may provide additional information [67].

Postconditioning may be more feasible in the trauma setting, with brief periods of ischemia and reperfusion performed prior to definitive restoration of flow and end-organ perfusion. Studies have demonstrated inflammatory modulation; however, further investigation is required [68].

Conclusion

IRI represents a complex and potentially lethal complication associated with restoration of flow after significant vascular trauma and hemorrhage. Mitigation strategies following repair and re-establishment of end-organ perfusion include surgical and pharmacologic considerations and adjuncts. Additional studies are required to define the metabolic and physiologic consequences of IRI, and subsequent optimal treatment following REBOA implementation.

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REBOA in Nontraumatic Cardiac Arrest

10

James Daley and Jonathan Morrison

10.1 Introduction

Nontraumatic cardiac arrest (NTCA) is a significant public health problem, affecting between 166,000 and 310,000 people annually in the United States [1]. The probability of survival to hospital discharge remains low, with one study reporting an average of 4.6% across ten different US states [1]. Despite significant advances in care, such as increased rates of bystander cardiopulmonary resuscitation (CPR), expanded access to automated external defibrillators, and postarrest targeted temperature management, the proportion of people surviving to hospital discharge has only minimally improved [1, 2].

Balloon occlusion of the aorta can be used in the critically ill as a method of temporizing the shock state and acting as a bridge to more definitive therapy such as the cardiac catheterization laboratory. It is accomplished via the femoral advancement and subsequent inflation of a compliant balloon into the aorta, obstructing distal flow, thereby increasing cardiac afterload and proximal aortic pressure [3]. The intermittent balloon occlusion of the aorta via intra-aortic balloon pumps (IABPs) provides support for the patient in cardiogenic shock. IABPs are timed to the cardiac cycle, inflating during diastole to support coronary perfusion, and deflating during systole to permit perfusion to the remainder of the body. Continuous aortic occlusion, termed resuscitative endovascular balloon occlusion of the aorta

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(REBOA), has recently been popularized as a method of controlling noncompressible bleeding in hemorrhagic shock.

During cardiac arrest, preclinical literature demonstrates that the occlusion blood flow to the distal aorta effectively redirects the patient's blood supply toward the heart and the brain, helping to preserve their function [4]. Increased flow improves coronary and cerebral perfusion and oxygenation. A significant body of preclinical evidence dating back to the early 1980s supports the balloon occlusion of the aorta during NTCA as an adjunct to improve traditional advanced cardiac life support (ACLS); however, human trials have been limited to case series [5]. Recent advances in percutaneous balloon technology have broadened this technique's feasibility and set the stage for promising research into its role as an adjunct to ACLS (Fig. 10.1).

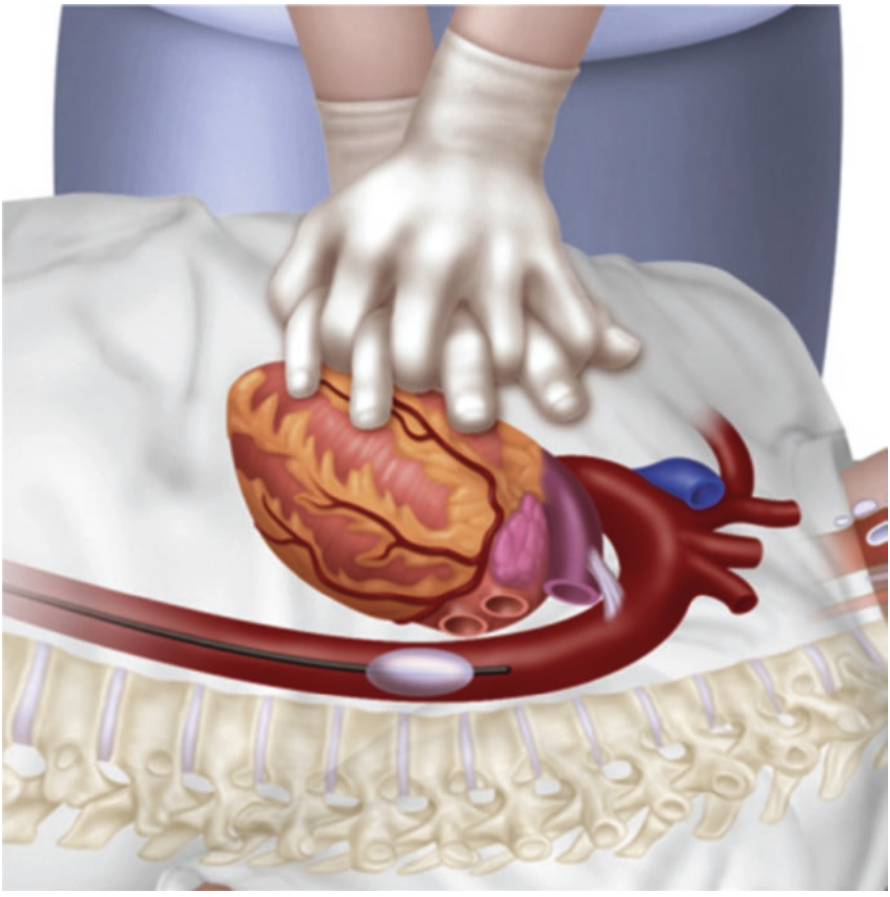

Fig. 10.1 Thoracic aortic balloon occlusion during cardiac arrest

10.2 Nontraumatic Cardiac Arrest

10.2.1 Epidemiology

While many patients who experience cardiac arrest are elderly with significant comorbidities, a large proportion of victims of NTCA are younger, relatively healthy, and could potentially survive their arrest with a meaningful quality of life. The mean age of arrest has been reported to range from 72 to 78 years old [6–8], while 33% of patients in NTCA are of working age (18–64 years old) [6]. A significant number of patients presenting in NTCA have a potentially reversible etiology of their arrest, while rates of associated terminal illness among victims of NTCA have been reported to be as low as 9.4% [7, 8]. A reversible etiology of cardiac arrest is defined as any cause of arrest that if rapidly and effectively treated may allow the patient to recover with significant quality of life. Examples include myocardial infarction, pulmonary embolism, hyperkalemia, and toxicological overdose.

Between 65% and 89% of NTCA have been estimated to be of primary cardiac origin with coronary artery disease as the leading cause of arrest [9]. One study estimated that 43% of arrests were due to acute myocardial infarction and 2% from pulmonary embolism [10]. Another study found that on postmortem examination, approximately 50% of patients had an obstructive coronary lesion that was the likely cause of their arrest [9]. Between 6% and 15% of cases are estimated to have a toxicological cause such as medication or illicit drug overdose [10, 11].

Historical information which can be obtained on patient arrival from the emergency medical system (EMS) providers can be of significant prognostic utility. Patients who survive with good neurologic function typically have at least one of the following significant positive predictors: initial rhythm of ventricular fibrillation or tachycardia, defibrillation attempted prior to arrival to the emergency department, early time to defibrillation, witnessed arrest, and/or received bystander CPR [9]. Physiologic data such as end tidal carbon dioxide (ETCO2) can also be of prognostic utility. Patients who have ETCO2 values greater than 10 mmHg have a significantly higher likelihood of return of spontaneous circulation (ROSC) and survival with good neurologic function [12].

10.2.2 Physiology

In the moments following a ventricular fibrillation arrest, blood flow throughout the body continues after cardiac activity has ceased. Over a period of several minutes, the pressure gradient between the aorta and the right atrium gradually equalizes [13]. These reductions in flow to vital organs cause cerebral and coronary perfusion pressures to plummet, hampering oxygen delivery and cardiac recovery.

Coronary perfusion pressure represents the gradient that drives blood flow through capillary beds that perfuse the myocardium. It is calculated by subtracting

the right atrial pressure from the diastolic aortic pressure, as the contracting heart prevents coronary perfusion during systole [14]. Coronary perfusion pressure and coronary artery flow are significant predictors of increased rates of ROSC and survival to hospital discharge [12–15]. In a landmark study of 100 cardiac arrest patients, Paradis et al. described a strong association between ROSC and a coronary perfusion pressure greater than 15 mmHg [14]. Increases in coronary perfusion pressure during a cardiac arrest are followed by improvements in cerebral perfusion pressure and enhanced cerebral oxygenation [16].

Traditional ACLS is often unable to maintain the circulatory support required for ROSC and preservation of neurologic function. During chest compressions, coronary perfusion pressure rises gradually over minutes and falls abruptly when CPR is interrupted, often becoming negative and impeding blood flow to the heart [17]. During NTCA, ACLS generates coronary perfusion pressures between 0% and 30% of normal values, which are associated with a low probability of ROSC and survival [18, 19]. Even when compressing to a depth of 6.25 cm, traditional CPR could only maintain 50% of prearrest coronary perfusion pressures in anesthetized pigs [20]. Coronary perfusion pressures achieved with ACLS are rarely enough to attain adequate levels of cerebral flow and oxygenation [16, 21], impeding neurologic recovery after ROSC.

While coronary perfusion pressure is critical to restoring cardiac activity, cerebral perfusion pressure is similarly important for neurologic preservation and recovery. Cerebral perfusion pressure refers to the gradient between the carotid artery and intra-cranial pressure, which drives cerebral blood flow and oxygen delivery to the brain. Increases in flow through the carotid arteries serve to bolster the cerebral perfusion pressure, increasing cerebral flow. Increased cerebral perfusion pressure, cerebral flow, and carotid flow are associated with improved neurologic outcomes in NTCA [12, 13, 22, 23].

Another more indirect marker of cardiac output and perfusion during NTCA is end tidal carbon dioxide, a measure of the partial pressure of carbon dioxide at the end of an exhalation. Its three main determinants are pulmonary ventilation, pulmonary perfusion (i.e., cardiac output), and cellular metabolism. During a cardiac arrest, pulmonary perfusion is the predominant factor driving any fluctuations and directly correlates with cardiac output [12]. Levels greater than 10 mmHg have been shown to be significantly associated with ROSC and can be trended to monitor CPR quality [12]. While end tidal carbon dioxide is of clear clinical utility during cardiac arrest, its sensitivity for ROSC has been reported to be between 70% and 90% and hence should not be used as the sole determinant of prognostication during resuscitation [12].

10.3 Evidence for the Use of Aortic Occlusion in Nontraumatic Cardiac Arrest

10.3.1 Preclinical Studies

Preclinical studies that examine the effectiveness of aortic occlusion use a ventricular fibrillation animal model of NTCA. Typically, the animal is placed under general anesthesia, followed by the induction of ventricular fibrillation using an electric

current. The animal is then left pulseless without intervention to simulate a period of time that a person might lie unattended without bystander CPR. Investigators then initiate either standard ACLS or ACLS with aortic balloon occlusion. Studies can be broadly divided into several categories based on the duration of aortic occlusion and whether a separate control group was utilized. Some studies involve intermittent aortic occlusion using short periods of balloon inflation and deflation, while others make use of continuous aortic occlusion. Additionally, many studies are of a crossover design, comparing the hemodynamic effect of aortic balloon inflation and deflation in the same animal and do utilize a separate control group. Other studies focus on outcomes such as ROSC and neurologic function and compare these outcomes in an experimental aortic occlusion group to a control group that received a standard resuscitation.

10.3.1.1 Intermittent Occlusion

Six preclinical studies have tested the effectiveness of intermittent aortic occlusion in animal models of ventricular fibrillation cardiac arrest [24–29]. The duration of aortic occlusion ranged from brief inflation during diastole (with systolic deflation) using IABPs to alternating periods of full aortic occlusion for up to 5 min.

Two crossover studies examined the use of IABPs that inflate during diastole and deflate with systole in a canine model. Authors found that during periods of IABP support (compared to when the IABP was switched-off), animals had significant increases in coronary blood flow [24]. One study noted a near doubling of coronary perfusion pressure as well as increased ETCO2, although no increase in systolic blood pressure [26]. This suggests that while IABP support may assist with increasing coronary perfusion, its effects on cerebral perfusion may be more limited.

Sesma et al. describe a crossover study where canines received two 5 min periods of aortic occlusion, interspersed by 5 min periods of traditional ACLS without aortic occlusion [29]. They noted improvements in hemodynamics during each period of aortic occlusion that were reversed with aortic balloon deflation. Coronary perfusion pressure increased from 10.2 to 29.0 mmHg in the initial period of aortic occlusion, while ETCO2 underwent a more modest (yet statistically significant) increase from 19.2 to 26.1 mmHg. The effects on coronary perfusion pressure and ETCO2 were similar for the second period of balloon inflation.

Tang et al. describe the only controlled experiment using intermittent aortic occlusion. Animals underwent 45 s of aortic occlusion 5 cm distal to the aortic valve (preventing blood flow to the brain) every 2 min and were compared to animals that received a standard resuscitation without aortic occlusion. Each period of balloon inflation demonstrated increases in coronary perfusion pressure from a baseline of approximately 10–50 mmHg. This increase is of greater magnitude than that seen in prior experiments, suggesting that the closer the balloon is placed to the heart, the greater the increase in cardiac perfusion. This increase in coronary perfusion led to a significant improvement in 48-h survival. All ten animals that underwent intermittent aortic occlusion remained alive at 48 h. Perhaps more impressive is that all of these animals had near-normal neurologic function, despite periods of 45 s during aortic balloon inflation where their brain did not receive blood flow. In comparison, only one animal out of ten survived to 48 h in the control group.

10.3.1.2 Continuous Occlusion

Nine studies of continuous balloon occlusion in animal models of NTCA have shown meaningful increases in hemodynamic outcomes or mortality [30–38], while one study failed to do so [39]. Several research groups investigated the effects of aortic occlusion on cardiac and cerebral perfusion using a crossover study design, where animals underwent both a period of balloon inflation and a period of standard resuscitation without balloon inflation. Gedeborg et al. demonstrated an 86% increase in coronary artery blood flow and a 33% decrease in cardiac output during periods of aortic occlusion [34]. The noted reduction in cardiac output is likely due to increased afterload caused by balloon inflation. In a similar study, Spence et al. reported increases in coronary and cerebral blood flow of approximately 100% during periods of aortic occlusion [31]. These results suggest that aortic occlusion is not only effective at increasing cardiac perfusion, but may have beneficial effects on cerebral perfusion as well. Gedeborg et al. reported similar findings, noting that carotid artery blood flow (a surrogate for cerebral blood flow) increased by 63% during periods of aortic occlusion.

Controlled preclinical studies of aortic occlusion note similar effects on hemodynamics, as well as significantly higher rates of ROSC and short-term survival with good neurologic status. Investigators found that groups treated with aortic occlusion had higher mean arterial pressures [34], increased cerebral perfusion [36–38], and improved coronary perfusion [33, 37], when compared to control animals receiving standard ACLS. Gedeborg et al. reported that mean arterial pressure (MAP) in experimental animals was 68 mmHg after inflation of the aortic balloon, compared to 48 mmHg in control animals that received a sham-balloon. In a similar experiment, Rubertsson et al. noted coronary perfusion pressure of approximately 25 mmHg in the aortic occlusion group, compared to that of only 10 mmHg in the control group.

Importantly, improvements in the hemodynamics of experimental aortic occlusion animals resulted in increased rates of ROSC as well as short term survival. In one study in swine with an 8 min simulated down-time where no CPR was performed, 9 out of 13 (69%) aortic balloon animals had ROSC compared to only 3 out of 13 (23%) animals from the control group [34]. A similarly conducted study noted a significant improvement in the rate of ROSC in aortic balloon animals. After 10 min of ventricular fibrillation without CPR, followed by either traditional ACLS or ACLS with aortic occlusion, 7 out of 8 (87%) experimental animals compared to 3 of 10 (30%) control animals achieved ROSC. There was a trend toward greater 24-h survival with 5 of 8 (63%) experimental animals surviving compared to 3 of 10 (30%) controls [33].

While the literature is replete with studies documenting the beneficial effects of aortic occlusion on hemodynamics and survival, there is one study that goes against this trend. In 2002, Liu et al. conducted an experiment where swine were subjected to ventricular fibrillation. After 8 min without any resuscitative efforts, the experimental group received balloon occlusion combined with an intravenous infusion of normal saline, while the control group only received sham balloon occlusion. Investigators found no difference in coronary perfusion pressure, rates of ROSC (6

out of 10 in experimental group, 7 out of 10 in control group), or 24-h survival. It is unclear why this experiment failed to replicate the results of those previously discussed. It is possible that by infusing normal saline in the experimental animals, investigators increased their right atrial pressure, in effect reducing their coronary perfusion pressure to the level of control animals. As there was no difference in coronary perfusion pressures, it is not surprising that rates of ROSC and survival remained similar between the two groups.

Several studies examined the use of the intra-aortic infusion of vasopressors and demonstrated positive effects on cardiac output, however, no effect on cerebral perfusion. Intra-aortic vasopressin and balloon occlusion was associated with an increase in coronary perfusion pressure during CPR in swine, but had no effect on cerebral cortical blood flow [37]. In a similar study by the same authors, the administration of intra-aortic epinephrine had no significant effect on cerebral cortical blood flow and possibly had an adverse effect, likely due to the vasoconstrictive effects of epinephrine [40]. A study by a different group found no difference in coronary perfusion pressure, rates of ROSC, or survival, when animals were given intra-aortic epinephrine. However, they did find that experimental animals had much higher rates of hemorrhagic myocardial necrosis on autopsy, suggesting that intra-aortic epinephrine may have a cardiotoxic effect.

10.3.1.3 Selective Aortic Arch Perfusion

Certain aortic balloon catheters are capable of infusing large volumes of various substances, such as hyper-oxygenated compounds and medications, directly proximal to the site of aortic balloon occlusion, a technique known as selective aortic arch perfusion (SAAP). Pioneers of SAAP believe that it may provide superior improvements in coronary and cerebral perfusion as compared to balloon occlusion alone. By delivering a high-volume infusion directly into the aortic arch, aortic pressures might increase further and bolster coronary perfusion pressure. Infusions with supra-normal levels of oxygen may provide additional benefits, such as increased oxygen delivery to the myocardium and brain. SAAP is a technique that is still under preclinical development and has not yet been tested in humans.

A study of cardiac arrest in canines with a prolonged no-compression down time (20 min) who received an infusion of stroma-free ultra-purified bovine hemoglobin in combination with aortic occlusion demonstrated significant differences in coronary perfusion pressures and survival. Animals that underwent aortic occlusion with a purified hemoglobin infusion had a mean coronary perfusion pressure of 62 mmHg and a 70% survival rate, compared to coronary perfusion pressure of 33 mmHg and survival rate of only 20% in those that underwent standard ACLS alone [41]. In a similar trial, the same authors demonstrated a dose–response relationship between increasing concentrations of the purified hemoglobin infusion and survival [42]. A separate research group investigated the use of aortic occlusion and infusion of an oxygen-carrying fluorocarbon emulsion and found similar effects on coronary perfusion pressure and survival in the SAAP animals [43, 44]. While SAAP may be more effective than aortic occlusion alone, it requires a much larger catheter (12Fr vs. 7Fr) than aortic occlusion alone, which increases the risk of extremity complications.

10.3.2 Clinical Evidence

The extent of the literature involving human subjects and aortic balloon support during NTCA is limited to several case reports and case series, three of which are from the 1980s [45–49]. The advent of the first percutaneous intra-aortic balloon pump in the late 1970s made it possible to utilize aortic balloon technology in cardiac arrest patients. Bregman et al. provided the first published account of this, describing the placement of IABPs in three patients undergoing cardiac arrest. All of the patients died, although they did not provide details of the circumstances of the patients' cardiac arrest [45]. Subsequently, Philips et al. reported on five patients that underwent IABP placement during cardiac arrest [46]. All were initially in asystole and one patient survived until hospital discharge; no complications of balloon insertion were reported.

Gottlieb et al. built upon their work when, in 1986, they describe using a modified ambulance to place IABPs outside of the hospital in three cardiac arrest patients [47]. Two patients, initially in a pulseless electrical activity rhythm, had ROSC and were subsequently discharged from the hospital with good neurologic function. The third suffered cardiac arrest from an ST-elevation myocardial infarction (STEMI). This patient achieved ROSC and notably, their ST-elevations improved or disappeared during periods of IABP support, suggesting a clinically significant increase in cardiac perfusion. Unfortunately, and likely due to their prolonged resuscitation prior to IABP placement, the patient had a poor neurologic outcome. Deakin et al. similarly described a report of two patients in cardiogenic shock, already dependent on IABPs, who had a cardiac arrest with their IABP in place [48]. In each, the aortic balloon was continuously inflated during their cardiac arrest and authors noted mild increases in coronary perfusion pressure (10 and 2 mmHg, respectively) after balloon inflation; however, both patients died. It is unlikely that these patients would have survived regardless of their treatment as their cardiac function was extremely poor even before their cardiac arrest.

The most compelling case report for the use of aortic occlusion in NTCA comes from Aslanger et al. in 2009 [49]. A 74-year-old female presented to the emergency department with a myocardial infarction and was taken to the cardiac catheterization laboratory. She was found to have a 95% stenotic lesion of her mid left circumflex coronary artery but due to vessel tortuosity, the interventionalist was unable to place a stent for revascularization. She was transferred to the cardiac care unit where her hemodynamics quickly decompensated. Investigators initiated a dopamine infusion, but the patient sustained a pulseless electrical activity (PEA) cardiac arrest that devolved into asystole soon after. After 25 min of ACLS, authors placed an oversized intra-aortic balloon pump and used it to continuously occlude the aorta. The authors noted that 45 s after balloon occlusion, the patient began to spontaneously gasp and had ROSC, with a normal sinus rhythm established after 1 min. She was placed on IABP support and eventually discharged from the hospital and had made a "good recovery" at a 3 months follow-up visit. It is unlikely that she would have had ROSC without the aortic balloon inflation, as patients who receive ACLS for greater than 20 min without ROSC have an extremely low probability of ROSC with

continued resuscitation [50, 51]. Furthermore, the temporal association between aortic balloon inflation followed by ROSC less than 1 min later suggests that it played a significant role in her successful resuscitation.

10.3.3 Feasibility of REBOA in Nontraumatic Cardiac Arrest

Femoral artery cannulation and aortic balloon placement during NTCA in the prehospital and hospital environment are technically feasible. The most difficult aspect of the REBOA procedure is obtaining femoral artery access, especially when patients are undergoing chest compressions [52]. The use of bedside ultrasound improves femoral artery cannulation success while allowing real-time confirmation of the location of the aortic catheter tip [3, 53]. The success of emergency department and prehospital extra corporeal membranous oxygenation (ECMO) programs further support the practicality of this concept, as these teams routinely place large femoral arterial catheters in patients undergoing ACLS for cardiac arrest [54–56]. There are an increasing number of centers in the United States and Europe who cannulate cardiac arrest patients for veno-arterial ECMO (often termed "E-CPR") [57]. Additionally, there are several case series that report the placement of IABPs in patients undergoing chest compressions [45–47], while the surgical literature contains many examples of REBOA use in patients in traumatic cardiac arrest [3, 58–60]. Manning et al. further demonstrated the feasibility of blind femoral arterial and venous cannulation and aortic catheter placement in 22 victims of NTCA in the prehospital environment. They utilized these catheters to measure coronary perfusion pressure in real-time to improve the delivery of CPR quality.

Conclusion: Implementation of REBOA for Nontraumatic Cardiac Arrest

Patients who undergo prolonged resuscitation without resumption of sustained cardiac activity have an extremely poor prognosis and can be considered to have failed traditional ACLS; however, these patients may still be neurologically viable [51]. In a study of 1204 cases of NTCA, 90% of those who achieved ROSC had done so by 24 min of CPR, with rates of ROSC declining significantly after that point. Further research shows that after 21 min of conventional ACLS in patients without ROSC, the probability of neurologically intact survival drops precipitously [6, 51, 61]. It is highly unlikely that patients without ROSC will survive their arrest with good neurologic outcome once traditional resuscitation has exceeded 21 min. Based on the compelling animal data and human case series, it is conceivable that these patients may still benefit from REBOA.

To maximize the probability of a patient's return to a good quality of life, detailed inclusion criteria must be applied before utilizing REBOA during a cardiac arrest. REBOA should only be considered if the physician believes that the patient has a reversible etiology of their arrest that may be immediately treated. For example, in a patient with acute myocardial infarction who is otherwise healthy, REBOA may be able to provide enough circulatory support to bridge the patient to definitive therapy, such as the cardiac catheterization laboratory or ECMO.

Physicians at the bedside must assess for contraindications, such as presence of an end-stage terminal illness, severe neurologic impairment at baseline, or suspected devastating neurologic injury as the etiology of arrest. Before initiation of REBOA, the patient must have failed therapy with traditional ACLS; a requirement that the authors consider satisfied after 20 min of resuscitation with ACLS and no ROSC. Finally, the ideal patient should show at least some signs of life prior to the initiation of REBOA, which may include findings such as reactive pupils, agonal breathing, end tidal carbon dioxide greater than 10 mmHg, arterial relaxation pressure greater than 17 mmHg, any cardiac activity on bedside echocardiogram, or a shockable rhythm.

While evidence for the use of aortic occlusion in NTCA in animal models is promising, experience in humans is too limited to advocate for immediate implementation of this technique outside of a research setting. What is clear is that REBOA in NTCA deserves future study on a larger scale to determine if it may be effective in humans. The selective perfusion of the heart and brain to augment traditional ACLS through aortic occlusion makes sense physiologically, as the laws of fluid dynamics dictate that when the same blood volume moves through a reduced vascular bed, the pressure will increase. The concept is supported by decades of preclinical research and has been shown to be feasible in humans. It is apparent that alternative therapies are required if we intend to significantly advance our ability to provide resuscitative care to patients in cardiac arrest. The use of REBOA as an adjunct to ACLS is an innovative strategy and is deserving of further consideration and rigorous clinical investigation.

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Endovascular Balloon Occlusion in Obstetrical Hemorrhage

11

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11.1 Introduction

Hemorrhage is the leading cause of maternal death worldwide. A "maternal near-miss" is defined by the World Health Organization as a woman who nearly died, but survived a complication that occurred during pregnancy, childbirth, or within 42 days of pregnancy. The median ratio of maternal near miss due to hemorrhage was 6 out of every 1000 live births (range 1–35) in one large, systematic review [1]. Another international systemic review estimated that approximately ten women suffer major morbidity for every mother who dies due to bleeding [2]. Women in developing nations are disproportionately affected; 99% of all deaths due to postpartum hemorrhage occur in low- or middle-income countries [3]. Hypothetically, between 66% and 73% of maternal deaths due to hemorrhage are preventable with early recognition and treatment [4, 5]. However, in lower-income countries lacking easy access to skilled medical and surgical care, blood-banking facilities, and transfusion capabilities, the ability to prevent death due to hemorrhage is hindered. Even in high-resource settings, the ability to radically reduce maternal morbidity and mortality due to hemorrhage with the implementation of management algorithms and massive transfusion protocols has proven challenging in practice [6, 7], highlighting the need for novel approaches to gain early hemostatic control.

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11.2 Physiologic Changes of Pregnancy

Pregnancy and the postpartum period are hypercoagulable states. Circulating levels of Factors VII, VII, IX, X, XII and von Willibrand factor and fibrinogen levels increase markedly by full term (20–1000%) [8]. Circulating levels or activity of anticoagulant proteins such as protein S, protein C, and tissue factor pathway inhibitor decrease [9, 10], and antifibrinolytic activity decreases due to increases in plasminogen activator inhibitors 1 and 2 (PAI-1 and PAI-2) [8, 11]. In two separate studies, low fibrinogen levels correlated strongly with the risk and degree of postpartum hemorrhage [12]. Specifically, women with a fibrinogen level <300–400 mg/dL were at a significantly increased risk for postpartum hemorrhage and development of disseminated intravascular coagulopathy, a risk that increased to 12-fold above baseline when fibrinogen levels fell below 200 mg/dL [13]. Notably, a drop in fibrinogen levels is often the first laboratory abnormality that can be detected in obstetrical hemorrhage.

During acute or ongoing hemorrhage, the time required to draw, send, process, and receive laboratory results creates a significant lag between the actual clinical status of a patient and the laboratory "evidence" of significant bleeding or disseminated intravascular coagulopathy (DIC). This is especially true when using traditional markers of coagulopathy, such as the prothrombin time (PT), activated partial thromboplastin time (aPTT), and fibrinogen levels. Thromboelastography (TEG®; Haemonetics Corp, Braintree, MA, USA) or rotational thromboelastometry (ROTEM®; Tem International GmbH, Munich, Germany) can be performed more quickly as point of care testing, and may identify specific derangements in clot formation, which may prove more useful to direct product replacement [14–16]. The blood supply to the pregnant uterus is necessarily robust in order to supply necessary oxygen, nutrients to and waste transport from the uterus and placenta. By full term, approximately 500–700 mL/min of blood course through the uterus [17]. When bleeding is active and brisk, even a 10-min delay in treatment may prove life-threatening. Often, transfusion must be started solely on the clinical scenario, while laboratory studies are simultaneously and sequentially run, in order to guide management.

In normal pregnancies, the total blood volume expands by approximately 20% by term, giving the average pregnant patient a blood volume of 4.5–5 L [18]. While the total red blood cell mass increases, the volume of plasma increases proportionally more, causing a physiologic anemia of pregnancy. Often, these changes provide adequate reserve for women to tolerate physiologic blood loss immediately following delivery. When bleeding is excessive, signs of hemorrhagic shock may ensue; however, a greater volume of blood (10–15%) must be lost in the pregnant compared to the nonpregnant state before overt signs or symptoms of shock are evident. Once women reach Stage III or IV in the Advanced Trauma Life Support classification of hemorrhagic shock (Table 11.1), however, decompensation may be rapid. Women who develop preeclampsia, however, do not exhibit the usual

Table 11.1 ATLS classification of hemorrhagic shock [19–21]

Class of hemorrhagic shock				
	I	II	III	IV
Estimated blood loss (mL)	<750	750–1500	1500–2000	>2000
Blood loss (% volume)	15	15–30	30–40	>40
Blood pressure	Normal or increased	Normal (tilt +)	Decreased (MAP <60)	Decreased
Heart rate (bpm)[a]	<100	>100	>120	>140
Capillary refill	Normal	May be delayed	Usually delayed	Always delayed
Respiratory rate	Normal	Mildly increased	Moderate tachypnea	Marked tachypnea or collapse
Urine output (mL/h)	>30	20–30	5–15	Anuric
Mental status	Normal or anxious	Anxious	Confused	Lethargic, obtunded

ATLS advanced trauma life support, *bpm* beats per minute
[a]In pregnancy, a heart rate of up to 110 may be normal and due to physiologic changes, but ≤120 is clearly abnormal

blood volume expansion and are particularly susceptible to shock despite relatively lower blood loss.

11.3 Uterine Blood Supply

The blood supply to the uterus must be sufficiently robust to bathe the developing placental bed, in order to supply adequate oxygen and nutrients to a growing fetus, and to carry away waste from the fetoplacental unit.

The main supply to the uterus is through the uterine arteries (Fig. 11.1). The uterine arteries branch from the anterior division of the hypogastric arteries, which in turn arise from the common iliac arteries distal to the aortic bifurcation. Each uterine artery divides into ascending and descending branches.

The ascending branch feeds the uterine corpus and anastomoses with the descending branches of the uterine artery, and the descending branch feeds the cervix and upper vagina. The ovarian arteries branch from the aorta, inferior to the renal arteries and superior to the mesenteric arteries. An aberrant branch may arise from the renal artery. The ovarian arteries run laterally along the psoas muscle through the infundibulopelvic ligaments and supply the ovaries and fallopian tubes from a posterior-lateral aspect.

The descending branch of the uterine artery feeds the upper vagina and connects with ascending branches of the vaginal artery, which is also a division of the anterior hypogastric artery. Additional aberrant vessels to the vagina, cervix, and bladder may arise from the deep circumflex artery, superior vesical artery, and inferior epigastric artery.

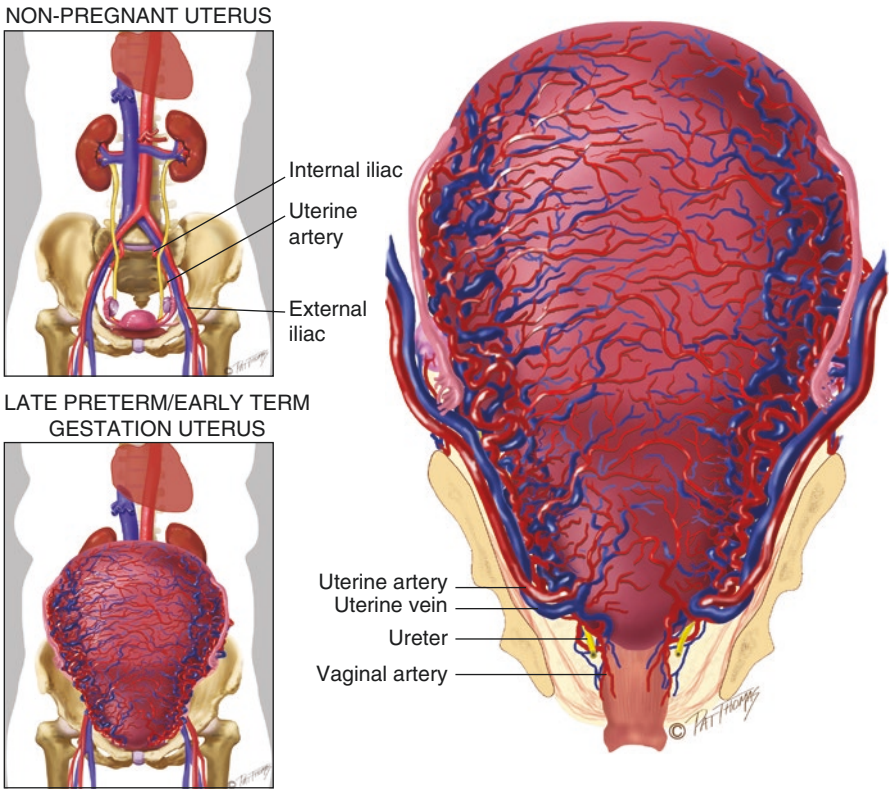

Fig. 11.1 This illustration demonstrates the blood supply to the pregnant uterus, with abundant sources for collateral circulatory supply. At full term, approximately 500–700 mL of blood courses through the uterus

The uterine myometrium consists of bundles of fibers of smooth muscle within fibrous tissue, throughout which multiple sinus channels and collateral vessels run. Many of these channels are not epithelial lined, but function rather like the pores in a sponge, allowing brisk flow of blood to the entire uterus even if one or two of the vessels that supply the uterus are ligated. Whenever blood flow is increased, such as with uterine fibroids, in the presence of diffuse cavernous sinuses, with pregnancy and especially pregnancy complicated by invasive placenta, these blood-filled spaces are especially engorged and prone to rapid blood loss.

11.4 Etiology of Obstetrical Hemorrhage

Obstetrical hemorrhage may occur at any time during pregnancy, most commonly at the time of delivery. Conditions in pregnancy associated with hemorrhage are listed in Table 11.2. The most common are listed below.

Table 11.2 Pregnancy-specific conditions associated with hemorrhage

Condition	Special considerations	Treatment
First trimester		
Ectopic pregnancy	– May rupture after medical management; significant hemoperitoneum, shock possible upon presentation	– Methotrexate (medical) – Salpingotomy with repair—Salpingectomy (surgery = definitive management)
Spontaneous abortion	– Greater risk of hemorrhage/DIC if >4 weeks from demise or if infected	– Misoprostol (medical) – Dilatation and curettage (surgical)
Hemorrhagic cyst rupture	– May be from corpus luteum or endometrioma – Large hemoperitoneum and shock possible	– Cystectomy or oophorectomy
Spontaneous hemoperitoneum	– Rare-associated with abdominal vessel aneurysm, endometriosis	– Exploratory laparotomy – Control any bleeding vessels
Second/third trimesters		
Placental abruption	– Commonly presents as painful vaginal bleeding. Maybe concealed – Associated with hypertension, trauma, cocaine use, placenta previa	– Close observation if stable and in early preterm – Rh immunoglobulin for Rh negative women – Expeditious delivery for heavy bleeding or fetal distress – Anticipate DIC and transfuse immediately (even prior to uterine evacuation) with RBC and FFP or cryoprecipitate if presents with abruption large enough to cause intrauterine fetal demise
Trauma	– Common cause of abruption	– Control bleeding – Surgery if necessary – Treat abruption as above
Abnormally invasive placenta	– Placenta accreta, increta, percreta	– Multidisciplinary team management – Anticipate massive hemorrhage and massive transfusion – Cesarean hysterectomy – Consider endovascular occlusion as adjunct to surgery
Intrapartum/early postpartum hemorrhage		
Abruption	– As above	– As above
Placenta previa	– Usually presents as painless vaginal bleeding	– Cesarean delivery
Placenta Accreta Spectrum	– As above	– As above
Uterine Atony	– Most common cause of early postpartum hemorrhage (80%) – Associated with chorioamnionitis, multiple gestation, prolonged labor	– Medical management with uterotonic agents – Intrauterine balloon tamponade – Uterine compression sutures – Uterine artery/hypogastric artery ligation – Intravascular embolization – Hysterectomy if continued bleeding

(continued)

Table 11.2 (continued)

Condition	Special considerations	Treatment
Genital tract laceration	– Associated with large fetus, operative vaginal delivery (use of vacuum or forceps), compound fetal presentation	– May require significant repair in OR for adequate visualization and control – Vaginal packing
Uterine inversion	– May cause significant bleeding and vasovagal shock	– Manual replacement of the uterus under relaxation – Surgical replacement if unable to manually reduce
Uterine rupture	– Complicates 5/1000 attempts at vaginal birth after cesarean – Rarely occurs spontaneously	– Surgical repair – Hysterectomy if bleeding otherwise uncontrollable
Amniotic fluid embolism	– Rare. Complicates 1 in 10- to 20,000 pregnancies – Causes sudden cardiovascular collapse and DIC	– Cardiovascular resuscitation – Intubation – Early fibrinogen replacement due to consumptive DIC
Delayed postpartum hemorrhage		
Retained products of conception	– Very small area may cause bleed	– Dilatation and curettage (D&C)
Subinvolution of placental bed	– 4–6 weeks postpartum	– Transfusion, D&C

11.5 First Trimester

11.5.1 Ectopic Pregnancy

In the first trimester, the most common cause of maternal death is due to bleeding that occurs secondary to rupture of an ectopic pregnancy [22]. Cases of hemorrhagic ovarian cyst rupture or vascular dissection and aneurysm rupture have also been reported [23, 24]. The intra-abdominal cavity can easily hold 1–2 L of blood and clot, therefore clinically significant intraperitoneal bleeding may occur. Adequate transfusion of blood and blood products, along with swift surgical control of the source of bleeding, is essential to prevent development or worsening of DIC.

11.5.2 Molar Pregnancy

A molar pregnancy arises when a triploid zygote (three complete sets of chromosome complement, as opposed to the normal double set of chromosomes) implants and develops. The pregnancy is considered a *complete mole* when there is no embryo and consists of abnormal trophoblastic tissue, and all three sets of chromosomes are paternal in origin. A *partial mole* is one from which one set of chromosomes is maternal and the remaining two are paternal in origin. A partial mole may consist of

an embryo/fetus and some combination of normal and abnormal placental tissue. Fetal growth restriction and the presence of a thick, hygropic placenta are common. Women who continue to carry a partial molar pregnancy are at increased risk for symptoms that mimic preeclampsia or thyroid storm. Molar pregnancy is associated with choriocarcinoma, a malignant form of this disease spectrum, and therefore is a medical indication for termination of pregnancy. Bleeding is the most common presentation [25]. At the time of uterine evacuation, heavy bleeding should be anticipated, and blood and blood products should be readily available in the operating room prior to the procedure whenever possible.

11.6 Second and Third Trimesters

In the second and early third trimester, placental abruption (premature separation of the placenta from the uterine wall) and placenta previa (placental tissue covering the cervical os) are the most common causes of vaginal bleeding prior to delivery.

11.6.1 Placental Abruption

Placental abruption complicates 50% of all cases of maternal trauma, and between 1% and 5% of minor injuries such as falls even those in which the abdomen is not affected. Both a direct "shearing" effect or an indirect "counter-coup" effect may occur. Displacement of the uterus causes a negative pressure effect due to the difference in elasticity between the placenta and the myometrium. This increases the risk that the placenta will separate prematurely, which results in bleeding [26, 27]. Placental abruption is characterized as third trimester vaginal bleeding associated with contractions and pain; however, bleeding may be completely *concealed* if the placental separation occurs centrally and the placental margins remain attached to the endometrial bed. Coagulopathy is common in cases involving fetal compromise and should be expected if a fetal demise has resulted from abruption. A drop in fibrinogen is the earliest detectable laboratory abnormality, and early replacement of fibrinogen containing blood products should be anticipated.

11.6.2 Trauma

Trauma is the leading nonobstetric cause of death in women of reproductive age in the United States, and includes injury due to motor vehicle collisions or falls (nonviolent trauma,) gunshot or other penetrating wounds, and blunt-force trauma due to assault (violent trauma) [28]. Pregnant women may be at nearly twice the risk of violent trauma and of death due to trauma compared to nonpregnant women, despite presenting for care with a lower average injury severity score [28]. Whenever trauma occurs, care must be focused primarily on the health and welfare of the mother, as the fetal status is wholly dependent upon maternal status. While it is reasonable and

necessary to quickly check for fetal cardiac activity, evaluation and treatment of the mother should not be delayed simply to obtain a formal and complete fetal ultrasound. Instead, a brief assessment of fetal heart rate could be performed very quickly with a Focused Assessment with Sonography in Trauma (FAST) examination, with minimal additional time, in order to inform the obstetrical and neonatal teams. Surgical intervention for control of hemorrhage should not be delayed simply because of pregnancy. Co-management with obstetricians or maternal-fetal medicine specialists and notification of a neonatology team is helpful, in order to monitor fetal status intraoperatively, if indicated, and to guide decisions and preparations surrounding delivery timing.

In the setting of cardiac arrest, the *only* modifications to cardiopulmonary resuscitation should include manual leftward displacement of the gravid uterus to prevent aortocaval compression from inhibiting venous return to the heart and use of a smaller endotracheal tube for intubation (6–7 Fr) due to airway edema. *Rescue* or *perimortem cesarean* should be performed early, ideally within 4 minutes, as this has been shown to improve the ability to restore maternal circulation. Delay in delivery beyond 4 min of maternal cardiovascular collapse significantly reduces survivability of a viable fetus [29, 30].

11.6.3 Postpartum Hemorrhage

Postpartum hemorrhage is defined as blood loss of 1000 mL or more at delivery, or blood loss accompanied by signs or symptoms of hypovolemia within 24 h after birth [31]. Uterine atony, or failure of the myometrium to contract after delivery of the placenta causes 80% of postpartum hemorrhage. Other sources of hemorrhage include lower or upper vaginal tract laceration, uterine rupture (especially in the setting of an attempted trial of labor after cesarean), uterine artery laceration (at the time of cesarean delivery), and rarely, amniotic fluid embolism.

11.6.4 Placenta Accreta Spectrum

Placenta accreta spectrum (PAS) affects approximately 1 in 1000–2000 live births in large, population-based studies [32, 33], and is associated with high risk of massive hemorrhage at delivery. The spectrum of PAS includes various depths of placental invasion, from placenta accreta (invasion of the endometrium and innermost myometrial layer), placenta increta (invasion of up to 50% of the depth of the myometrium, and placenta percreta (invasion through the uterine serosa, sometimes into adjacent bladder, bowel, or vessels.) PAS occurs when the placenta implants over a prior uterine scar, where the normal endometrial layer is absent or thinned. The most common risk factors are: prior (especially multiple) cesarean deliveries and the presence of placenta previa. Other risk factors include any other prior uterine surgery, endometrial ablation, radiation, in vitro fertilization, and smoking [34, 35]. Definitive management includes hysterectomy at the time of cesarean without any

attempts to separate the placenta [36]. Increasingly, conservative, nonextirpative approaches have been used in an attempt to reduce blood loss and morbidity, and in some cases to preserve fertility [34]. Conservative management is often attempted in conjunction with femoral artery endovascular balloon occlusion, uterine artery embolization, sequential arterial ligation, and/or planned interval (delayed) hysterectomy [37–40].

Blood loss approaches 2–5 L on average and can be significantly higher in complex cases [36, 38, 41] and transfusion is often required. The invasive placenta is associated with irregular neovascularization surrounding the lower uterine segment, broad ligaments, and cervicovaginal junction, as well as enlargement of the uterine vascular supply. The abnormal neovasculaturization is different in every case, and can make dissection within the already narrow lower pelvis tenuous. The placenta will bleed profusely even if the integrity is compromised with only a small puncture or tear. Even after control of the uterine arteries, one must consider that in cases of PAS, supply from the adherent or invaded bladder and from the vagina still may be a source of significant bleeding even after the uterus is removed.

The risk for complications at the time of delivery, the volume of blood transfusion required, and maternal mortality can all be reduced when abnormally invasive placenta is identified antenatally [41, 42] and when women are cared for in experienced centers with a multidisciplinary approach [43–45].

11.7 Management of Obstetrical Hemorrhage

Clinical guidelines for blood replacement therapy in postpartum hemorrhage have largely been extrapolated from lessons learned from combat and trauma [46–49]. The volume and speed with which a peripartum patient bleeds are similar to that seen in such settings [50]. Large, high-quality randomized controlled trials have been difficult to conduct in pregnant patients due to the traditional categorization of pregnant women as "vulnerable subjects." It was not until 2017 that the call for greater inclusion of pregnant women in research trials was recognized, specifically citing that many pregnant women see value in participating in research [51] and that the lack of adequate evidence-based data actually poses a greater threat to pregnant women than inclusion in well-designed clinical trials [52, 53]. Maternal mortality remains relatively rare, even though it is considered unacceptably high in terms of the resultant devastating emotional and socioeconomic cost. More commonly occurring proxy measures such as estimated blood loss, volume transfused, length of stay, intensive care admission, or the use of population-based, epidemiologic studies are often utilized in obstetrics research. In obstetrics, as in trauma, control of the source of bleeding is the cornerstone of treatment. This may be achieved using manual pressure, medical management of uterine atony, tamponade, or surgery, depending upon the etiology (Table 11.2). Adjunctive measures are often necessary to ensure maintenance of intravascular volume and oxygen carrying capacity, to prevent consumptive or dilutional coagulopathy, and to maintain cardiovascular stability until bleeding is successfully controlled and the patient stabilizes.

11.8 Massive Transfusion Protocols

The use of a transfusion ratio of 1:1:1 of red blood cells (RBC): fresh frozen plasma (FFP): platelets (PLT) was first supported by studies evaluating military casualties of war. An analysis of 10 years of data from US military hospitals supports the survival benefit for patients who receive a higher ratio of both FFP and PLT [54]. Over this time, combat mortality rates decreased over time despite increased injury severity scores, as practice patterns changed favoring a higher component: RBC ratio. Similarly, in trauma, a higher ratio of FFP to RBCs was associated with an increased rate of hemostasis and decreased rate of death due to exsanguination [48]. While the optimal ratio of fractionated products to red blood cell units for obstetrical hemorrhage remains up for debate [55], it is clear that early administration of fibrinogen-containing products and platelets offer a more hemostatic approach to transfusion than the classical approach of using red blood cells and crystalloid, and delaying transfusion of FFP or cryoprecipitate until overt clinical signs of coagulopathy are identified [56]. The incorporation of a standardized protocol for the management of postpartum hemorrhage as a part of local hospital policy is strongly encouraged by most large organizations that aim to improve obstetrical safety, including the American College of Obstetricians and Gynecologists [31], the Royal College of Obstetricians and Gynaecologists [57], and the World Health Organization [58].

11.9 Adjunctive Medications

11.9.1 Tranexamic Acid

Tranexamic acid is an inexpensive, widely available antifibrinolytic agent that has been shown to reduce death due to hemorrhage [59, 60]. It is available for intravenous or oral administration and is an inexpensive medication. Two large, multicenter trials have brought the use of tranexamic acid to the forefront: the CRASH trial from trauma literature and the WOMAN trial [61], specifically designed to test its use in postpartum hemorrhage. Both studies showed that when tranexamic acid is given intravenously within 3 h of injury or delivery, the risk of death from hemorrhage was significantly reduced; however, administration thereafter showed little benefit or potential harm, suggesting that early administration is essential, and that the mechanism of action is due primarily to its effect on cessation of bleeding rather than an anti-inflammatory effect [62]. Importantly, unlike other fractionated products, the use of tranexamic acid has not demonstrated an increased risk for thrombotic complications and appears to be a safe effective, and highly cost-effective treatment [63].

11.9.2 Lyophilized Fibrinogen Concentrate

Lyophilized fibrinogen concentrate (RiaSTAP®) is derived from pooled human blood and is a fibrinogen concentrate for intravenous administration that requires

reconstitution. It is indicated for the treatment of acute bleeding in patients with congenital fibrinogen deficiency, afibrinogenemia, and hypofibrinogenemia. The most commonly reported adverse reactions are headache and fever; however, thrombotic events and anaphylaxis have also been reported [64]. Results of early observational and small, randomized controlled trials evaluating the use of fibrinogen concentrate in postpartum hemorrhage have been mixed, with some showing a reduction in total number of units of blood products transfused, others showing no significant difference, especially [65, 66] when the fibrinogen level is >200 mg/dL [67]. The value of fibrinogen concentrate may be to bridge to thaw fibrinogen-containing products; however, the price per dose remains very high. Further randomized controlled trials are planned and are needed to better evaluate the efficacy and optimal role for fibrinogen concentrate in the setting of postpartum hemorrhage.

11.9.3 Prothrombin Complex Concentrates (PCCs)

Prothrombin complex concentrates (PCCs), which contain a combination of vitamin-K dependent clotting factors may be given in the setting of warfarin reversal, and have been used in the setting of massive hemorrhage due to trauma or surgery; however, data about its use for obstetrical hemorrhage is limited [56].

11.9.4 Activated Recombinant Factor VII

Activated recombinant Factor VII (rVIIa) has also been reported in massive obstetrical hemorrhage. Activated recombinant factor VII is only effective when adequate fibrinogen is present (fibrinogen replacement must precede rVIIa use) and it has been associated with both venous and arterial thromboembolic complications. Survival benefit with rVIIa is questionable [68]. The cost for both of these products is very high, and with limited or conflicting data regarding survival benefit, many experts recommend that the use of PCCs and of VIIa be limited to approved indications, or in settings of hemorrhage refractory to more proven resuscitation measures [69, 70].

11.10 Endovascular Balloon Occlusion

Endovascular balloon occlusion of the internal iliac arteries has been utilized primarily for control of hemorrhage as an adjunct to both surgical and conservative management of abnormally invasive placenta; however, data regarding their utility is mixed [71–75]. Successful control of hemorrhage has been reported in some small, single-center studies; however, others have found that estimated blood loss did not differ significantly between women who had femoral artery balloon occlusion and those who did not [72]. It is possible that this is due to extensive collateral

circulation within the pelvis supplying the uterus that arises from arteries superior to the origin of the femoral arteries [76].

Balloon occlusion of the aorta has been proposed as a potential solution to control collateral bleeding in the management of abnormally invasive placenta [76]. The setting of planned, multidisciplinary team delivery for placenta percreta is ideal for endovascular balloon placement prior to the onset of bleeding.

In the trauma setting, balloon placement is performed after significant loss of intravascular volume has already occurred, and thereby technically more difficult than when the intravascular tree is full and vessels expanded. Emergent placement is more of a salvage maneuver, whereas in the planned, presurgical setting for invasive placenta, the introduction of an intravascular sheath and balloon is prophylactic. The balloon can be placed, positioned, and level verified prior to delivery of the fetus, and the balloon can remain uninflated until hemorrhage ensues. Although some pregnant women have pre-existing comorbid disease, a majority of women of childbearing age are relatively young and healthy, and therefore likely to respond to well-timed interventions that render hemostatic control, and tolerate prophylactic placement well. Early arterial access for endovascular balloon occlusion has been shown to improve survival in trauma settings [77] and in the setting of invasive placenta [78] as demonstrated in a meta-analysis of its use in over 1200 patients [79].

Rare but potentially serious complications have been reported after endovascular arterial balloon occlusion including vascular dissection, thrombosis, aneurysm rupture, and loss of a lower limb [80, 81]. In one meta-analysis, groin access complications were identified in approximately 5% of cases, and included cases in which the femoral access was performed by emergency room physicians [82]. The decision to place an intra-aortic balloon must be reserved for cases in which the risk of hemorrhage outweighs the risks of the balloon, and appropriate backup planning must be in place should serious complications arise, and strategies should be in place to mitigate risk of complications [81]. With proper planning and selection, the risk-benefit ratio may tip in favor of balloon placement in those cases in which torrential hemorrhage is likely, or in which the ability to rapidly transfuse is limited.

11.11 Multidisciplinary Team Management of Endovascular Balloon Occlusion

Multidisciplinary team management has proven effective in reducing morbidity and mortality in the most complex obstetrical cases, and is essential for optimal management of endovascular balloon occlusion for the obstetrical patient. We have learned in our work with abnormally invasive placenta that the specific make-up and systematic programming of multidisciplinary teams must be tailored to each individual hospital and system [83]. The subspecialists included in one team may differ somewhat from another team, as the focus should be less on the titles or subspecialties of team members, but rather on the combined skills, training, and ability to respond rapidly in an emergency [83].

Ultrasound-guided, vascular access with a needle is performed by maternal-fetal medicine specialists, but usually limited to within the intrauterine cavity. When performing amniocentesis, only the amniotic cavity is entered, and amniotic fluid removed. For percutaneous umbilical cord sampling, the umbilical vein (rarely the umbilical artery) is accessed for fetal blood sampling just prior to and during intrauterine transfusion, such as for fetal anemia due to isoimmunization due to Rh-mismatch or infection. The umbilical vein is entered at a fixed point, whenever the placenta inserts anteriorly on the uterus, and provides easy access to the fixed placental insertion site of the cord. When the placenta is posterior, a free loop of cord must be cannulated, which is significantly more challenging, as the cord may float freely in amniotic fluid, unless pressed against the uterine wall or fetus. The risks of percutaneous umbilical cord sampling are not insignificant, which is why this procedure is only done rarely, when absolutely necessary to improve the odds of fetal survival.

Piercing through the thick-walled maternal femoral artery, which is fixed within muscle, adipose, and connective tissue, provides a very different tactile sense than puncturing the amnion or fetal umbilical vein. More importantly, while maternal-fetal medicine specialists are highly trained in antenatal diagnostic and therapeutic procedures and obstetrical surgery, repair of vascular injury is not within the scope of most. We recommend partnering with experienced vascular surgeons, trauma surgeons, and/or interventional radiologists with extensive experience in the placement of intravascular balloons and capability to readily manage vascular complications.

Endovascular aortic balloons have been placed successfully by nonsurgeons in the emergency setting (such as in the emergency department or military settings) to gain control of hemorrhage to "buy time" until the surgical team arrives; however, the number of times that one must place an intra-aortic balloon under supervision to attain the requisite skills to place them safely is unclear. At our institution, we are developing a credentialing process by which maternal-fetal medicine specialists and obstetricians who undergo appropriate didactic and simulation training, such as the "Endovascular Skills for Trauma and Safety" course [84], may begin femoral sheath placement under the direct supervision and co-management with either a trauma surgeon or interventional radiologist. We aim to train a core group of obstetrical surgeons to gain the requisite skill to place a sheath and aortic balloon for women with postpartum hemorrhage while a staff member calls in the vascular access team for acute emergencies, in the rare event the vascular access team is not immediately available. Whenever an obstetrician is performing surgery or holding bimanual pressure on the uterus to arrest hemorrhage, it is critical to have another well-trained specialist (i.e., the vascular surgeon, interventional radiologist) place and inflate the balloon, as any movement away from the surgical field will be at the expense of additional hemorrhage.

While data is needed to further elucidate the ease of use, efficacy, and risk of complications, endovascular balloon occlusion in the proper setting has the potential to shift the paradigm from one in which *liters* of blood and fluid are given to one in which a mere 2–8 *milliliters* of fluid, strategically placed, slows bleeding enough to save a mother's life.

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Prehospital and Austere EVTM

12

Viktor A. Reva

The wounded patient needs to undergo the right operation at the right time and in the right place.
–Vladimir Oppel, Russian Military Surgeon, 1916.

12.1 Introduction

Noncompressible junctional and torso hemorrhage (NCTH) is caused by the vascular disruption of a named torso or junctional vessel, or grade IV or greater abdominal solid-organ injury, or thoracic cavity injury, or severe unstable pelvic fracture, supplemented by hemodynamic instability. It is one of the leading causes of potentially preventable deaths in civilian and military trauma [1–3]. Permissive hypotension and hemostatic resuscitation, early whole-blood and packed red-blood cells transfusion, tranexamic acid administration and active rewarming, the fitting of pelvic binders, and rapid transportation with appropriate en-route care have become regular practices and have been shown to save many lives.

Endovascular surgery and catheter-based techniques have also been demonstrated to be minimally invasive, well-tolerated, and safe and effective in controlling hemorrhage and reducing mortality and morbidity [4, 5]. Advanced endovascular procedures are now a standard form of in-hospital care for blunt traumatic aortic injury, abdominal solid-organ injury, severe pelvic hemorrhage, and junctional arterial injury, all of which can be managed via a percutaneous intervention. This involves, among other procedures, angioembolization, stent implantation, and temporary proximal balloon occlusion [6]. Endovascular surgery, however, usually requires a well-equipped angiographic suite, and a variety of different sheaths,

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wires, catheters, embolic agents (coils, gelfoam, etc.), balloons, and stents (stent grafts), which are supplemented by expedient manual skills, a multidisciplinary approach, and a well-organized trauma system.

Having such a sophisticated armamentarium is hardly achievable at the prehospital stage of care, although there is a need to bring minimally invasive life-saving interventions closer to the point of injury. Some studies have shown that most trauma patients die in the first 30 min after trauma, before reaching a hospital or soon after arrival in a hospital [3, 7]. Until now, there has been no trauma system that provides fast enough care to perform NCTH control within this time frame and, up to now, there has been no prehospital method of NCTH control that is proven and effective.

Along with self-expanding polyurethane foam [8, 9], an abdominal aortic and junctional tourniquet [10–12], a few endovascular methods (with varying terminology) have been proposed for early temporary NCTH control and resuscitation [13]. They are currently in use or have a role to play in potential future applications:

- REBOA.
  - Prehospital/out-of-hospital REBOA.
  - Transfer/en-route REBOA.
  - Austere/military REBOA.
  - Battlefield/combat REBOA.
- Selective aortic arch perfusion (SAAP).
- Extracorporeal membrane oxygenation/extracorporeal life support (ECMO/ECLS).

12.2 Prehospital EVTM

Prehospital care is crucial to improving injury-related mortality and morbidity. To achieve improvements, prehospital interventions have to be fast, effective, and life-saving. In this regard, endovascular techniques, which are usually time-consuming, are of limited value. REBOA is the only prehospital intervention that might have a role to play in improving the mortality of severely injured trauma patients with a life-threatening hemorrhage below the diaphragm.

The intervention is usually performed in-hospital by an acute-care or vascular surgeon [14, 15]. However, a few recent studies and Japanese experiences have demonstrated that REBOA may be successfully performed by nonsurgeons (emergency medicine physicians, intensive care specialists, interventional radiologists) or even by nonphysician providers [16]. In appropriately skilled hands, it becomes a fast and reliable procedure, providing a temporary bridge to surgery.

The most important aspects for successful prehospital REBOA are appropriate patient selection and an understanding of what the next step is to achieving definitive hemorrhage control. Although there is huge debate over the pros and cons of early aortic occlusion, London's Air Ambulance Service established a multidisciplinary group to investigate a potential role for prehospital REBOA [17, 18].

A London Helicopter Emergency Medical System (HEMS) team, consisting of a trauma surgeon, anesthetist or emergency physician, and a paramedic, pioneered 13 Zone III REBOA procedures in a prehospital setting using a compliant balloon (or Fogarty) catheter, and eight of them survived [18]. The severely injured patients, with either a pelvic injury or a lower extremity hemorrhage, who were unresponsive to initial resuscitation and treatment, underwent Zone III REBOA, either prehospital or in the emergency department [17, 18].

Following the positive experience of London's Air Ambulance Service, the Russian (Saint-Petersburg) helicopter and ground EMS launched a pilot study to investigate the feasibility and effectiveness of prehospital REBOA in trauma care. The following algorithm for prehospital REBOA was proposed (Fig. 12.1). If an injured patient is severely hypotensive at the scene or en-route, and has no obvious severe traumatic brain and/or chest injury, the patient may undergo femoral arterial access and REBOA depending on the medical, tactical, and logistic situation (Fig. 12.2). A decision to perform REBOA can be made immediately (for a critically unstable patient) or after telephone consultation with a REBOA coordinator working in a trauma center (a relatively stable scenario).

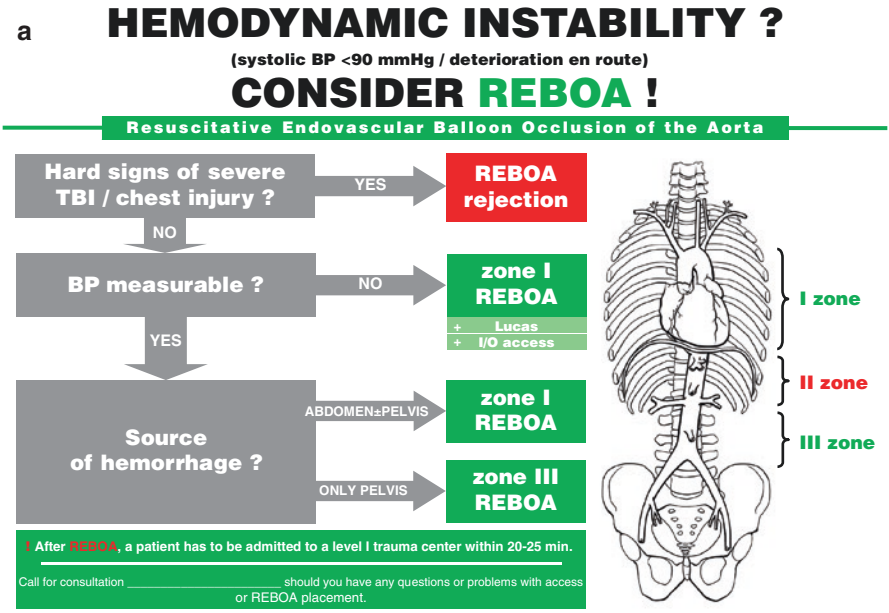
A low threshold is recommended for prehospital procedure rejection at any step. Three to five minutes is the maximum time for attempts to gain femoral arterial access using a blind or ultrasound-guided puncture. If resistance is felt during wire or /and balloon catheter insertion, if venous cannulation is suspected, or if there is no backflow after sheath insertion, then the REBOA procedure has to be discontinued. Prolonged time for transportation to a Level-I Trauma Center is also considered to be a contraindication for REBOA.

REBOA placement in a moving ambulance is challenging, and may cause additional damage; hence, it cannot be recommended [19]. Instead, on-the-scene catheter insertion or REBOA placement in a stationary ambulance before transportation might be an option. To reduce occlusion time, a balloon can be inflated as soon as evacuation is started.

Once the decision for performing REBOA is made, a zone of occlusion is chosen according to the results of an abdominal ultrasound (FAST) examination (abdominal or pelvic REBOA protocol), followed by arterial access and balloon placement. A femoral arterial puncture is critical, but it is the longest and the most challenging part of the procedure. Early arterial access for REBOA has been demonstrated to significantly improve survival [20]. Blind puncture is difficult to accomplish in a setting of shock, and ultrasound guidance has now become the recommended method for gaining arterial access in a safe and reliable manner [21, 22]. A "hybrid" or so-called "semi-Seldinger" technique (where a femoral cut-down is made and superficial tissues over the femoral artery are slightly dissected, followed by a direct or ultrasound-guided puncture) can also be considered.

Training in vascular access and ultrasound-guided intervention is essential for successful prehospital REBOA application (see Chap. 18). Emergency physicians undergo expedience training in a dry lab (simulator) and wet lab (an animal facility equipped with a C-arm), and their live-tissue training can be extended for a flying helicopter (Fig. 12.3). On-duty physicians are able to receive remote consultation

a



b

1	Clean, prep and drape both inguinal areas		
2	Prepare a needle, a sheath and a balloon catheter, saline, a bottle of contrast medium.		
3	A small skin incision is made 1-2 cm below the inguinal crease in projection of the CFA	Local anesthesia with Lidocaine if a patient is alert	
4	Perform a blind or ultrasound-guided puncture	**2 mins** one side + **1 min** another side **failure**	
5	Advance a wire via the needle	Resistance!	REBOA REJECTION
6	Remove the needle, insert a sheath	Venous blood from side-arm	
7	Measure a length required to reach external landmarks	Zone I (xyphoid process) / Zone III (umbilicus)	
8	Advance the catheter into predetermined position	Resistance!	
9	Inflate the balloon with saline (or saline:contrast = 1:1-3:1) until moderate resistance is felt		
10	Secure both a balloon and a sheath (apply suture or Curafix plaster or a chest seal)		
11	Record time of occlusion. Transportation as fast as possible		

Fig. 12.1 Decision-making protocol (**a**) and algorithm (**b**) for prehospital REBOA

Fig. 12.2 A typical case for prehospital REBOA. A severely injured patient with blunt pelvic trauma, extensive soft tissue loss, and a noncompressible junctional hemorrhage. A long 23-cm 11-Fr sheath is inserted into the right common femoral artery; a balloon (Reliant® stent graft balloon catheter, Medtronic Vascular, USA) is inflated in Zone III, followed by wound packing and bilateral hypogastric artery embolization with N-bytilcyanacrilate. The right brachial artery is cannulated for continuous invasive blood pressure monitoring

Fig. 12.3 Live tissue training of a HEMS team to perform REBOA on board a helicopter during evacuation. A portable ultrasound device (FujiFilm SonoSite® iViz™, Bothell, WA, USA) is used for vascular access. An intercommunication system is required for better communication while in flight

about a clinical case. Every case appropriate for, or with potential for, REBOA is discussed afterward to work out future strategies, to address problems, and to avoid mistakes. After appropriate training (simulators, perfused cadavers, live tissues), our physicians were able to perform a whole procedure in 5 min, which is our time limit. A few studies have recently demonstrated that procedural times are decreasing from trial to trial, reaching a plateau with an average time of less than 9 min even for nonphysician personnel [19, 23]. According to a recent study, the average time required to insert an aortic catheter in the case of cardiac arrest was shown to be less than 5 min in most patients [24]. Manning has described a prehospital percutaneous femoral arterial access technique for blind aortic catheter deployment [24]. In only one of 22 patients who failed to undergo blind arterial access was there a necessity for an open procedure, via a surgical cut-down, to identify the femoral artery. A few investigators have found that half of all REBOA procedures require an open cut-down for femoral artery cannulation [19, 25]. Although an open approach is barely appropriate in prehospital settings, REBOA is certainly feasible from a technical point of view.

A prehospital REBOA kit has to contain at least the following items: a 18 G puncture needle, an introducer sheath (of a size compatible with the balloon catheter, but smaller than or equal to 8 Fr), a REBOA catheter, a sterile fenestrated drape, a scalpel (No. 11), and 10 and 30 mL syringes. A minispike, a Curafix plaster, and a small bottle (20 mL) of contrast media can also be included.

Contrast media with saline injected into a balloon in a 1:1–1:3 ratio is regarded as optimal for better subsequent in-hospital balloon visualization. However, in a difficult scenario, the balloon can be inflated with saline only. It is obvious that fluoroscopy-free techniques are necessary to perform a whole procedure, and, especially in a prehospital setting, balloon positioning must rely on what is practically possible. To navigate a balloon catheter in the aorta, the simplest available methods might be used, such as using external landmarks (a xyphoid process for Zone I and an umbilicus for Zone III) [24]. However, ultrasound may be of value to assess a wire/balloon catheter crossing the “liver window” or distal aorta.

Since REBOA is a temporary maneuver, the question “What to do next?” always arises. When prehospital total aortic occlusion is performed, then access to an operation room and surgical control has to be achieved as quickly as possible. Air transportation of the REBOA patient is preferable, since it significantly reduces time to definitive hemorrhage control. Time to surgery after Zone I aortic occlusion is said to be between 15 min [26] and 1 h [27]. The former seems to be unrealistic even in a developed trauma system, while the latter might have deleterious effects due to significant ischemia-reperfusion injury. While most of the literature supports 40 min as a threshold for the duration of Zone I occlusion, we propose that estimated time to surgery should be 20–25 min, which requires significant effort from every team member (Table 12.1). In the case of prolonged prehospital care, Zone I aortic occlusion, if indicated, can be performed when the estimated time for arrival in hospital is less than 30 min.

The whole trauma system has to be highly developed in order to adopt REBOA as an early hemorrhage control strategy, since an aortic occlusion by itself—being a

Table 12.1 An in-hospital algorithm to follow when a REBOA patient is admitted

Zone/time of occlusion	Less than 20 min	More than 20 min
Zone I[a]	OR or CT[b]	OR and Deflation[c]
Zone III	CT[d]	

OR operation room, *CT* computed tomography
[a]When abdominal hemorrhage is confirmed by ultrasound
[b]When a whole CT-angiography can be performed within 10–12 min and the patient is relatively stable
[c]Slow balloon deflation is initiated upon admission with appropriate resuscitation
[d]A procedure is slowly switched to partial occlusion to allow good visualization of the iliac arteries. According to results, the patient is referred either to the OR or to an angio suite (a trauma hybrid OR is optimal)

bridge to surgery—does not solve the problem. Trauma centers must be well prepared to take a patient with aortic balloon occlusion at the prehospital stage of care (a so-called REBOA patient). An in-hospital major hemorrhage ("Code Red") protocol has to be activated. There are a few crucial factors for its safe implementation: (1) availability of a highly motivated and highly professional multidisciplinary team; (2) an operation room and an angio suite readily available at the time of admission (a hybrid operation room is optimal); (3) proper REBOA training, and full understanding of the patient's physiology, indications, the technique to be used, pitfalls, and possible complications on the part of all team members.

In our center, when a call from a dispatch center is received saying that a REBOA patient is arriving soon, the emergency algorithm (code) below is followed, and roles are distributed between a team leader, surgeons, anesthetists, nurses, registrars, etc. The tasks are as follows:

BEFORE arrival:

- To activate a trauma team.
- To take full consideration of an aortic occlusion time, a zone for balloon inflation.
- To prepare imaging to confirm position of the balloon and to do extended FAST (X-Ray, C-arm, ultrasound).

UPON arrival:

- ABC…
- To activate a massive transfusion protocol.
- To define whether the patient is transportable to a CT-scanner.
- To set invasive blood pressure monitoring.
- To call for available OR (preparation for laparotomy, to check a cell-saver is readily available).

To mitigate a reperfusion insult after balloon deflation, alternative techniques have been described, that is, intermittent and partial aortic occlusion. The former is easier to accomplish, but short-term balloon deflations can scarcely diminish a reperfusion burden. The latter has been proven to be feasible in both experimental

research and clinical practice, and is thoroughly described in a specific chapter in this book (see Chap. 7). A few cases of transfer REBOA (in-hospital and between hospitals) have been described where a combination of total and partial occlusion was successfully used for NCTH, thereby demonstrating value and feasibility [28].

Invasive blood pressure monitoring is recommended for titrating partial REBOA to balance between central pressure stabilization and distal organ perfusion. Proximal pressure monitoring is often used by Japanese emergency physicians [29], while an assistant is working with a syringe connected to the balloon, inflating and deflating it for pressure support. This places an additional workload on prehospital care providers, and may affect or even disturb other life-saving interventions. Another target, which is used by London HEMS in the prehospital environment as a very simple marker of partial occlusion, is the return of the pulsatile waveform in the distal arterial sheath [S. Sadek, personal communication] [17]. Animal studies have shown that femoral pulse pressure can be used for approximate titrating of Zone I aortic occlusion to reach an appropriate 80–90% occlusion, although these parameters have not yet been validated [30]. Seemingly, an electronic automated device connected to a balloon and titrating the level of aortic occlusion according to the proximal/distal pressure or flow gradient might be beneficial for prehospital care. It frees a couple of hands to work on what is critically needed for the patient, especially during longer transportation, for example, tactical evacuation during combat operations.

Another emerging aortic catheter resuscitation technique—SAAP—has been shown to be feasible in a prehospital setting [31–33]. SAAP is a method of Zone I aortic occlusion and isolated perfusion of the heart and brain with an oxygen carrier or blood via the catheter lumen. It is designed to treat impending cardiac arrest and achieve return of spontaneous circulation (ROSC). This technique has been thoroughly investigated in animal models, but clinical applications are lacking.

A further possible prehospital intervention for cardiac arrest is extracorporeal membrane oxygenation (ECMO). This stabilizes respiratory function (veno-venous ECMO) and circulation (veno-arterial ECMO) by removing carbon dioxide from tissue and organs when the patient's lungs and heart have stopped working or are severely damaged. Although it is widely used in civilian settings, and even in advanced forward military medical facilities (combat support hospitals) for acute respiratory distress syndrome, ECMO has also been demonstrated to be effective in improving ROSC and enabling nontrauma cardiac arrest even in a prehospital scenario [34–37]. ECMO has also been in early use for trauma and for the transportation of trauma patients [38–40]. Prehospital or ambulatory ECMO requires a multidisciplinary team, involving a perfusionist, anesthetist, cardiac surgeon, and vascular surgeon, and is a very advanced procedure that is available mostly for specialized ECMO teams (see Chap. 15 for details).

For any endovascular procedure, including REBOA, SAAP, and ECMO, prompt and stable vascular access is of great importance in a prehospital and austere environment. In the future, an automated robotic system for vascular imaging and access may make arterial puncture easily attainable in any far-forward (remote) setting [41].

12.3 Austere EVTM

Endovascular surgery has currently limited applicability in a combat zone and other austere settings. Some low-quality evidence is, at least, available to evaluate the safety and effectiveness of austere EVTM; most of the published literature is presented in case reports or case series. However, guided by the crucial importance of NCTH for potentially preventable deaths in Iraq and Afghanistan [2, 7], the military has initiated the concept of early enhanced or advanced resuscitative care [42, 43]. A modern paradigm of patient-oriented care, rather than territory-oriented care, has extended the "golden hour" and expanded the tactical combat casualty care protocol, putting hemorrhage control at a very early stage [44].

It is now well-documented that torso and junctional hemorrhage is a leading cause of potentially preventable deaths in combat, and that early hemorrhage control improves prehospital and overall survival [2, 7]. It has been shown that every fifth casualty may have benefitted from early REBOA placement, which is especially important for severe blast injuries, including pelvic injuries and high uni−/bilateral amputations [7].

To address surgical hemorrhage, mobile medical groups, such as a special operations surgical team (SOST) or a surgical resuscitation team (SRT), comprising at least a general surgeon, an emergency physician, a nurse anesthetist, and a physician assistant (4–6 members in total), have been created [45–47]. These groups work in an austere environment in close proximity to the possible point of injury, delivering damage control resuscitation and surgery so as to facilitate transfer to the next echelon of care. Since it is one of the current technologies, REBOA is in the armamentarium of these groups. To implement basic endovascular resuscitation (i.e., REBOA) as an element of surgical care, members of any such team must be appropriately trained.

Clinical application of REBOA performed in a far-forward military medical facility was first described during the Korean war (1950–1953) [48]. After a 65-year break, the SOST performed 19 successful prehospital REBOAs (Zone I, $n = 17$ and Zone III, $n = 2$) to control abdominal and pelvic hemorrhage with an average occlusion time of 21 min (range, 7–34 min) [49]. Casualties were admitted to Role 1 from 15 to 90 min after injury by ground transport, and underwent immediate REBOA followed by a laparotomy. Eight REBOAs were treated as mass casualty (MASCAL) events, and six procedures were performed by emergency medicine physicians. Most of the arterial accesses were achieved using ultrasound guidance, and no access-related complications were noted.

Another series of two successful REBOA cases, performed at a Role 2 facility to control abdominal (gunshot splenic injury) and pelvic (blunt trauma) hemorrhage, has recently been described, which also includes REBOA in a MASCAL event (49) (Fig. 12.4). The number of military REBOA cases is increasing, and initial results are encouraging [45, 49–51].

Pushing EVTM forward to the point of injury has been in the focus of many investigators [19, 23, 27, 44] (Fig. 12.5). Battlefield REBOA, which can be performed even by well-trained nonphysicians, is a reality these days. A few feasibility studies have demonstrated that REBOA can be used at the point-of-injury, in either

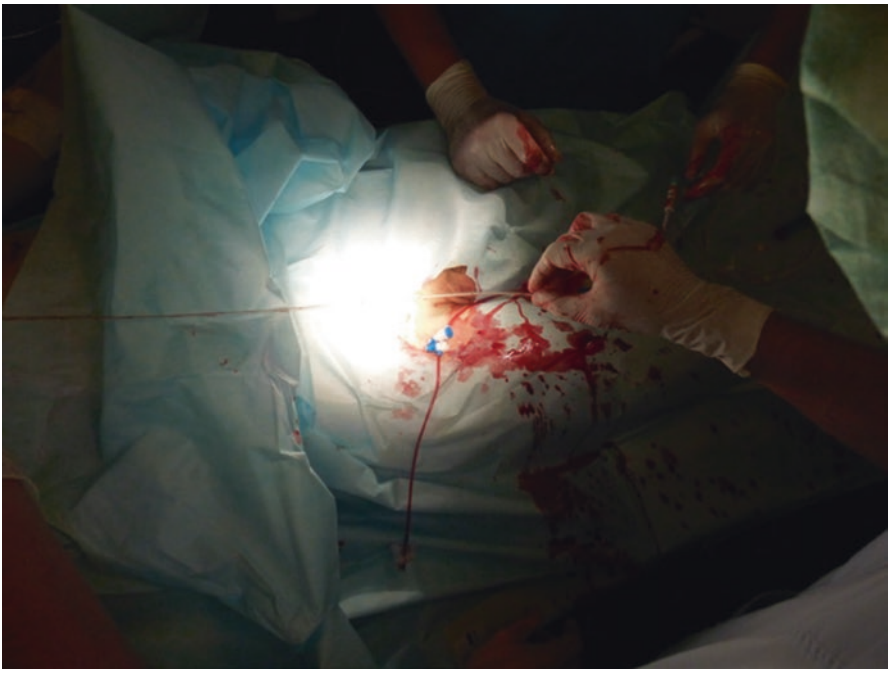


Fig. 12.4 A successful REBOA placement (Rescue balloon®, Tokai Medical Products Inc., Japan) at a Role 2 MTF for a severe intra-abdominal hemorrhage. No imaging was available due to mass casualties. Primary inadvertent femoral vein cannulation followed by blind arterial access. The distance between a sheath and a xyphoid process was measured. A splenectomy was performed afterward with a total occlusion time of 25 min, followed by vascular closure using a fascia suture technique, strategic evacuation, and full recovery

Fig. 12.5 An illustration of a future tactical evacuation module (The "Evacuation Cocoon", designed by the Central Research Institute of Robotics and Technical Cybernetics, Saint-Petersburg, Russia) that includes an automated device for titrating partial balloon occlusion during delivery to a Role 2/3 medical treatment facility

a stationary or moving ambulance (the latter is much more difficult), or en-route during flight on board a helicopter [19, 52].

Austere REBOA has many features, pitfalls, and limitations. Unintentional movements during transportation, flight turbulence, aircraft vibration, poor light or bright sunlight, noise, limited space, suboptimal surgical sterility, time pressure, enemy fire, and prolonged field care are among the factors making this life-saving intervention challenging, even unsafe.

Vascular access is a very important and, in an austere environment, the most difficult step in an endovascular procedure. Although a percutaneous puncture might be achieved even when blood pressure is undetectable, ultrasound-guided arterial access is not to be overestimated in austere settings [19, 27, 44]. However, along with other investigators [19], we found that sunlight makes the screen of an ultrasound device almost impossible to see and the vessels very difficult to visualize, making the procedure much more difficult. This is relevant to both field and flight applications. On the other hand, headlamps are necessary for the procedure in poor light conditions [19, 53], which have been shown to impede en-route interventions [52].

Once arterial access is achieved, stable securing of a sheath and a balloon catheter in place during transportation is very important, as their unintentional displacement will lead to severe hemorrhage. As part of every individual first-aid kit, a chest seal can be successfully used to secure the balloon and sheath to the body [19].

As soon as definitive surgical hemostasis is achieved, the question of balloon and sheath removal arises. A technique for vascular closure defines completion of the procedure and the safety of subsequent evacuation. Which vascular closure technique is used depends on certain medical, tactical, and organizational aspects related to the military conflict in question. Different techniques for vascular arterial closure have been proposed in the literature: manual compression [16], use of vascular closure devices [54, 55], and the fascia suture technique [56, 57]. These are described in a chapter of their own in this book (see Chap. 6). While the first two techniques are reliable and effective in "ideal" settings, that is, when a patient can be closely monitored on a continuum of care, the fascia suture technique is a safe and effective femoral vascular closure procedure after REBOA and is feasible in military settings [50]. Employing this technique may be particularly useful for strategic evacuation by air to minimize the risk of puncture-site bleeding. If, however, delivery time to the next echelon of care is short, if a vascular surgeon is available there, and if no immediate strategic evacuation is planned, then a standard lateral suture is an option at a Role 3 medical treatment facility (MTF), and there is no need to remove the sheath earlier.

EVTM in an austere environment is not limited to REBOA. Within the concept of resuscitative physiology-based surgery, some simple endovascular and minimally invasive techniques have a potential role to play in truncal and peripheral hemorrhage control at far-forward MTFs.

Role 2 is characterized by the ability to perform life- and limb-saving interventions and damage-control procedures. While temporary shunting is a standard technique for the treatment of vascular injuries at a Role 2 MTF, a new temporizing method has been recently proposed for rapid open revascularization. This is the so-called direct site "sutureless" repair [58, 59]. Utilizing an expandable

polytetrafluoroethylene stent graft for the "sutureless" endovascular repair of an injured artery has been demonstrated to be an alternative to traditional temporary shunting using a polyvinylchloride tube [59], and is effective in clinical practice [58]. Such a simple technique may have a role in military settings.

Early access to surgery at a Role 2 MTF may provide a good opportunity for implementation of simple EVTM techniques (stent/stent graft placement or angio-embolization) for some indications, including torso and junctional hemorrhage control (Fig. 12.6).

A possible role for ECMO (ECLS) has been recently recognized for combat casualty care at Role 1 or Role 2 MTFs [60]. It has been used in civilian practice for decades, and a few cases of strategic evacuation of combat casualties have been described. Despite a major concern about the role of veno-arterial ECMO in acute trauma, it is expected that the procedure may shift the current paradigm and become a reality in the near future [60] (Fig. 12.7).

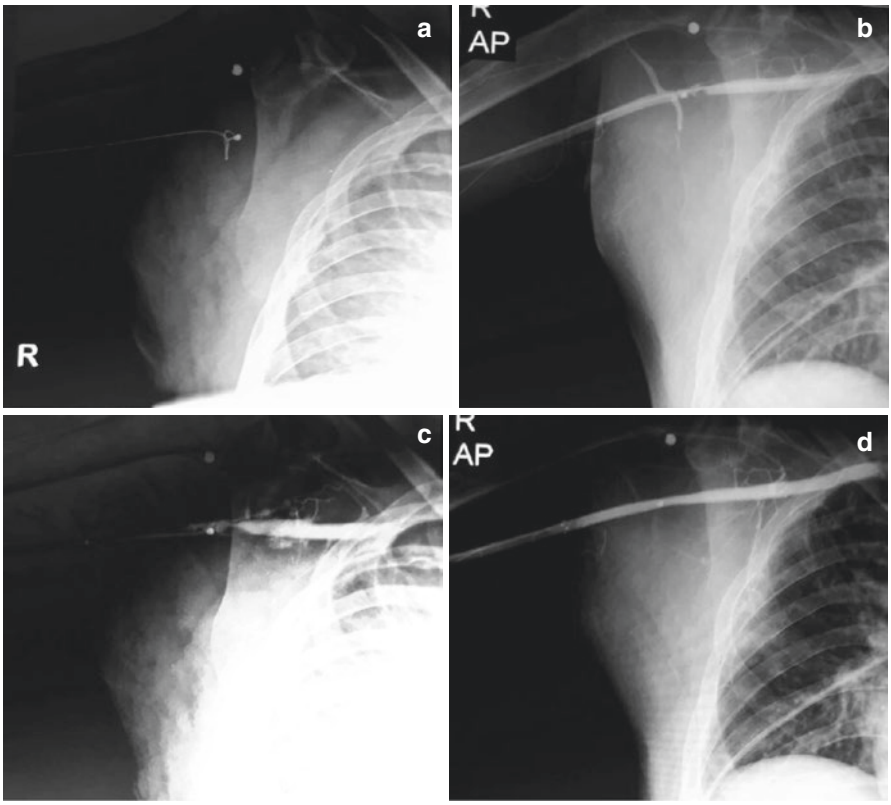


Fig. 12.6 Fluoroscopy-free stent-graft implantation in a Role 2 medical treatment facility using plain chest X-Ray for a combat, penetrating cervico-thoracic axillary-artery injury. (**a**) A wire is twisted while meeting an obstacle at the level of axillary artery injury caused by two small fragments; (**b**) a pre-recanalization angiogram demonstrating subocclusion of the artery; (**c**) a post-recanalization angiogram revealing an arterial wall defect; (**d**) a completion angiogram after stent graft implantation demonstrating good antegrade flow. No further intervention was required until discharge

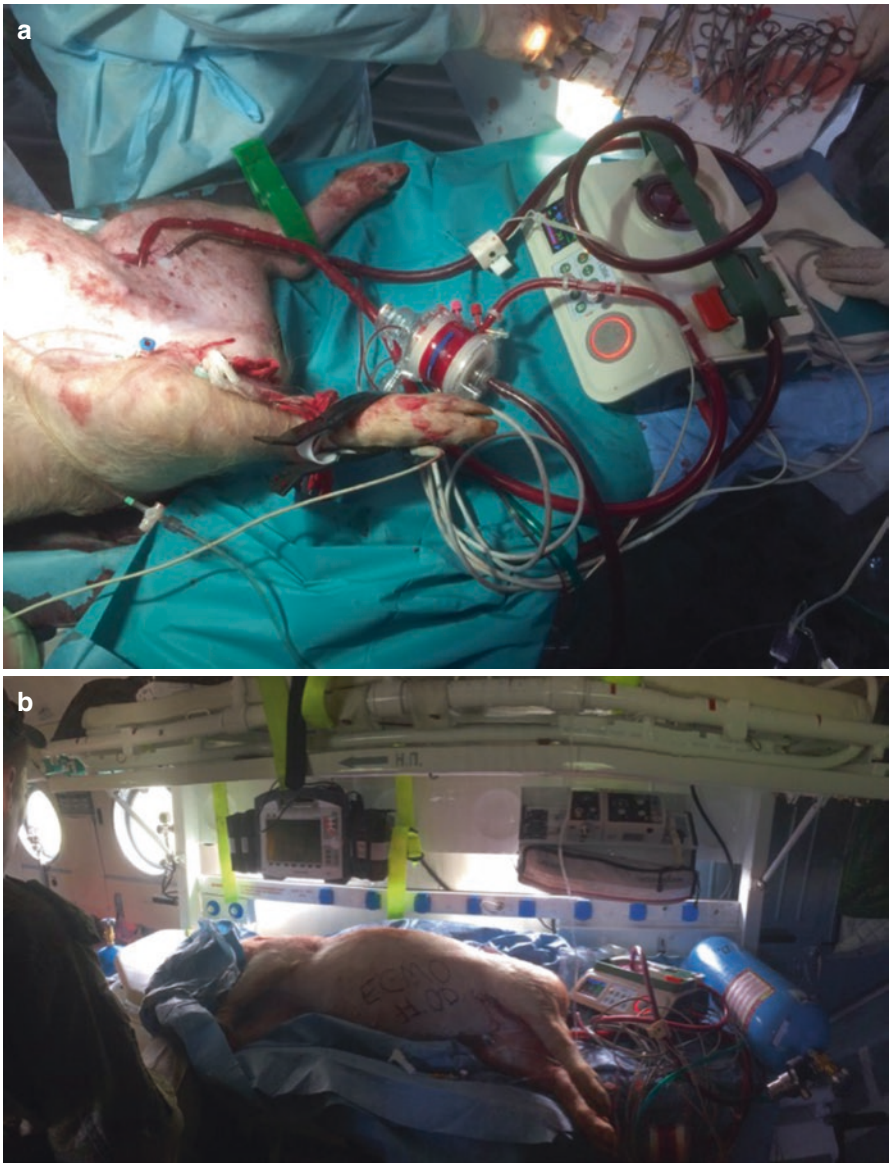


Fig. 12.7 A hemorrhagic cardiac arrest porcine model for extracorporeal membrane oxygenation during military medical exercises in Saint-Petersburg Kirov Military Medical Academy, 2018 (Russia). A portable perfusion device for emergency life support (Russian Ex-Stream®, created by TransBioTech. Ltd. with support from Skolkovo), is a lightweight (3 kg) ultracompact system with a power supply of 6 h. Both femoral artery and vein are exposed and instrumented with 10- and 18-Fr cannulas, respectively, for veno-arterial ECMO at Role 1 (**a**), followed by aeromedical evacuation to a Role 2 medical treatment facility in a high-capacity Mil Mi-8 helicopter (**b**)

A broad armamentarium and spectrum of modern equipment, including high-quality fluoroscopy imaging, are needed for successful advanced intervention, which is available at Role 3 only. EVTM has been used in combat zones since 2004, when Rasmussen and Fox started performing endovascular procedures in combat-support hospitals in Iraq [61, 62]. A Role 3 MTF has hospital-response capability and more robust resources, which provide for almost the whole possible spectrum of endovascular interventions in trauma (aortic or peripheral stent graft placement, angioembolization, vena cava filter placement, foreign body removal, etc.). These are beyond the scope of this chapter (see Chaps. 3–5).

Conclusion

EVTM is a fast-developing area for research, clinical practice, and marketing, and for integration into different specialties. Its implementation is believed to improve mortality and morbidity in civilian and military settings. Taking into account technological breakthroughs and the development of EVTM, a well-known saying (from the time when there was no endovascular-surgery option) can be rephrased as follows: the wounded patient needs to undergo the right intervention, at the right time, and in the right place.

With understanding of the value of early hemorrhage control, maturation of trauma systems and combat casualty care, development of new equipment and techniques, expedient training, and a multidisciplinary approach, the doctrine of EVTM will shift and life-saving interventions in prehospital and austere environments will certainly play an important role in saving civilian and military patients worldwide.

Expert's Comments by Miklosh Bala

No One Should Die from Uncontrolled Hemorrhage

As advocated by the Hartford Consensus on improving survival from active shooter incidents, no one should die from uncontrolled hemorrhage [63]. Techniques and interventions that have been validated as effective following years of experience in both military and civilian emergency facilities allow improving survival for bleeding victims.

This chapter helps to summarize the applicability and efficacy of different endovascular techniques published in recent literature.

Treatment options for ongoing hemorrhage in the prehospital arena are limited. In the case of blunt trauma and closed extremity injuries, splinting of limbs and stabilizing the pelvis reduces blood loss until definitive care. External blood loss can be limited by the use of extremity tourniquets, with excellent results in both the military and civilian setting [64–66]. Hemostatic suturing, direct digital pressure, packing junctional bleeding with a Foley catheter, and the application of pressure bandages can all help to stop continued hemorrhage. Other advancements include damage control resuscitation with balanced blood products or the 1:1:1 concept, junctional tourniquets (JETT and others), and Resuscitative Endovascular Balloon Occlusion of the

Aorta (REBOA). All of these techniques and adjuncts may help result in an increased survival rate if the patient reaches a surgeon at an appropriate facility. REBOA has evolved and been implemented in both the military scenario and civilian care in multiple countries. We know that the concept is valid, and the technology has now caught up. Now it is just a matter of training and optimal application.

When comparing the high mortality rate following hemorrhage with the infrequent side effects of REBOA use, the risk–benefit balance is positive. Three percent of all patients with trauma have been eligible for REBOA [67].

There is no question that REBOA is beneficial for pelvic fractures and bleeding once the skill has been acquired. But the debate for its use in hemorrhage control in the upper abdomen and chest remains vigorous. I don't believe REBOA will replace resuscitative thoracotomy for injuries in Zone I where relief of pericardial tamponade, hilar clamping to prevent air embolism, or immediate mechanical control of bleeding are life-saving. In general, contraindications for the use of an endovascular balloon are few. REBOA is technically easier than performing a thoracotomy. It requires operator training and skills to add to the beneficial effect of damage control resuscitation and surgery. Additionally, continuity of care at the receiving facility is extremely important and is perfectly strengthened in this chapter. This technology is not wildly available, but instead limited to developed trauma systems.

So, what is next? Selective Aortic Arch Perfusion (SAAP) is an example of an advanced technology with promising results in cardiac arrest, cardiac emergencies, and trauma. Both REBOA and SAAP could potentially improve survival from uncontrolled bleeding after trauma, but they have yet to be proven good enough when blood loss has resulted in cardiac arrest [33]. *ECMO restores normal physiology and unloads the venous system.* In multi-trauma patients it sounds like asking for complexity and lots of oozing blood, but it seems to have potential for actually stabilizing the patient's systems resulting in a better outcome [68]. As Bedeir et al. noted: *"The risk from bleeding-related mortality in trauma patients on ECLS seems to be overestimated"* [69].

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Endovascular Embolization in Trauma and Bleeding

13

Brandon Dean Lohman and Junichi Matsumoto

13.1 Background

Uncontrolled bleeding is the leading cause of potentially preventable death among trauma and nontrauma patients [1, 2]. Increasing positive outcomes for these types of patients require efficient hemorrhage source identification and expeditious hemostasis in order to restore hemodynamics and tissue perfusion. Interventional radiology is one of the most recognized and universal hemostatic methods for hemodynamically stable (HS) bleeding trauma and nontrauma patients. Its purpose is to halt bleeding and preserve organ/limb function with less tissue damage and stress than surgery.

However, multiple-vessel bleeding and hemodynamically unstable (HU) trauma patients belong to a more severe category within trauma injuries. They require a different attitude and mindset whereby implementing an aggressive, time-conscious strategy would lead to more efficient hemostasis than the current endovascular methods.

This chapter will first introduce the reader to the importance of vessel injury categorization, followed by evaluation methods for determining the proper protocol and adequacy of endovascular techniques based on patient status. The chapter then goes on to discuss the shortfalls of conventional IR (CEIR,) and finally will introduce the concept of time-conscious Trauma IR (TIR) and Damage Control IR (DCIR) guidelines in depth.

Performed properly, adhering to the TIR protocols outlined in this chapter can substantially reduce the procedural time from admission to hemostasis and possibly improve mortality.

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13.2 Categorizing Bleeding Severity

Uncontrolled bleeding is often associated with complex conditions in very dynamic situations. A clear understanding of the kind of hemorrhage sustained will determine its severity, as well as the treatment modality best suited to control the bleeding.

Of course, the type, size, and blood flow of a vessel are the primary factors for determining the severity of bleeding. However, considerations of the space around a leaking vessel are also critical in determining the urgency of a hemorrhagic event.

These are categorized as (1) the *free space*: where a massive amount of blood may rapidly spread, such as the peritoneal cavity, pleural cavity, and lung parenchyma; (2) *loose space*: where blood spreads at a slower pace, such as the retroperitoneal cavity, extraperitoneal cavity, mediastinum, and splenic parenchyma (without capsular disruption); and (3) *tight space*: areas with limited blood collection within a confined space such as a liver injury without capsular disruption and intramuscular injury (younger or athletic patients). Additionally, age and coagulation status are other elements to consider when preparing for endovascular treatment, for example: intramuscular tight space extravasation without coagulopathy in a younger patient would resolve alone due to the elevated intrinsic pressure from the accumulated blood, while the same event in an older patient would be different. The musculature in older patients is usually looser, and therefore any intramuscular hemorrhage will lead to *loose space* bleeding rather than the usual *tight space* bleeding found in younger patients, and will likely require treatment.

From those dynamic parameters, it is easy to understand that hemorrhage categorization is wide-ranging and could vary from relatively benign "low flow into tight space" to lethal "high-flow into free space."

Every parameter must be carefully considered and analyzed in order to forecast an accurate "bleeding status" and plan the adequate treatment workup (Fig. 13.1).

13.3 IR: Which Method to Use?

The realm of IR consists of distinct and independent subcategories of specialized IR protocols and techniques. We have defined them as in Fig. 13.2:

13.3.1 Emergency IR (EIR)

1. Primary Categorization
   (a) Trauma IR (TIR)
   (b) Non-Trauma IR (nTIR)
2. Secondary Catergorization
   (a) Damage Control IR (DCIR)
   (b) Conventional endovascular bleeding control Emergency IR (CEIR)

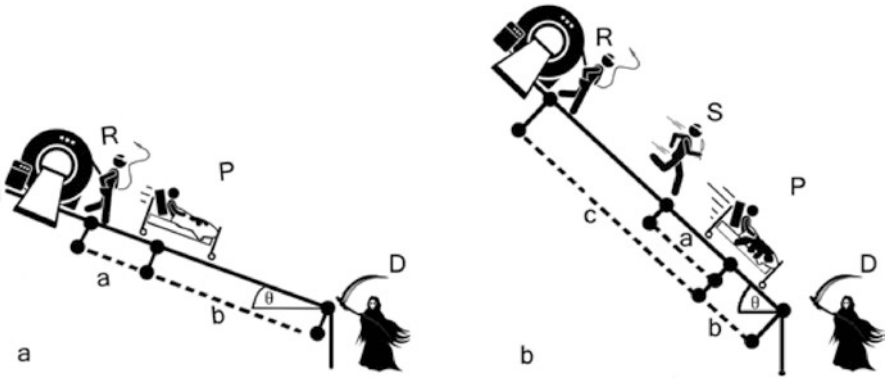


Fig. 13.1 (**a**, **b**) Categorizing bleeding severity. The concept of urgency when treating bleeding patients can be summarized by this illustration which depicts a bleeding patient on a gurney rolling down a slope leading to a cliff where death awaits; the radiologist holding a catheter (R) and surgeon holding a scalpel (S) are trying to catch and save the patient. There are two types of bleedings: nonlethal bleedings (**a**) and lethal bleedings (**b**). Both require different care and treatment strategies. The degree of urgency is represented by the incline of the slope in which the angle θ depends on parameters such as the number of bleeding sources and blood flow of affected vessels, tightness of spaces affected, patient's age, and coagulation status. (**a**) Single traumatic and nontraumatic bleeding patients suffer from a single vessel bleeding and are usually not coagulopathic. This is represented by a gentle slope θ. The patient (P) is at a far distance '*b*' to the edge of the cliff and is relatively safe from death (D). The radiologist (R) is at a close distance '*a*' to the patient (P) and may safely catch and save the patient (P) from death (D) utilizing conventional emergency IR (CEIR) techniques. (**b**) Severe trauma bleeding patients are multiple-vessel bleeders, HU and coagulopathic. All these parameters are represented by the very steep θ slope. The patient (P) is at a very close distance '*b*' to the edge of the cliff and nearing death. It also depicts a radiologist (R) at a far distance '*c*' (time before angioembolization) to the patient (P) and hence cannot reach and save the bleeding patient. Without a specific time-conscious IR protocol, endovascular embolization cannot save such patients who are rapidly nearing death (shorter *b* and large θ). Surgery (S) is closer to the patient at a distance '*a*' (time before surgery) and hence may save those patients. Without a time-conscious IR protocol, trauma surgery being available on an in-house 24/7 service is the treatment of choice

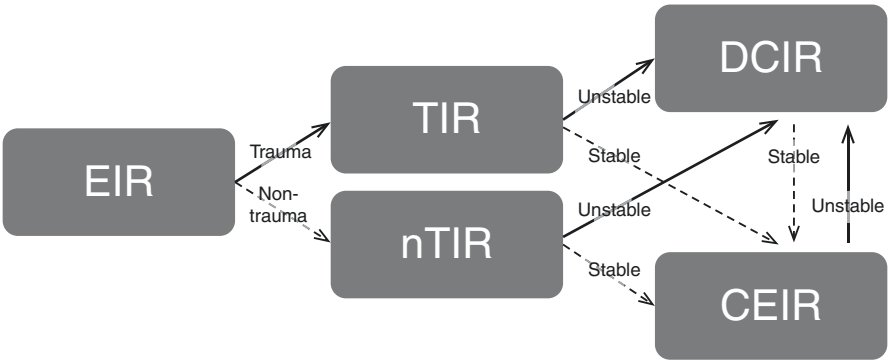


Fig. 13.2 Selecting the right IR method according to trauma and hemodynamic stability. The flowchart provides guidance in selecting the most appropriate endovascular method according to the patient's hemodynamic status. Hemodynamic status may change during procedure and the IR method will accordingly adapt to the patient's hemodynamics. TIR encompasses the entire management and guidelines for the potentially severely injured patient while nTIR merely refers to the techniques/procedures for nontraumatic illnesses

Each of these IR subcategories is based on the needs of specific types of patients and thereby governed by different methods and guidelines. The ability to distinguish the appropriate IR subgroup suitable for the appropriate patient is paramount for all physicians involved in trauma care, regardless of specialty.

13.4 Conventional Emergency Interventional Radiology (CEIR): When Conventional Methods Fall Short

Endovascular embolization targets HS patients and considerably decreases hospitalization time and mortality [3]. Instances where CEIR yields successful results include: gastrointestinal bleedings, intramuscular hemorrhage, postoperative hemorrhage, postpartum hemorrhage, hepatocellular carcinoma rupture, and bronchial arterial embolization in case of hemoptysis (Figs. 13.3 and 13.4).

An important determinant for successful endovascular embolization is the reliability of a functional coagulation-cascade (although somewhat debilitated in trauma patients) as well as coagulation-dependent embolic agents that will control the ongoing bleeding. CEIR patients mostly suffer from a single bleeding source and are treated with super-selective embolization, so as to preserve local tissue and organ function while also minimizing complications.

However, it is important to note that applying CEIR techniques on multiple-vessel bleeding, HU, and coagulopathic trauma patients would not only result in excessive time loss (waiting time for the IR physician's arrival to hospital, patient transport, and pre-/post-commotions surrounding angiography procedure) but also put the patient in potential peril. Therefore, contrary to CEIR, a trauma-specific IR protocol with a different ethos should be put in place: prioritizing saving life over limb/organ while establishing time-consciousness as the primary concern.

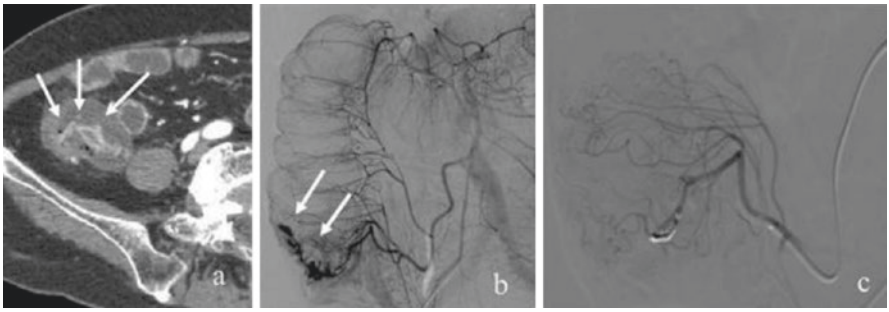


Fig. 13.3 nTIR case managed with CEIR: 72-year old male with diverticular bleeding. (**a**) Contrast-enhanced CT reveals extravasation (arrows) in the ascending colon, suspected to originate from a diverticulum (not shown). (**b**) Superior mesenteric arteriography showed extravasation (arrows) at the distal branch of the ileocolic artery. (**c**) Active bleeding was successfully controlled with super-selective coil embolization. No sequelae were noted after the procedure

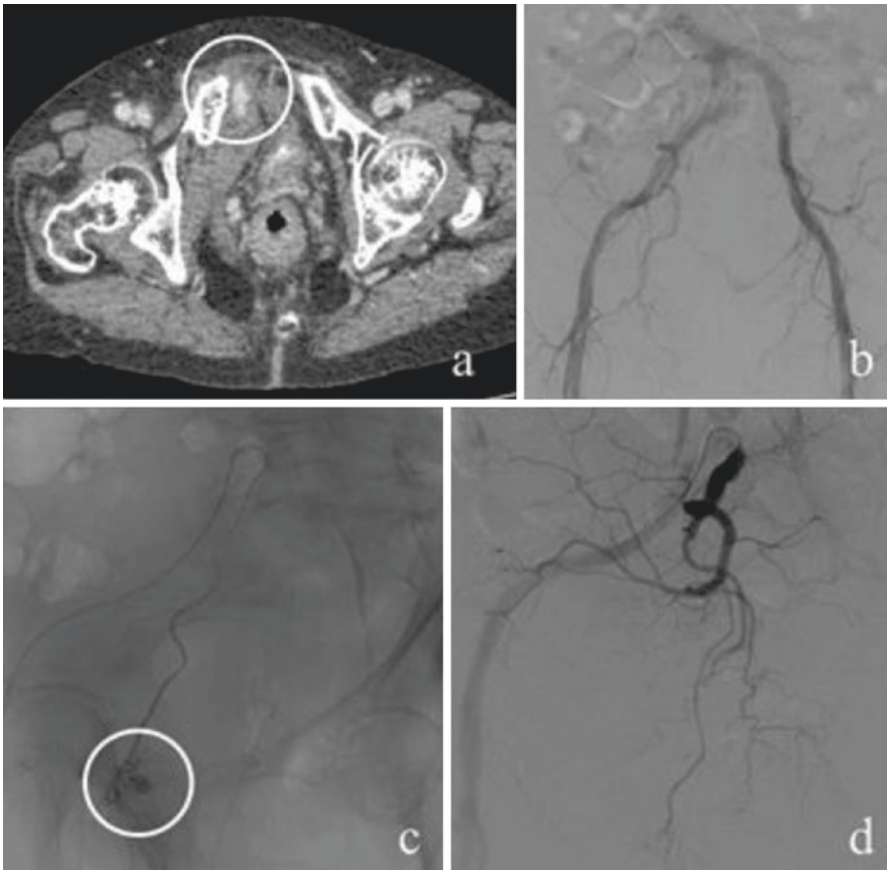


Fig. 13.4 TIR case managed with CEIR: 81-year old female with pelvic fracture. (**a**) Contrast-enhanced CT showed extravasation at the site of the right pubic bone fracture (circle). (**b**) Angioembolization was initiated with pelvic arteriography to identify the bleeding source. (**c**) Super selective arteriography in the internal pudendal artery showed extravasation (circle). (**d**) The active bleeding was selectively controlled

13.5 Trauma IR (TIR)

13.5.1 Overview

As with endovascular aneurysm repair (EVAR), a major treatment modality for aortic aneurysm rupture which operates according to a time-conscious and regulated protocol [4], a trauma-specific algorithm with comprehensive time-rigorous guidelines should be put in place and customized for the presumably severely bleeding HU patients. It should consist of prompt team activation alongside an early and swift CT scan; this should be followed by a rapid image evaluation scheme and

early management of life-threatening injuries. This time-conscious protocol should be initiated from the earliest stages of injury (before the patient's arrival to trauma bay) until completion of hemostasis and restoration of hemodynamics. It should be noted that TIR is both applicable to HU and HS patients. However, the severely injured patient is more likely to become unstable, which justifies TIR strict guidelines regardless of the patient's hemodynamics. The TIR protocol will be covered below and is divided into the following four sections and covers preadmission, patient arrival, trauma imaging, and patient selection.

13.5.2 Preadmission

The concept of trauma interventional radiology, as its name implies, requires the active participation of the radiologist from the earliest phase of treatment, and addresses trauma as well as nontrauma patients. Its foundation is time-consciousness and expects the readiness of all physicians, nurses, and medical technicians to cooperate with one another, regardless of whether the admitted patient is HU or HS. The trauma team consists of an in-hospital panel of specialists (diagnostic/interventional radiologist, emergency physicians, intensive care physician, trauma surgeon, orthopedic surgeon, neurosurgeon, anesthesiologist, radiology technician, and trauma nurse) that can be instantly mobilized 24/7 [5]. The team should be (pre)alerted and on standby at the ED with all the necessary equipment and instruments prepped before the arrival of the patient (Fig. 13.5).

Fig. 13.5 (**a**, **b**) Team on standby waiting for patient. (**a**) Immediately after the activation call, the entire trauma team is on standby in the trauma bay waiting for the patient's arrival. The early participation of the radiologist (white arrow) from the very initial phases of TIR, is a significant prerequisite that ensures a prompt and successful completion of embolization. (**b**) Specific "endovascular kits" (black dotted arrow) containing all the necessary instruments (e.g., sheaths of various sizes, various types of catheters as well as REBOA catheters) are assembled during off hours and stored in a designated cabinet (white asterisk) within the trauma bay. The kit is placed on the portable C-arm fluoroscopy table ready for patient arrival

13.5.3 Patient's Arrival to Trauma Bay

Simultaneously, while the primary survey is being conducted, bilateral femoral arterial sheaths are to be placed as early as possible because of possible rapid patient deterioration, for example, the slowly expanding groin hematoma from a pelvic fracture may rapidly turn into a large bulging mass, or the loss of femoral pulse from severe shock may render femoral sheath placement difficult. The importance of always placing femoral sheaths in pairs and bilaterally cannot be over-emphasized. Early femoral sheathing potentiates and supplements ongoing resuscitative efforts by providing a quick access route for resuscitative endovascular balloon occlusion of the aorta (REBOA), embolization, arterial pressure monitoring, and so forth.

13.5.4 Trauma Imaging

Most guidelines do not recommend CT for severely injured HU trauma patients [6–8]; however, these are the patients who would gain the most from the diagnostic accuracy of an early CT scan. CT imaging may provide valuable information that could influence the course of treatment. A recent study demonstrated that early CT imaging swayed the management decision from surgery to IR regarding penetrating and blunt trauma patients at almost 40% and 70%, respectively [9].

13.5.4.1 Sub-Seven-Scan: Scan Within 7 Minutes

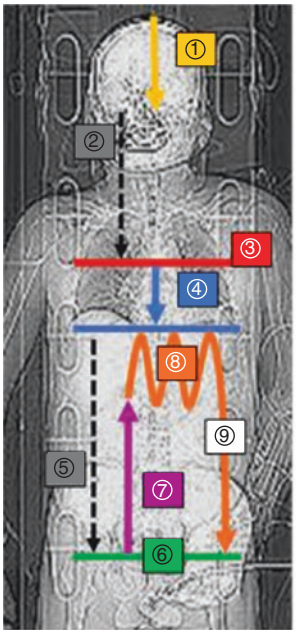
Regardless of the location of the CT room in relation to the trauma bay, reducing the CT room entry-to-exit time by a few minutes will contribute to a faster hemostasis. Training can considerably reduce the CT room entry-to-exit time, so as not to exceed 7 min.

While the patient is still on the CT table, the acquired cross-sectional imaging data will be analyzed by the trauma team who will localize the site(s) of active bleeding and deliver a consented diagnosis before the patient leaves the CT room. Based on hemodynamics, mechanism of injury, and the presence or lack of hemoperitoneum, patients will be triaged into surgical, IR, or a combined procedure.

13.5.4.2 Focused Assessment with CT for Trauma (FACT)

The image evaluation should be brief yet comprehensive, so that all anatomical regions most susceptible to lethal injury can be examined within a short time window. A trauma-specific CT imaging evaluation method, namely the focused assessment with CT for trauma (FACT), is a rapid CT trauma evaluation protocol consisting of pan-scan CT images of the head, chest, abdomen, and pelvis that will identify or exclude preselected severe injuries within 3 min (Fig. 13.6).

Simultaneously, throughout the procedure, an appointed radiologist will extensively review the CT images in uninterrupted isolation, with the intention of providing relevant information that was not initially detected with FACT (e.g., intricate vascularization, portal-venous injuries, atherosclerotic vessels, etc.) as well as other undetected injuries (bowel injuries and minor intracranial hematoma) or other



FACT

Focused Assessment with CT for trauma

① Surgical intracranial hematoma
② *Down to aortic arch level*
③ Aortic injury
④ Severe lung injury and hemo / pneumothorax
⑤ *Down to pelvic floor*
⑥ Douglas' pouch: hemoperitoneum
⑦ Pelvic and spinal fracture with retroperitoneal hematoma
⑧ Solid organ injury
⑨ Mesenteric hematoma

* ***Complete within 3 min***
* ***Never stop when in doubt***

Fig. 13.6 Focused assessment with CT for trauma (FACT). FACT is a rapid method that evaluates the entire body at anatomical locations susceptible to life-threatening injuries. The results are immediately communicated to the team who will initiate the preliminary treatment. FACT's objective is to provide a rough estimate of the imaging data within 3 min. It consists of nine steps that will be conducted without interruption. In step (6), blood collection within the Douglas' pouch (peritoneal *free space*) may be indicative of severe bleeding. Therefore, it is recommended to evaluate the Douglas' pouch which is the most gravity-dependent area in the peritoneal cavity, before evaluating abdominal organs. The amount of blood collected will reveal the severity of bleeding. FACT is now accepted by the Japanese Trauma Guidelines as a standard CT evaluating method for trauma Panscan

information that could potentially influence or alter the undergoing course of treatment. Anatomical abnormalities, impracticable vascular terrain that is not endovascularly accessible, or unfeasible as well as rapidly exsanguinating subjects will be transferred directly to surgery.

13.5.5 Patient Selection

The factors determining intervention by the endovascular route depend on a multitude of parameters, which include selecting the right patient (clinical stability, type, and location of bleeding, accessibility/feasibility of IR, and coagulopathy). Additionally, an unbiased aptitude-assessment of the immediately available personnel is mandated. TIR may deal with a specific trauma patient population: those for whom *time is of the essence* and can be (1) severe trauma subjects in extremis; (2)

hemodynamically unstable (HU); (3) coagulopathic; and (4) suffering from multiple bleeding sources.

Patients displaying arterial/aortic abnormalities on imaging, such as atherosclerotic arteries (older patients), median arcuate ligament syndrome (MALS), replaced hepatic arteries, venous, portal-venous, or greater venous injuries and so forth, will be carefully screened to see whether or not they are IR-suitable. Any case that cannot be contained with IR will either be directed to immediate surgical or IR/surgery combined care.

13.6 Damage Control IR (DCIR) (Table 13.1)

13.6.1 Overview

DCIR is a trauma-specific protocol that requires its own unique approach and heightened sense of urgency. It targets the bleeding HU patient in extremis and is extremely time conscious, emphasizing a more aggressive bleeding control, focused on saving the patient's life, even at the expense of sacrificing organs or limbs [10].

DCIR may be combined with additional surgery and/or IR.

Ideally, super-selective embolization is employed; however, in situations with narrow time windows, it could be difficult to achieve or repeatedly fail, and hence be dangerously time-consuming. Therefore, rapid nonselective proximal embolization is the recommended option [10].

Table 13.1 Comparison between conventional emergency IR and damage control interventional IR (DCIR)

	Conventional emergency IR (CEIR)	Damage control IR (DCIR)
Goal of procedure	Slop bleeding and preserve limb/organ function	Stop bleeding and save life, not preserve limb or organ function
Method	As selective as possibleCan be applied in hemodynamically stable trauma	Wide range proximal embolization as needed
Invasiveness	Less invasive than surgery	Can be more invasive than surgery and can require additional surgery and/or embolization after stabilization
Number of bleeding sources	Usually single vessel or organ	Often multiple
Hemodynamics and coagulopathy	Relatively stableCoagulopathy less severe	Always unstableMostly coagulopathic
Preferable embolic agent	Gelatin sponge particle, metallic coil, and vascular plug	NBCA ONYX®
Time allowed for procedure	30–60 min for whole embolization procedure	10 min for single arterial embolization (catheterization, embolization, and confirmation)

The following sections outline procedure (including CT room, angiography suite, and embolic agents), the key elements of successful DCIR, and lastly, results regarding DCIR duration.

13.6.2 Procedure

The DCIR guidelines have been specifically designed so that a single vessel catheterization, embolization, and arteriography confirmation may be completed within less than 10 min. This is achievable by skipping the diagnostic angiography whenever the sources of bleeding are already identified from anatomy, CT images, or surgery.

From the moment the patient enters the CT room, a series of actions will be put into motion.

13.6.2.1 In the CT Room

After acquiring the CT images, a specific 3D workstation will process the imaging data and, in less than 5 min, create a virtual angiographic image with a clear catheter route trace-out that will provide guidance to the bleeding site (Fig. 13.7).

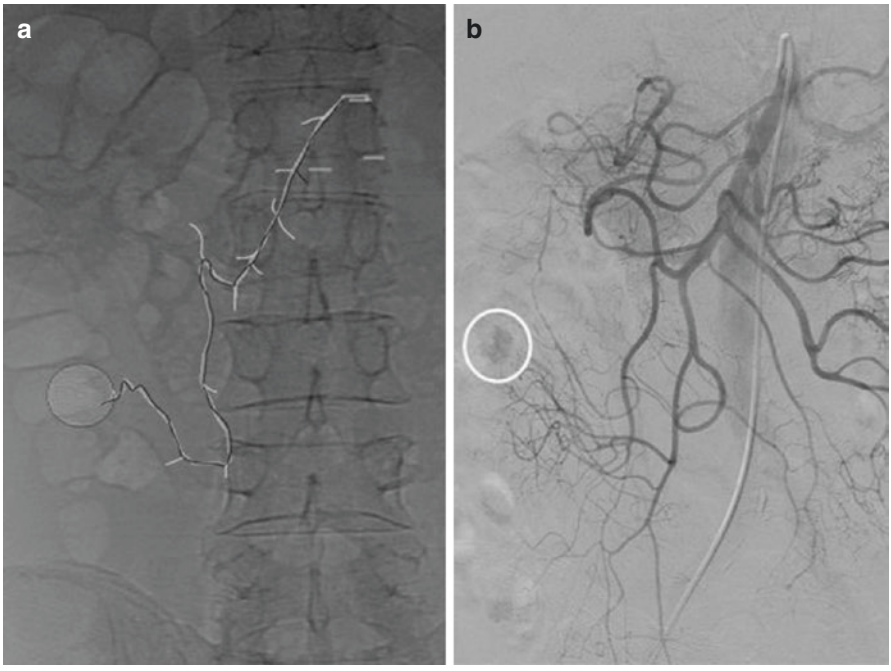


Fig. 13.7 Preprocedural-planning: virtual angiographic trace-out. A specific workstation will process the CT data and trace a virtual angiographic image (**a**) catheter course for the site(s) of extravasation replicating the angiography image (**b**). This virtual angiographic catheter trace-out can be attained within 5 min and is achieved before the patient's arrival to the angiography suite

13.6.2.2 In the Angiography Suite

Subsequently, a team of three IR physicians will form a Conductor-Operator-Assistant (COA) triad (Fig. 13.8) whereby the conductor, in consultation with the trauma surgeon sitting behind a glass window and microphone, orchestrates and guides the operator in the angiography suite along the acquired catheter trace-out. The role of the operator is to follow the conductor's instructions "word for word" and not act on his/her own, thereby eliminating any operator's decision-making time and any ancillary time-consuming maneuvers to optimize procedural efficiency. The assistant will also follow the conductor's instructions and prepare the appropriate device (guidewire, microcatheter, etc.) and embolization material in a timely fashion.

The presence of an intensivist or anesthesiologist will recreate an ICU/OR-like environment within the angiography suite. The intensivist/anesthesiologist may detect and correct any change in the patient's status, provide any necessary and continuous care (e.g., transfusions, etc.), and consequently make the angiography suite a "safer" environment for the HU patient.

13.6.2.3 Embolic Agents

Selecting the appropriate embolic agent is another crucial part of DCIR, especially with coagulopathic patients. Most of the commonly utilized agents in CEIR (metallic coils, gelatin sponge particle, and vascular plugs) are coagulation-dependent and yield satisfactory results in stable patients, but embolize poorly on coagulopathic patients and are associated with an increased risk of recanalization. HU patients are mostly coagulopathic and benefit most from liquid agents such as N-butyl cyanoacrylate (NBCA,) which is coagulation-independent. Hydrocoils and ethylene vinyl alcohol copolymer (ONYX) are other alternative embolizing agents in coagulopathy and are comparatively easy to handle. NBCA requires some training and experience; however, it is affordable and polymerizes within seconds. NBCA can also penetrate and easily disperse within intricate vascular territories [11]. NBCA permanently occludes distant bleeding sites and is less likely to re-canalize, hence making it the ideal embolic agent in the DCIR arena.

13.6.3 Key Elements of DCIR

1. Frequent stopping points (every 5–10 min) should be announced and shared, to re-assess each maneuver. Failing or time-consuming procedures (>5 min) should be discontinued and replaced by alternative procedures.
2. In the case of multiple bleeding vessels, if an initial nonselective embolization normalizes the hemodynamics, the subsequent vessels may be embolized superselectively. Hence, all throughout a procedure, a DCIR protocol may switch into a CEIR protocol and vice versa. DCIR is not solely limited to HU patients and may be applied in cases such as open fracture and brain trauma injuries.
3. DCIR is not, and must not, be considered as the main nor sole treatment method. Therefore, exercising a certain degree of mental flexibility is another prerequisite.

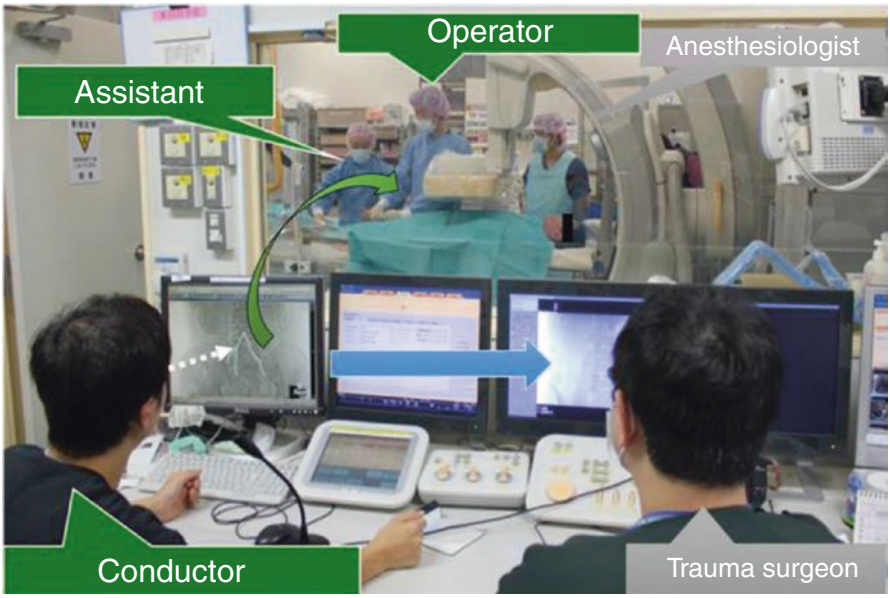


Fig. 13.8 Conductor–operator–assistant (COA) triad. The conductor in consultation with the trauma surgeon orchestrates and guides the operator during the procedure. This eliminates the operator's decision-making time as well as the time-consuming maneuvers while performing catheterization. The COA triad optimizes the procedural efficiency while minimizing human error and preventing loss of critical time. The assistant anticipates subsequent maneuvers of the operator by preparing the appropriate device (guidewire, microcatheter, etc.) and embolization material in a timely fashion. An anesthesiologist/ICU physician is also present recreating an ICU-like environment within the angiography-suite

4. The liberal use of catheters and the preparedness to abandon any time-consuming procedure (>5 min) in favor of another is accepted and recommended.
5. Changing operator in mid-procedure should also be envisaged when fatigue is suspected after repeated procedural failures.
6. Balloon occlusion of the internal iliac arteries or abdominal aorta/its branches, as well as the aorta (REBOA), may be done to either provide the physician enough time to assess and consult with colleagues or as a temporary adjunct to definitive surgery in cases of life-threatening hemorrhages prior to laparotomy.

13.6.4 Results: Duration of Procedure

Integrating a DCIR workflow with CT scan and endovascular intervention can deliver effective diagnoses and treatments to severe exsanguinating injuries. Careful implementation of DCIR key maneuvers will considerably shorten procedural time (Fig. 13.9). Previous studies demonstrated that the median time from admission to embolization ranged from 80 min to as much as 5 h [12–14]. However, only

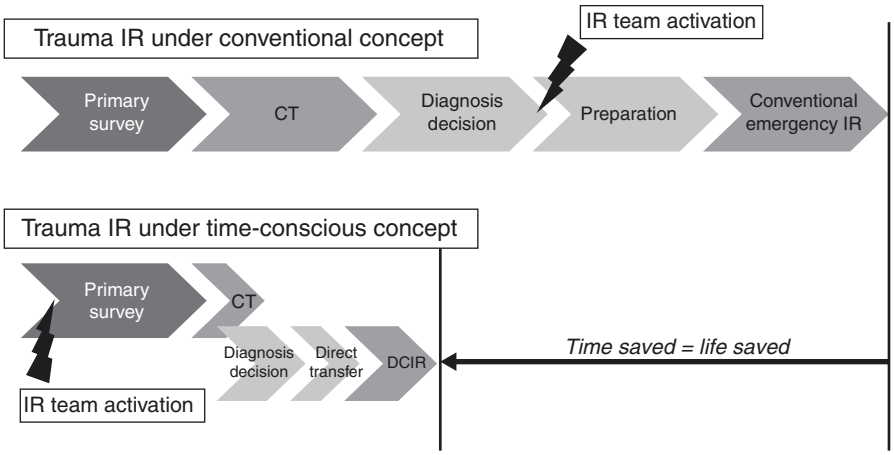


Fig. 13.9 Conventional IR for trauma versus time conscious IR for trauma. Time conscious IR guidelines effectively target every step of the management scheme that offers any opportunity for time optimization. Early activation of the IR trauma team, a shorter CT room time, a trauma-specific CT imaging evaluation algorithm, and a time rigorous damage control IR are capital parameters which reduce the wasted procedure time that could be the difference between life and death in multivessel bleeding HU coagulopathic patients

angiography within 90 min of admission improves survival rates [15]. Angiography within 60 min has a 16% mortality rate, with the rate increasing to 64% when angiography is delayed [16].

At our institution, the implementation of a time-conscious IR on a 10-year old boy run over by a 20-t truck, resulted in a 30-min embolization time for the right and left internal, splenic, and left adrenal arteries. Namely, the time for a single arterial embolization was 7.5 min, for a total of four vessels embolized (Fig. 13.10).

13.7 Future Trends

13.7.1 Hybrid ER Room

In recent years, the development of hybrid ERs consisting of an angiography suite/operating room with an integrated CT scan have significantly reduced the time between diagnosis and intervention [17]. These improved ergonomic measures applied alongside a trauma-specific workflow allow the team to efficiently perform rapid bleeding control without patient transfer and improve mortality in severe trauma [18]. However, without a time conscious IR workflow, any hybrid resuscitation room will not fully exploit its true potential and, therefore, a time rigorous and specifically designed trauma IR protocol for HU patients is a matter of the utmost importance in order to successfully increase survival rates.

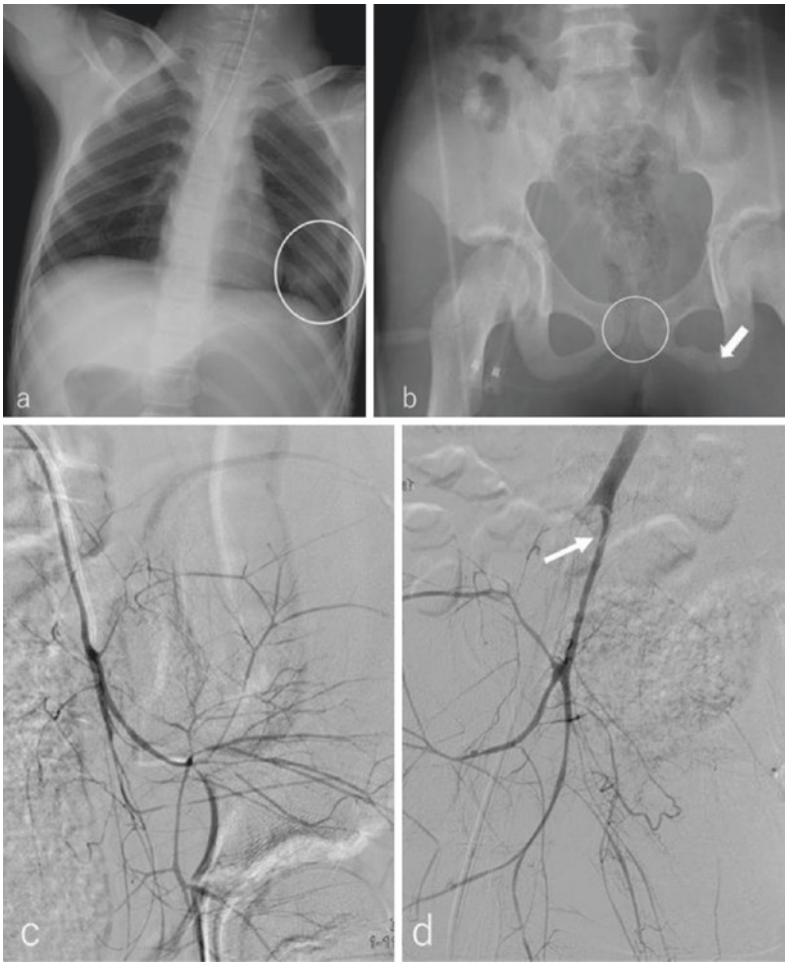


Fig. 13.10 Case of a 10-year old boy struck and run over by a 20-t truck. A 10-year old boy was run over by a 20-t truck and was admitted with a systolic blood pressure of 60 mmHg. Initial portable X-rays (**a** and **b**) showed subtle left lower lung contusion (circle), separated symphysis pubis (circle), and left pelvic fracture (arrow). FAST (focused assessment with sonography for trauma) was negative. The left internal iliac artery embolization (**c**) was followed by aortography (**d**) revealing splenic (circle) and renal artery extravasation (arrow). Right internal iliac artery embolization was performed before changing catheters and embolized the splenic artery and the left adrenal artery (**e**) thereby sacrificing the left adrenal gland and part of the renal artery. Postembolization aortography did not exhibit any extravasation, confirming successful splenic and left adrenal embolization (**f**). A double COA system (two conductors/two operators/two assistants) angioembolization was implemented and resulted in a four-vessel embolization time of 30 min whereby the patient stabilized, which is the main purpose of DCIR. Postprocedural CT examination (not shown), revealed additional minor extravasations and a large bowel injury. Additional angioembolization followed by immediate surgery were performed

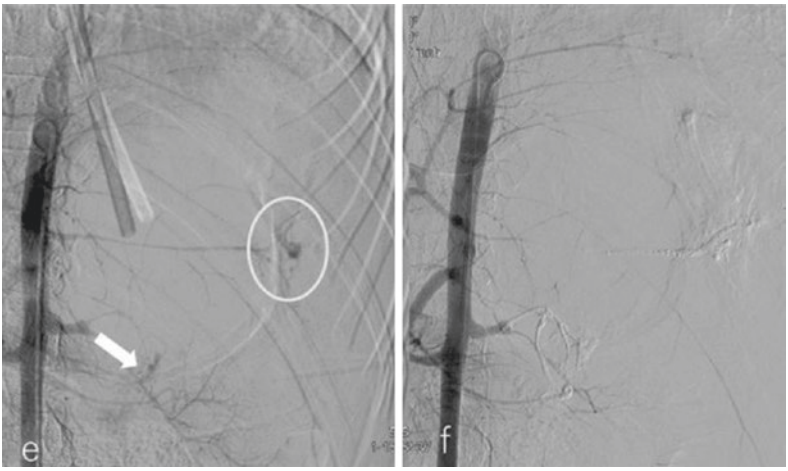


Fig. 13.10 (continued)

13.8 Hybrid Trauma Specialist

Additionally, cross-training "hybrid trauma specialists" with combined proficiency in surgery, IR, and emergency medicine, would further improve the trauma care process with shorter diagnosis and intervention. This concept is a challenge for all the medical specialties involved. Unlimited interdisciplinary cooperation and mutual exchange of information are the fundamental principles for successful IR care and management. Putting aside all interdepartmental contention and developing periodical cross-educational and training workshops among specialties will bring about a new specialty: the "trauma hybrid physician" which could potentially improve future trauma care medicine.

Such strategy may help further expand and redefine key concepts and indications of endovascular techniques within the realm of trauma, as well as nontrauma settings, as a valid adjunct to surgical care.

Recently, the EndoVascular resuscitation and Trauma Management (EVTM) Society has advocated a multidisciplinary approach, utilizing a hybrid surgery-endovascular concept to control massive bleedings; this approach has been steadily growing in popularity among trauma physicians and interventional radiologists worldwide. EVTM conducts yearly meetings and several workshops in Sweden and has recently created a North American EVTM branch. This is a clear indication of the growing awareness that severe trauma HU patients necessitate specific care and that new methods in trauma care are warranted.

Conclusion

Uncontrolled bleeding patients may be either single- or multiple-vessel bleeders. CEIR is the commonly utilized method for single-vessel HS noncoagulopathic patients while TIR can target multiple-vessel HU coagulopathic patients. TIR

patients may possibly be death-bound and time is of the essence. The TIR protocol consists of early activation of the multidisciplinary trauma team, time-conscious CT imaging evaluation followed by damage control IR. Despite the advent of modern hybrid trauma ER, the successful implementation of such a protocol may be feasible only with inter-departmental collaboration. Cross-training and education will create certified "hybrid" cross-certified emergency, trauma and radiology specialists. Despite its utopic appeal, time conscious trauma IR is achievable with the right amount of motivation, the right trauma team, and a strong dedication to saving the dying patient.

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Management of the Unstable Patient During EVTM and REBOA

14

Albert Pierce and Jan O. Jansen

14.1 Introduction

Most trauma patients who require Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) will be cardiovascularly "unstable"—whatever that means. The term is typically used to describe a physiological state characterized by hypotension, hypoperfusion, and tachycardia, often—but not invariably—brought on by blood loss. REBOA is used as part of a damage control resuscitation approach, when blood loss has reached critical levels, to obtain temporary hemorrhage control, while hemostatic resuscitation is instituted. Understanding the physiological consequences of REBOA, and the relationship between anesthesia and aortic occlusion, is therefore critically important.

14.2 Understanding the Physiology of Aortic Occlusion

Superficially, aortic occlusion is an appealing concept: if there is insufficient circulating blood volume to fill the circulatory system, then reducing the capacity of the system, and redistributing the remaining blood volume to those organs most susceptible to hypoperfusion—the brain and the myocardium—makes sense. However, as always, human physiology is more complex than the concepts used to describe it. First and foremost, the circulation is not a single pipe, but

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consists of systemic and pulmonary arterial and venous systems—arguably four different circulatory systems. The differential effects of REBOA on these circulations are incompletely understood.

The most obvious consequence of REBOA (and the best-researched) is an increase in systemic (arterial) vascular resistance, but the impact on the other three, probably mediated through a combination of neurological and endocrine effects, is harder to predict, especially in the context of severe hypovolemia [1]. The effect of a sudden increase in afterload on the myocardium which, until this point, had been struggling with insufficient end-diastolic volume is also not clear, although there is some evidence to suggest that it may be injurious, or at the very least associated with troponin release. Lastly, excluding part of the circulation invariably results in ischemia, which can only be tolerated for a certain period of time. Release of the occlusion will result not only in dramatic changes to vascular resistance and redistribution of circulating blood volume, but also in the release of inflammatory mediators. The magnitude of this insult is proportional to the completeness and duration of balloon inflation, as well as the preocclusion depth and duration of shock [2]. Ischemia results in depletion of cellular energy stores. When perfusion is restored, a post-reperfusion syndrome ensues, which includes the activation and adhesion of leukocytes and platelets, generation of inflammatory mediators, calcium influx into cells, disruption of cellular membrane ion pumps, generation of free radicals, and apoptosis. Clinically, the syndrome is characterized by increased vascular permeability, further exacerbating intravascular volume depletion, and washout of myoglobin, potassium, lactate, and microthrombi into the systemic circulation, exacerbating hyperkalemia and hypocalcemia, and causing rhabdomyolysis and renal failure, compartment syndromes, and cardiac arrhythmias. Recognition can be difficult when the sequelae of post-reperfusion syndrome are superimposed on the manifestations of hemorrhagic shock and hypoperfusion, and requires experience and mature judgment. Injury, REBOA, operation, and post-reperfusion syndrome will all contribute to systemic inflammation.

In short, the physiological impact of aortic occlusion is profound, and incompletely understood, but has to be managed. The remainder of this chapter deals with clinical strategies to help surgeons and anesthesiologists when managing the resuscitation of patients who required REBOA. However, evidence to support these actions is in short supply, and much of it is based on personal experience and extrapolation from other settings.

14.3 Communication

Damage control resuscitation requires excellent communication between surgeons and anesthesiologists, adding REBOA further increases this need. Anesthesiologists must be told when temporary and definitive hemorrhage control has been attained, and when attempts will be made to deflate the balloon. Surgeons must be told how resuscitation is progressing, and whether balloon deflation can be attempted. However, the team managing the patient also has many other members. In our

experience, a very rapid brief on entering the operating room, before transferring the patient to the table, works well. This is often a period of intense activity and conflicting priorities, and requires a firm "Listen in!" to capture everybody's attention. The brief does not have to cover all aspects of the patient's history, but should include aspects relevant to the subsequent surgical and anesthetic management, as deemed by the attending surgeon and anesthesiologist.

14.4 Crew Resource Management

Along with good communication, it is important to ensure that there are sufficient staff available to take on all necessary roles, and that staff understand which roles they have been allocated. In addition to the attending surgeon, there should be two experienced assistants. It is often useful to have a second scrub nurse, and more than one circulating nurse. It is also helpful to have a "REBOA guard," to protect the arterial sheath and catheter during transfer, and while the patient is being prepped and draped, to prevent accidental dislodgement. As far as the anesthetic team is concerned, it is helpful to have at least three anesthesiologists. This allows the senior clinician present to maintain a "30,000-foot" perspective, while others are focusing on gaining venous and arterial access, and managing anesthetic and transfusion management. The latter is further helped by designating a "blood monitor" with the sole responsibility of facilitating the infusion of blood and blood products, and keeping track of what has been administered. If cell salvage is being used, an additional person may be required. Many of these roles should be allocated and commenced before the patient arrives in the operating room, that is, while still in the emergency department.

14.5 REBOA Before or After Anesthesia?

One of the most important and earliest decisions to make is whether to institute REBOA before or after the patient is anesthetized and intubated—unless this has already occurred prior to arrival in the emergency department. Both approaches have advantages and disadvantages.

Early anesthesia and intubation ensure that operative treatment can commence almost immediately. It also reduces patient awareness and discomfort, if the patient is still conscious. A theoretical disadvantage is that induction may precipitate a further decrease in preload, and precipitate a worsening of the patient's cardiovascular status, or even a "cardiac arrest" (although the spectrum between severe hypotension and lack of a palpable pulse is a continuum). However, experience from the wars in Iraq and Afghanistan has shown that "the patient is too unwell to anesthetize" is probably no longer a valid concept. In experienced hands, with appropriately chosen and dosed agents (see below), any patient can be anesthetized and intubated, which undoubtedly facilitates endovascular (and subsequent surgical) management.

However, there may be occasions when endovascular balloon occlusion prior to anesthesia and intubation should be considered. Examples include delays in the

arrival of the anesthetic team, whether caused by multiple casualties, or the setting—in particular, when REBOA is used in prehospital care. In these instances, initial REBOA, facilitated by sedation and local anesthesia, may well be a suitable strategy. However, it should be borne in mind that these patients are often obtunded as a result of cerebral hypoperfusion, and that aortic occlusion and restoration of cerebral perfusion may result in a sudden improvement in the patient's level of consciousness, requiring proactive management.

14.6 Nonarterial Circulatory Access

Typically, large central venous access is preferred; however, if this is unavailable, large bore peripheral IVs can suffice. This access is preferably placed in the upper body venous system, as venous return from the lower body is probably impaired. Paradoxically, during aortic occlusion, volume resuscitation sometimes has to be limited, due to the concern for upper body circulatory overload. As a result, there is an expected need for rapid resuscitation immediately following balloon deflation, with return of the dilated and relatively empty lower circulatory system. This is facilitated by good venous access. Lastly, if vasoactive drugs are required, central venous access is also helpful.

14.7 Induction of Anesthesia

Anesthetic induction must be performed with the patient's cardiovascular and neurologic status in mind, with the goal of maintaining and optimizing perfusion. Achieving this goal requires careful consideration of the available medications and their pharmacological properties, and continuous observation of the patient's hemodynamic state, along with preparations for rapidly responding to sudden hypotension. All medications used for anesthetic induction are capable of causing an abrupt and deleterious decrease in blood pressure and perfusion. Patients who are facing imminent death exhibit a strong "stress response," with high catecholamine output. Induction of anesthesia results in a loss of sympathetic tone, which can result in profound hypotension. Another consideration is that these patients exhibit a decreased volume of distribution, secondary to blood loss, and also decreased mental acuity. Both of these conditions necessitate significant reductions in sedative medication dosing.

The most common agents chosen for Rapid Sequence Induction (RSI) of anesthesia in the severely injured are ketamine and etomidate. Generally, these agents cause less hypotension and thus less hypoperfusion than other induction agents (such as propofol and thiopental), but are not without their own concerns, which require careful consideration [3]. Ketamine has historically been said to be associated with increases in intracranial and intraocular pressures. Currently, however, these concerns are deemed to be either unfounded or clinically irrelevant [4]. While

Ketamine is a direct myocardial depressant, it maintains perfusion by stimulating endogenous catecholamine release. This is not the case in patients who are so incredibly ill that they have depleted their intrinsic stores of catecholamines. That said, in this situation, every other induction agent would likely cause hypotension and hypoperfusion too.

Etomidate has been shown to cause decreased cortisol synthesis, even after a single dose, and has been associated with increased mortality in noncardiac surgical patients [5]. Concomitant steroid supplementation has been attempted, but may not overcome these issues, and brings with it additional problems. Ketamine is therefore intrinsically simpler, and thus more attractive [3]. Either way, outcomes in severely injured patients have been shown to be similar, regardless of whether etomidate or ketamine was utilized for RSI [6, 7].

14.8 Maintenance of Anesthesia

Various techniques exist for the maintenance phase of anesthesia. Some centers promote the use of high dose opioids, where others utilize a mostly volatile agent-based anesthetic. Both provide vasodilation, albeit via different mechanisms: opioids result in decreased sympathetic tone, while the effect of volatile agents is more direct. No specific anesthetic technique has been shown to be definitively superior.

Occasionally, the patient is deemed too tenuous to survive the inevitable vasodilation and myocardial depression associated with all anesthetic agents. The patient's cardiovascular state is so incredibly fragile at these times that maintenance of "anesthesia" may only be attempted with small doses of medications that are typically considered anesthetic adjuncts, such as midazolam and scopolamine. Aggressive attempts to improve perfusion through continued resuscitation are the main focus and will, hopefully, lead to an improved state where the patient might tolerate further opioid dosing and other anesthetic agents [8].

14.9 Analgesia

Fentanyl is the preferred opioid analgesic utilized during REBOA. As stated above, it lowers sympathetic tone, allowing for down-regulation of the vasoconstrictive state typical of the severely injured, thus promoting better tissue perfusion. Hypoperfusion drives the metabolic consequences of shock—such as coagulopathy—and "resuscitation of the microcirculation" is therefore a key concept. Patients who require REBOA thus benefit from opioid effects particularly after the aorta has been occluded, surgical repairs have been performed, and the initial reperfusion insult has passed. Its use prior to this would likely promote hypotension either during the initial resuscitation phase or immediately following balloon deflation. Ketamine also possesses significant analgesic effects—yet another reason to consider its use for induction of anesthesia as well as a low dose infusion after reperfusion.

14.10 Hemostatic Resuscitation

Hemostatic resuscitation broadly follows the principles of other trauma resuscitations, while bearing in mind the upcoming reperfusion of the lower body. Institutions using REBOA should have a Massive Transfusion Protocol, which facilitates the administration of units of red blood cells, plasma, and platelets in a 1:1:1 ratio, while also considering fibrinogen supplementation.

14.11 Afterload Reduction

During aortic occlusion, the rapid increase in systemic vascular resistance leads to a significant increase in myocardial oxygen demand. In elective aortic procedures, this is accompanied by concomitant volume overload of the upper body circulatory system. These effects are more dramatic the closer the aortic occlusion is to the heart and can be tempered by active vasodilation [9]. Nitroglycerin is often used to provide venodilation to offset the volume overload in these elective cases.

REBOA patients differ from those undergoing elective aortic procedures. Volume overload, at least early after aortic occlusion, would not be expected in the setting of hypovolemic shock. Venodilation may be considered, but is not usually necessary. Should active arterial vasodilation be required, clevidipine may be the best choice. Nitroprusside, a combined arterial and venodilator, is also an option. The infusion duration is typically neither long enough, nor at sufficient doses, to cause cyanide toxicity, although with renal dysfunction as a common complication of aortic occlusion and massive trauma, this may become an issue. Both nitroprusside and clevidipine have the advantage of being easily titratable, with rapid on/off effects. Experience with clevidipine, although largely derived from non-REBOA aortic occlusion cases, has been positive. Onset occurs in less than 1 minute, and the dose is adjusted after a 90 s infusion period. We usually start the infusion at 1–2 mg/h and double the dose every 90 s until the blood pressure goal is achieved. When approaching the pressure desired, one can finely titrate by 0.5 mg/h. Active communication with the surgeons allows cessation of the drip with optimal timing for the best response to balloon deflation.

Nitroglycerin is a poor choice of agent for afterload reduction in emergency cases or hemorrhagic shock, as it predominantly acts on the venous system. However, it has been shown to improve cardiac performance through decreasing preload (increased venous capacitance), increasing coronary flow (coronary vasodilation) and augmentation of the Anrep effect (increased contractility secondary to increased afterload related to improved endocardial perfusion) [9].

14.12 Monitoring

Cardiovascular monitoring is best achieved through a combination of invasive arterial pressure monitoring, EKG monitoring, and transesophageal echocardiography (TEE). Arterial pressure should, ideally, be measured both above/proximal to the

balloon (which, depending on the device used, can often be done through the catheter, thus obviating the need for a peripheral arterial line) and below the balloon, through the arterial sheath sidearm. Following both arterial waveform changes provides useful information on a rapidly changing system. Transesophageal echocardiography provides real-time assessment of contractility, volume status, and the ability to detect segmental wall motion abnormalities. This additional information is extremely valuable when managing the complex and rapid changes in volume status. Aortic occlusion creates significant left heart strain, and it is therefore also important to observe for signs of ischemia, including dysrhythmias, on EKG and TEE.

Samples for laboratory analysis are typically drawn from arterial lines. Upon arrival, first round tests include arterial blood gas analysis, hemoglobin/hematocrit, lactate, base excess, pertinent electrolytes (Na^+, K^+, ionized Ca^{++}), platelet count, fibrinogen, viscoelastic testing (thromboelastography or thromboelastometry), and basic coagulation studies (prothrombin time/international normalized ration, partial thromboplastin time). These tests are repeated as indicated, typically every hour during active resuscitation.

14.13 Electrolyte Management

Reperfusion is accompanied by an increase in serum potassium levels. This, on top of the significant potassium load incurred with a massive transfusion, especially in the setting of an acute kidney injury, can result in critical hyperkalemia, dysrhythmias, and cardiac arrest. For this reason, IV calcium should be administered "prophylactically" during the initial phase of balloon deflation/reperfusion. Calcium acts to abrogate the effects of hyperkalemia on the myocardium, as well as supporting contractility and coagulation. Ionized calcium levels also typically drop significantly during massive resuscitation, as a result of the administration of citrated blood products, and must be supplemented as indicated.

14.14 Balloon Deflation

Balloon deflation is as important as inflation. It is a perilous time of reperfusion and determination of adequacy of surgical bleeding control. If uncontrolled bleeding ensues, or if hemodynamic compromise requires it, the balloon should be reinflated until reocclusion occurs. Resuscitation should continue and additional attempts at balloon deflation should follow.

Deflation of the balloon may be performed by the anesthesiologist or surgeon, while mindful of the possible need for reinflation and reocclusion, should the situation require it. Stepwise or partial deflation is conceptually attractive, but difficult given current, highly compliant balloon designs, which tend to behave in an "on/off" manner. This rapid reperfusion of the ischemic portions of the lower body washes deleterious metabolites into the systemic circulation, potentially leading to severe cardiopulmonary dysfunction and systemic cardiovascular collapse. Newer systems with improved partial reperfusion profiles are in development. Measuring

distal blood pressure may be helpful. Recent research in a porcine hemorrhagic shock model shows that distal arterial pressures provide much better estimation of distal aortic blood flow due to the finding that it linearly correlates with flow beyond the balloon whereas proximal arterial pressures do not [10].

Since over-resuscitation prior to balloon deflation is probably detrimental, it is likely that rapid volume resuscitation with blood products will be needed following deflation. Adequate vascular access is therefore imperative. Therapeutic vasodilation is discontinued at the time of reperfusion. This allows the normal compensatory mechanisms of the vasculature to return. However, should the patient continue to exhibit hypoperfusion, as indicated by stable or increasing lactic acid and a worsening base deficit, attempts should be made to dilate the circulation. Increased doses of fentanyl help to ensure that excessive sympathetic tone is not the source of microvascular vasoconstriction, while reversible vasodilation with a volatile agent may also prove helpful. Both of these treatments may lead to reperfusion of areas excluded from prior resuscitation efforts. This is evidenced by a relatively acute drop in perfusion pressure that mimics acute blood loss. Calcium chloride and epinephrine have been found to be helpful in maintaining hemodynamics during reperfusion.

Conclusion

Experience with the intra-operative and anesthetic management of REBOA patients is still limited. Nevertheless, there are a number of key principles which, if adhered to, will help anesthesiologists and surgeons manage these complex and demanding patients.

Experts' Comments by Luca Ansaloni and Federico Coccolini

Traumatic torso hemorrhage (TTH) is an important cause of morbidity and mortality in the field of trauma and emergency medicine and surgery [11, 12]. In recent times, there has been a renewed interest in the adoption of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) in association with the Endovascular resuscitation and Trauma Management (EVTM) approach for patients who present with TTH [13]. Like all medical interventions and procedures, there are not only benefits, but even risks associated with the REBOA technique. However, in the case of REBOA, these complications are not unanimously agreed upon with varying viewpoints and studies. This chapter aims to indicate the correct management of REBOA placement in hemodynamically unstable patients with TTH, in order to reduce the well-known complications of the REBOA technique at each step of its application. Although REBOA is an emergent and increasingly accepted technique used as a less invasive alternative (than surgical interventions) for controlling bleeding in patients with TTH, in order to allow for this procedure to be used in widespread practice, a better understanding of the potential complications that can arise in all stages (arterial access, balloon positioning, inflation, during occlusion,

deflation, and removal of the sheath) must be well recognized. The understanding of the physiology of temporary aortic occlusion, an excellent grade of communication between trauma team members, an integrated management of anesthesia, hemostatic resuscitation and fluid balance during REBOA application (especially during balloon deflation times), and finally an appropriate monitoring of the patients with TTH, can allow identification of specific complications and adequate measures to be taken to avoid these complications and reduce potential morbidity and mortality associated with REBOA.

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Extracorporeal Membrane Oxygenation in the Unstable Trauma Patient

15

Emily J. MacKay and Jeremy W. Cannon

15.1 VV and VA ECMO Circuit Overview

An extracorporeal membrane oxygenation (ECMO) circuit consists of drainage and return cannulae, a pump and a membrane oxygenator with heat exchanger (Fig. 15.1a) [1, 2]. Venoarterial (VA) ECMO drains deoxygenated blood through a venous cannula to a centrifugal pump, arranged in series with a membrane oxygenator and returns oxygenated blood via an arterial cannula [2, 3]. In contrast, venovenous (VV) ECMO returns oxygenated blood via a second venous cannula [4].

15.2 VV ECMO

The use of VV ECMO for acute respiratory distress syndrome (ARDS) has expanded dramatically following positive outcomes published in the CESAR trial [5] and the favorable experience during the H1N1 influenza pandemic of 2009–2010 [6–8]. More recent evidence clarifying its role in the management of adults with severe ARDS will likely contribute to increased use of VV ECMO in the future [9]. Despite the expanding role of VV ECMO for ARDS in the nontrauma patient population

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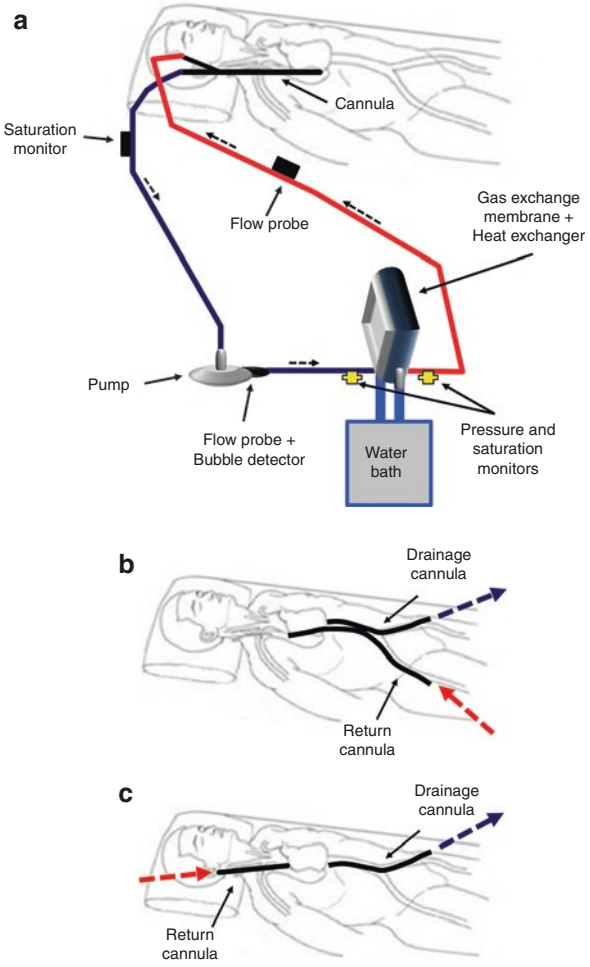

Fig. 15.1 Common circuit components and cannulation strategies for VV ECMO. (**a**) Single site internal jugular cannulation. (**b**) Dual site femoral-femoral cannulation. (**c**) Dual site femoral-internal jugular cannulation

[5–8], VV ECMO use in the trauma patient population has been somewhat limited due to continued concerns over bleeding complications associated with systemic anticoagulation and the inflammatory response incited by the ECMO circuit [10–12], particularly in patients with traumatic brain injury (TBI) [4, 5, 13]. However, recent observational studies have demonstrated promising results for the use of VV ECMO in both the poly-trauma and TBI patient population with very few reported bleeding complications [18–26]. Table 15.1 summarizes the evidence for the use of VV ECMO for ARDS specific to the trauma patient population.

According to the 2017 Extracorporeal Life Support Organization (ELSO) guidelines [14], VV ECMO should be considered when risk of mortality exceeds 50% [14], and indicated when risk of mortality exceeds 80% [14]. 50% mortality in ARDS is associated with: (1) $PaO_2/FiO_2 < 150$ on $FiO_2 > 90\%$ [15]; (2) Murray

Table 15.1 Evidence for use of VV ECMO specific to trauma patients

Author	Year	Type of study	*N*	Indication	Anticoagulation (AC)	Target (aPTT or ACT)	Outcome: survival (*N*%)
Cordell-Smith [18]	2006	Retrospective cohort	28 (VV ECMO)	ARDS	Yes	ACT: 180–220 s	71%
Muellenbach [19]	2012	Case series	3 (VV ECMO)	ARDS (& TBI)	Yes (all cases delayed by 1–5 days)	aPTT: 50–60 s	100%
Biderman [20]‡	2013	Retrospective cohort	5 (VV ECMO)	ARDS (& TBI)	Yes (certain cases delayed up to 48 h)	Not specified	60%
Ried [21]‡	2013	Retrospective cohort	26 (VV ECMO)	ARDS (& TBI)	Yes (certain cases delayed up to 48 h)	aPTT: 40–50 s	81%
Guirand [22]	2014	Retrospective cohort; PS matched (VV ECMO vs. Conventional ventilation (CONV))	102 unmatched (26 VV ECMO vs 76 CONV) 34 matched (17 VV ECMO matched to 17 CONV)	ARDS	Yes	ACT: 180–220 s	Unmatched: 58% (VV ECMO) vs. 55% (CONV) Matched: 65% (VV ECMO) vs. 24% (CONV)
Bosarge [23]	2016	Retrospective cohort; "matched" (VV ECMO vs. Conventional ventilation (CONV))	29 (15 VV ECMO vs 14 CONV)	ARDS	Yes	TEG; R time twice that of unheparinized blood	86.7% (VV ECMO) vs 36% (CONV)
Munoz [24]	2017	Retrospective case-control	67 (15 VV ECMO vs. 52 CONV)	ARDS	Yes	ACT ≤160 s	47% (VV ECMO) vs 77% (CONV)
Ahmad [25]	2017	Retrospective cohort	39 (VV ECMO)	ARDS	Yes	ACT: 160–180 s. or aPTT 60–80 s. (lowered to 45–55 s. if high bleeding risk)	44%
Menaker [26]	2018	Retrospective cohort	18 (VV ECMO)	ARDS	Not specified	Not specified	78%

VV venovenous, *ECMO* extracorporeal membrane oxygenation, *aPTT* activated partial thromboplastin time in seconds (s), *ACT* activated clotting time in seconds (s), *ARDS* acute respiratory distress syndrome, *TBI* traumatic brain injury, *CONV* conventional mechanical ventilation, *TEG* thromboelastography
‡ indicates a study with cohort consisting entirely of thoracic trauma patients

Table 15.2 The Murray score is obtained by averaging the parameter scores for each of the following four areas [15]

	Score				
Parameter	0	1	2	3	4
PaO_2/FiO_2 (on FiO_2 = 100%)	≥300	225–299	175–224	100–174	<100
Chest consolidation (Quadrants involved)	0	1	2	3	4
PEEP required (cm H_2O)	≤5	6–8	9–11	12–14	≥15
Compliance (mL/cm H_2O)	≥80	60–79	40–59	20–39	≤19

ARDS acute respiratory distress syndrome, *FiO_2* fraction inspired oxygen, *PaO_2* partial pressure of arterial oxygen, *PEEP* positive end-expiratory pressure
Table modified from: Murray JF, Matthay MA, Luce JM and Flick MR. An expanded definition of the adult respiratory distress syndrome. Am Rev. Respir Dis. 1988;138:720–3

score of 2–3 (Table 15.2) [15]; (3) Age-adjusted oxygenation index (AOI) >60 [16]; and (4) ARDS prediction score (APPS) ≥5 [17]. 80% mortality in ARDS is associated with: (1) PaO_2/FiO_2 < 100 on FiO_2 > 90% [15]; (2) Murray score of 3–4 (Table 15.2) [15]; (3) AOI >80 [16]; and (4) APSS ≥8 [17]. While ELSO states there are no absolute contraindications to VV ECMO [14], severely injured poly-trauma [10–12] or TBI [4, 13] are considered by many to have relative contraindication to the systemic anticoagulation used in VV ECMO. It is worth noting that the CESAR trial [5], the single randomized controlled trial demonstrating a survival benefit for VV ECMO referrals compared to no-ECMO (relative risk (RR) 0.69, [95% confidence interval (CI): 0.05–0.97]; p = 0.03), included trauma patients (6% of the ECMO cohort) but excluded patients with intracranial bleeding or any contraindication (relative or absolute) to systemic heparinization [5].

15.3 VV ECMO Circuit Management

15.3.1 VV ECMO Cannulation Strategies

The elements of a typical VV ECMO circuit and the three most common cannulation strategies employed in VV ECMO are shown in Fig. 15.1. The cannula orientation should maximize flow and minimize recirculation [14, 27–29] and should be placed under fluoroscopic and echocardiographic guidance if at all possible. In all cases, a bolus 5000 units of Heparin should be administered prior to cannulation to minimize the risk of clot formation and possible circuit thrombosis [1, 14].

Single site dual-lumen cannulation (AvalonElite Bi-caval Dual Lumen Catheter; Maquet, Gothenburg, Sweden) is performed with a 27 or 31 French cannula (depending on the patient's size and cardiac output) typically using the right internal jugular (IJ) vein. The tip of the cannula is positioned in the mid-IVC a few centimeters below the hepatic veins with drainage occurring through side-ports in the SVC and IVC. The return lumen is approximately 10 cm above the distal tip and should be positioned such that the oxygenated return will flow through the tricuspid valve [29]. This cannulation strategy enables early ambulation but can be somewhat difficult to position.

The other cannulation strategies use single lumen catheters. In bilateral femoral cannulation, venous drainage occurs from a cannula introduced into the femoral vein with the tip placed 5–10 cm below the IVC-RA junction within the intra-hepatic vena cava (drainage side-holes positioned above the collapsible intra-abdominal vena cava). Oxygenated return occurs from a cannula introduced into the contralateral femoral vein with the tip in the RA at the level of the tricuspid valve [14, 27]. This strategy is commonly employed in urgent situations where access to the neck is limited and early ambulation is unlikely. This cannula orientation requires a large caliber vena cava to ensure adequate space for two cannulae. The other 2-site strategy is termed "bi-caval cannulation." In this approach, venous drainage occurs from a cannula introduced into the femoral vein with the tip placed 5–10 cm below the IVC-RA junction, again within the intra-hepatic vena cava. Oxygenated return occurs through a small caliber, short cannula introduced into the right internal jugular (IJ) vein with the tip at the SVC-RA junction [14, 27, 28]. This approach is ideal for controlled cannulation in most trauma patients who will not be candidates for early ambulation.

15.3.2 Monitoring Targets

Following cannulation and heparinization, the VV ECMO circuit should be unclamped and flows gradually increased to the target flow range, typically ≥60% of the calculated cardiac output (CO) (approximately 50–80 mL/kg/min [3.5–5 L/min]) [14]. Inlet saturation (sampled from the drainage cannula immediately prior to the oxygenator) is a surrogate for SvO_2 and should be maintained ≥70% [14, 36]. Outlet saturation (sampled from the return cannula immediately after the oxygenator) should be ≥95% with a $PaO_2 > 300$ mmHg [14, 36]. If the outlet saturation is less than 95%, the oxygenator should be investigated for potential clot formation [14, 36]. FiO_2 on the VV ECMO circuit should be titrated to achieve a patient-level arterial saturation of ≥88% [14, 36]. Sweep gas flow (oxygen flow through the gas exchange membrane) on the VV ECMO circuit should be titrated to achieve a patient-level $PaCO_2$ between 30 mmHg and 40 mmHg [14, 36]. VV ECMO does not provide hemodynamic support and therefore will not mitigate the need for inotropic and/or vasopressor support. Inotropes are typically titrated to targets such as $SvO_2 \geq 65\%$ or cardiac index (CI) ≥2.0 L/min, and vasopressors titrated to a MAP ≥65 mmHg. In many cases, the patient's hemodynamics will improve with decreased ventilator pressures and increased systemic oxygen levels.

15.4 VV ECMO Patient Management

15.4.1 Anticoagulation Range

In the absence of any contraindications to systemic anticoagulation, a heparin bolus of 5000 units should be administered prior to cannulation to minimize risk of clot

formation while the circuit is clamped [1, 14]. A heparin infusion should then be initiated with a goal ACT of at least 160 s, [1, 14] ideally between 180 s and 220 s [14, 22]. Although aPTT may be used, ESLO guidelines do not recommend its use because it is susceptible to derangements in coagulation factor levels and platelet function which commonly occur in VV ECMO patients [14]. If aPTT is used to monitor ECMO anticoagulation, it should be maintained between 40 s and 50 s [14]. In the setting of TBI, heparin-boned circuitry [19, 30–33] and a period of heparin-free support have led to successful management of VV ECMO for ARDS in several case series [19, 33–35].

15.4.2 Ventilator Management

Ventilator FiO_2 should be set on "lung rest" settings with an $FiO_2 \leq 0.4$ [14, 36], a plateau pressure of ≤25 cm H_2O [5, 14, 36], and a PEEP between 5 and 10 cm H_2O [5, 14, 36]. Although the ELSO guidelines [14, 36] and the CESAR Trial [5] promote pressure control ventilation (PCV) [5, 36], volume controlled ventilation (VCV) is acceptable, as long as tidal volumes are set at 4–6 mL/kg/ideal body weight and plateau pressures are maintained at ≤25 cm H_2O [4]. Debate on the safety of allowing the lungs to "white out" by minimizing ventilator support continues. Regardless, PEEP levels should be decreased judiciously to avoid losing recruited alveolar units that may still be contributing to gas exchange.

15.4.3 Sedation Strategies

For the first 24–48 h after VV ECMO initiation, heavy sedation is recommended [14, 36]. After initial stabilization, a tapered sedation plan should be implemented to allow for early and frequent assessment of neurologic status [37]. Pharmacokinetic and pharmacodynamic changes in the critically ill result in significant variability between drug dosing and response [38]. These pharmacologic derangements are further exaggerated in ECMO patients [39]. The ECMO circuit increases the volume of distribution by either hemodilution and/or sequestration of drugs [39, 40], particularly highly lipophilic drugs [39–42]. Existing data for appropriate anesthesia and analgesia drug choices on ECMO remains somewhat sparse [43]. Initiating a continuous infusion of an opioid (e.g., fentanyl or hydromorphone) and a sedative (e.g., propofol) during VV ECMO is a reasonable first step [43]. Propofol buildup may start to appear as white streaks in the membrane lung after several days, but the impact of this on membrane efficiency is unknown. If hemodynamically stable, daily sedation interruptions are recommended, especially in anticipation of ECMO weaning and ultimately decannulation [44].

15.4.4 Peri-procedural Management

Surgical procedures can be done successfully while on VV ECMO. When possible, the heparin infusion should be discontinued 6 h prior. If urgent or emergent surgery

is necessary, fresh frozen plasma (FFP) should be infused prior to and during surgery; however, pharmacologic reversal with protamine is never recommended because of risk of circuit thrombosis [14]. Electrocautery should be used liberally in surgical cases, and even in minor procedures such as chest tube insertion performed on VV ECMO, to minimize bleeding [14]. For patients who require open surgery while on ECMO, we recommended temporary cavitary closure with intermittent washouts until ECMO has been discontinued, as the patient is very likely to bleed significantly into the closed cavity during ECMO support.

15.4.5 Tracheostomy Timing and Technique

According to the 2017 ELSO guidelines [14], both "early" extubation and tracheostomy (i.e., at 3–5 days post-cannulation) are recommended for those on VV ECMO [14]. Candidates for endotracheal extubation (or no endotracheal intubation) [45] while on VV ECMO support are typically pre-operative lung transplantation cases [46–50]. Unlike pre-operative lung transplant patients, severely injured, polytrauma patients with ARDS are more likely to benefit from early tracheostomy airway management. Although early tracheostomy does not necessarily confer a mortality benefit or decreased duration of mechanical ventilation, it can permit decreased sedation and earlier mobilization [51–53]. Careful planning and meticulous hemostasis are essential to the success of a tracheostomy in a patient on VV ECMO and the advised technique differs from a standard tracheostomy [14]. A "hybrid" open/percutaneous technique minimizes the risk of bleeding: (1) hold heparin for 6 h, (2) set the ventilator to room air, (3) expose the anterior trachea through a small incision made with an electrocauter, (4) insert the tracheostomy using a percutaneous dilational technique with a Ciaglia Blue Rhino® (Cook Medical, Bloomington, IN) under bronchoscopic guidance, and (5) resume heparin at the previous infusion rate without a bolus once hemostasis is assured.

15.4.6 Early Mobilization and Physical Therapy

The literature for early physical therapy while on VV ECMO is accumulating [54]. Evidence for the efficacy and safety of early mobilization while on VV ECMO is in the pre-operative lung transplantation population [46–50] facilitated largely by using a dual-lumen cannula in the right IJ (AvalonElite Bi-caval Dual Lumen Catheter; Maquet, Gothenburg, Sweden). Recently, the scope of physical therapy during VV ECMO support has expanded and proven to be both efficacious [55] and safe [56].

15.5 VA ECMO

While the evidence for the use of VV ECMO for ARDS in the trauma patient population is accumulating with positive outcomes [18–26], the evidence for VA ECMO following cardiothoracic trauma or traumatic cardiac arrest from exsanguination is inadequate. Table 15.3 summarizes two retrospective, observational cohort studies

Table 15.3 Evidence for use of VA ECMO specific to trauma patients

Author	Year	Type of study	*N*	Indication	VV ECMO	VA ECMO	Anticoagulation (AC)	Target (aPTT or ACT)	Outcome: survival (*N*%)
Arlt [30]	2010	Retrospective cohort	10	ARDS (VV) Hemorrhagic shock (VA)	7	3	Yes (all cases delayed by 4–6 h)	ACT: 120–140 s	60%
Jacobs [57]	2015	Retrospective cohort	85	ARDS (VV) Hemorrhagic shock (VA)	63	21	Yes	Not specified (registry data limitation)	74.1%

VA venoarterial, *ECMO* extracorporeal membrane oxygenation, *aPTT* activated partial thromboplastin time in seconds (s), *ACT* activated clotting time in seconds (s), *ARDS* acute respiratory distress syndrome

investigating outcomes of a combined VV and VA ECMO cohort [30, 57]. VV ECMO cases in both studies had a survival benefit, but the VA patients in each study were very heterogeneous with respect to their underlying diagnoses [30, 57]. Future randomized controlled trials comparing VA ECMO to the current standard in a select trauma patient population are warranted.

To address this evidence gap for the utility of VA ECMO following traumatic arrest, Tisherman and colleagues are actively enrolling in a multicenter clinical trial [58]. This trial is an innovative, parallel assignment, interventional clinical trial comparing "usual care" to "emergency preservation and resuscitation (EPR)" in trauma patients who have exsanguinated to the point of cardiac arrest requiring resuscitative thoracotomy [58, 59]. The investigators define usual care as an emergency thoracotomy, open cardiac massage and fluid resuscitation, and EPR as going onto cardiopulmonary bypass (CPB) by central aortic cannulation in the ascending aorta and central venous cannulation in the right atrium for those patients who fail to achieve return of spontaneous circulation after aortic clamping [59]. These investigators plan to enroll 20 trauma patients (10 assigned to each arm) with a primary outcome of survival to hospital discharge without major disability, and secondary outcomes of (1) feasibility, (2) survival, (3) neurologic functional outcome, and (4) multiple organ dysfunction [58]. This trial represents an important first step in understanding how ECMO may be applied to the management of severely injured trauma patients outside of the typical indications of respiratory failure and the surgical management of tracheobronchial injuries.

Conclusions

VV ECMO for ARDS is feasible and safe in the trauma patient population and appears to confer a significant mortality benefit based on retrospective data. In the setting severe ARDS refractory to conventional mechanical ventilation, VV ECMO with delayed systemic anticoagulation is acceptable in those with TBI

when combined with vigilant monitoring for circuit thrombosis. ECMO alters the pharmacokinetics and pharmacodynamics of lipophilic and protein-bound medications; so sedation strategies often need to be adjusted significantly during ECMO support. Surgical interventions can be performed, but the techniques used require modification to include liberal use of cautery and damage control techniques with open cavitary management. VA ECMO following traumatic arrest is being evaluated in a single pilot study. Taken together, use of both VV and potentially VA ECMO has the potential to substantially improve outcomes in the severely injured.

Experts' Comments by Emiliano Gamberini and Alessandro Circelli

There has been a significant increase in the use of extracorporeal life support (ECLS) in adult patients who are in a state of shock and pulmonary failure. It has been proven to be effective and safe in acute cardiopulmonary failure, even when conventional therapies fail. Advanced management of polytrauma patients should include extracorporeal membrane oxygenation (ECMO) in cases of persistent circulatory and/or respiratory failure despite adequate conventional treatments [30, 60, 61].

Technical advances and compact devices have led to the increased use of ECLS as an advanced option in severe trauma treatment. The improvements in devices allow safer and easier ECLS, for example, anticoagulation can be safely delayed for 48–72 h after trauma due to improved biocompatibility.

ECMO can be used in severe multiple trauma patients as a multi-approach management in respiratory failure (lung contusions, chest wall disruption, acute respiratory distress syndrome), traumatic brain injury (TBI) with associated respiratory failure and impossibility of maintaining normo-hypocapnia with lung protective strategies, post-traumatic cardiogenic shock (providing full hemodynamic support), and tracheobronchial injury.

In patients with severe TBI and hemodynamic instability, ECLS can be used with the purpose of saving time for brain death assessment, and should be continued in order to support an eventual organ donation program.

ECMO is also used to ensure adequate perfusion in cardiopulmonary failure in patients with severe trauma, even in the context of hemorrhagic shock. The surgeon can perform damage control surgery, and coagulation abnormalities can be treated according to the recommendations for blood component transfusion.

ECLS is also used in post-traumatic cardiac arrest requiring resuscitative thoracotomy, but the evidence for this is still inadequate.

The evidence for the benefits in terms of survival is still lacking, although we think that ECLS plays an important role in trauma patients, although the exact role is yet unknown. The use of ECMO in the treatment of trauma patients should be considered in patient populations where conventional treatments fail to result in more benefits than risks.

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Postoperative Critical Care Management Considerations

16

Kristofer F. Nilsson and Birger Axelsson

16.1 Introduction

Intensive care after severe hemorrhage managed by EndoVascular resuscitation and Trauma Management (EVTM) will have many similarities with standard intensive care in bleeding patients. This chapter does not aim to review all aspects of intensive care; instead, the aim is to pay attention to the special considerations that must be regarded in an EVTM patient. The most significant differences between standard and EVTM care, which will affect intensive care, are the use of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA), and of endovascular methods in bleeding management, including embolization and endografts [1]. Importantly, due to its indications, REBOA is applied as an adjunct in the most severely bleeding patients, which promotes complex postischemic reperfusion critical care. Additionally, REBOA introduces a severe challenge to the circulatory system in the reperfusion phase, i.e., vasodilatory (distributive) shock, and disturbance of the acid-base status and electrolyte balance of circulating blood. Furthermore, ischemia-reperfusion injury to the lower body threatens distal organ function and may cause devastating abdominal compartment syndrome as well as a systemic inflammatory response syndrome (SIRS). The anesthesiologic intraoperative considerations of REBOA usage have recently been reviewed, including consideration of the physiology of balloon inflation and deflation [2, 3]. Immobilization, use of endografts in combination with potentially bleeding traumatic injuries, and possible intracranial bleeding, mean that the use and timing of anticoagulants must be thoroughly taken into account in an EVTM trauma patient, in addition to the expected transfusion-induced coagulopathy. Use of sheaths for femoral access introduces a risk of groin access complication, which can be limb threatening.

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Taken together, in the intensive care of an EVTM patient, special considerations include monitoring, management, and complications. In many respects, evidence is lacking, since EVTM is a new concept. However, where possible, the authors reference existing EVTM research and also incorporate evidence from surgical intensive care, and vascular and trauma surgery into the EVTM concept.

16.2 Physiological Alterations and Organ Complications After REBOA

According to animal studies of REBOA in hemorrhagic shock, the following physiological disarrangements may be expected in the reperfusion phase: severe acidosis, lactatemia, systemic hypotension requiring vasopressor infusion and exaggerated fluid resuscitation, transient hyperkalemia, increased wet lung weight to body weight ratio, decreased arterial partial pressure of oxygen to fraction of inspired oxygen ratio, increased cardiac troponin, increased lactate dehydrogenase, and increased cytokine release [4–11]. On measurement, many of these changes were found to be less pronounced when utilizing the partial REBOA technique [4–6].

Animal studies have indicated that many organs are at risk of damage when using REBOA, including increased incidence of acute respiratory distress syndrome, acute tubular necrosis in the kidneys, increased blood urea nitrogen, increased aspartate aminotransferase and creatine kinase levels, necrosis of intestinal epithelial cells, centrilobular liver necrosis, lumbar spinal cord necrosis, and functional neurological dysfunction in limbs [4, 5, 7, 8, 12]. One animal study did not find that REBOA increased intracranial bleeding in a traumatic brain injury [6]. Compared to total REBOA, partial REBOA generates more physiological proximal pressures and distal blood flow, and therefore probably spares both proximal and distal organ function [4, 5, 13].

Trauma and hemorrhagic shock alone promote postresuscitation organ dysfunction. In blunt injury trauma patients, multiple organ failure (MOF) is common, reaching approximately 30%, and develops within the first postresuscitation days [14]. Risk factors for MOF in trauma patients are, among others, high trauma severity and physiological derangement [14]. Therefore, since REBOA is applied to the most injured patients [15, 16], organ dysfunction and failure are to be expected.

DuBose et al. [17] found, in a cohort of 46 trauma REBOA patients, that 4.3% developed the conditions necessary for dialysis, sepsis or septic shock, pneumonia, and/or MOF, and that 2.2% developed bacteremia. Early mortality in this cohort was high, and the true incidence is therefore difficult to estimate. Saito et al. [18] reported that 64% of 14 REBOA patients who survived 24 h after blunt trauma developed at least a risk of acute kidney injury, and in all but one case this was part of MOF. In the same study, 64% of the patients developed MOF, which was also a major cause of death beyond 24 h [18]. Romagnoli et al. [19] found 3% of cases of mesenteric ischemia in a study group of 74 trauma REBOA patients, and Sato et al. [20] observed one case of mesenteric ischemia in 24 trauma REBOA patients. Sadeghi et al. [15] reported MOF in 10 trauma REBOA patients, out of 96 patients in their cohort. Stensaeth et al. reported no systemic complications of REBOA usage in postpartum hemorrhage patients, indicating that Zone III occlusion is less

harmful [21]. A clinical case study reported increased intracranial bleeding in a trauma REBOA patient [22].

Presently, tentative organ complications in REBOA use are well described in animal studies, but not well documented with regard to incidence in REBOA patients. Unfortunately, organ complications in REBOA patients are often not reported in detail, and the numbers are derived from registry cohort studies, making estimates of incidence difficult. Furthermore, the studies are either observation studies or retrospective comparisons, and therefore lack adequate control groups. Despite their limitations, however, the numbers give a picture of what an EVTM intensivist can expect.

16.3 Important Information for the Intensivist from the Trauma Team

When enrolling a trauma EVTM patient for intensive care, the intensivist must gather information on the duration of aortic occlusion and the level of occlusion (Zones I, II, or III), and whether complete, partial and/or intermittent occlusion strategies have been used. Simplified, the longer the duration of complete occlusion in Zone I, the worse the physiological status and complications in the patient that can be expected. To adequately foresee complications in EVTM patients, markers or algorithms for the prediction of complications are needed.

16.4 Access-Related Complications

In a recent meta-analysis and systematic review, groin access-related complications were estimated at approximately 5% [23]. Complications include arterial thrombosis, vessel injury, dissection, pseudoaneurysm, and compartment syndrome and are associated with a substantial risk of limb amputation [19, 23]. The risk of arterial thrombosis may be higher in postpartum hemorrhage REBOA cases, perhaps reflecting hypercoagulation in obstetric patients [21]. Therefore, a high awareness of access-related complications is warranted in the intensive care of EVTM patients. Frequent monitoring includes examination of access-site bleeding, and clinical and Doppler examination of distal perfusion of the lower limbs. Near- infrared spectroscopy of the calves may be useful for continuous monitoring of distal oxygenation to early detect ischemic events [24]. Importantly, the access-related complications may be decreased by using smaller sheaths, longer sheaths, and the percutaneous puncture technique instead of surgical cut-down on insertion [21, 23, 25]. Removal of the sheath as fast as possible is indicated when bleeding source control is achieved.

16.5 Cardiovascular Monitoring and Treatment

Basic cardiovascular monitoring of an EVTM patient requires an arterial line, which facilitates continuous invasive blood pressure measurement and repeated arterial blood analyses. A trauma patient must also be equipped with large bore

venous catheters for fluid and blood resuscitation, and preferably a central venous access for drug infusions. In the hypotensive REBOA patient, adequate treatment should be based on distinguishing persistent hemorrhagic shock, vasodilatory shock, relative hypovolemia due to SIRS, and cardiac dysfunction causing a low cardiac output. Several bed side methods, in addition to clinical examination, are available to estimate volume status, cardiac output, and systemic vascular resistance. A simplified and focused assessment of cardiac performance and volume status by echocardiography may be the fastest and easiest way of differentiating the effects of the vascular and cardiac components of systemic hypotension. In previously healthy patients who promptly respond to treatment, advanced hemodynamic monitoring is not needed, but in severe cases and/or with heavy comorbidities, it may be recommended. Direct measurement of cardiac output with a pulmonary arterial catheter can be an option in institutions where it is available, but there are many less invasive alternatives, e.g., pulse wave analysis with or without thermodilution calibration [26]. If sophisticated methods are unavailable, the saturation in the venous blood from the central line is helpful, but the interpretation may be complicated [27]. A large retrospective registry study found increased survival in aged severely injured shock trauma patients managed with a pulmonary arterial catheter, showing the potential benefit of advanced cardiovascular monitoring in selected patients [28].

16.6 Fluid Resuscitation

Patients with uncontrolled bleeding undergo a massive transfusion; perhaps, a societal massive transfusion protocol is initiated [29]. Since the REBOA patient is at extremis per definition, it is not surprising that cohort data show that most REBOA patients undergo extensive resuscitation with packed red blood cells, fresh-frozen plasma, and platelets [15, 17, 21]. To avoid prolonged massive transfusion that leads to complications in REBOA patients, the authors suggest that the massive transfusion protocol should be terminated when acceptable surgical bleeding source control is acquired, although absolute hemodynamic stability has not been achieved. Postdeflation REBOA physiology by itself gives rise to a compromised circulation that may not benefit from overresuscitation of fluids and transfusions. Therefore, the authors advocate that, in hemodynamically unstable REBOA patients with bleeding source control, further volume resuscitation must be guided by a goal-directed strategy using the cardiovascular monitoring described above, and laboratory test resuscitation targets [30].

16.7 Cardiovascular and Circulatory Support

Use of vasopressors is recommended for life-threatening bleeding as a complement to aggressive volume resuscitation [30]. After initial resuscitation, vasodilatory shock may be a consequence of SIRS after hemorrhagic shock and REBOA. It is preferably counteracted by vasopressor infusion to avoid volume overload. Indeed, 50–75% of the trauma REBOA patients in two cohort studies received

vasopressor treatment [17, 31]. If the cardiovascular monitoring shows low systemic vascular resistance with preserved cardiac output, vasopressor infusion should be initiated. Norepinephrine is often the first choice of vasopressor drug, but if insufficient, vasopressin or epinephrine may be added, as in cases of septic shock [32]. Recently, angiotensin II has been suggested as an adjunct vasopressor to norepinephrine for patients in severe vasodilatory shock [33]. However, it is noteworthy that too early a use of vasopressors instead of fluid resuscitation may be detrimental in trauma patients, indicating the importance of use of advanced cardiovascular monitoring [34].

If cardiac dysfunction or injury, resulting in low cardiac output, is suspected from the cardiovascular monitoring, inotropic drugs may be an option [30], but no studies have shown any long-term beneficial effects of these drugs in intensive care patients [35]. Inotropic catecholamines with short half-lives, epinephrine and dobutamine, cause tachycardia and raise myocardial oxygen consumption and produce an unpredictable response in the presence of beta-blockade treatment [36]. Although not well studied in the setting of trauma, the inotropic agents, levosimendan (intracellular calcium sensitizer and phosphodiesterase inhibitor) and milrinone (phosphodiesterase inhibitor), may also be used [37, 38]. They are a better choice in patients on beta-blocking therapy, but they may produce vasodilation and have longer half-lives [36].

16.8 Extracorporeal Membrane Oxygenation

An emerging endovascular method in the treatment of severe trauma patients is extracorporeal membrane oxygenation (ECMO), which replaces pulmonary and/or cardiac functions. Thus, indications for ECMO treatment in the severe trauma population may include severe hypoxemia (venovenous ECMO) and cardiovascular collapse (venoarterial ECMO) [39, 40]. By using a heparin-coated ECMO, EMCO may be initiated even in patients at high risk of bleeding, since systemic heparin treatment can be delayed a few days [41]. Often a femoral vessel and the right jugular vein are cannulated, and to avoid ischemic complications in the cannulated leg in venoarterial ECMO, a distal perfusion catheter is connected to the arterial line. The required duration of ECMO treatment in severe thoracic trauma patients with pulmonary failure is relatively short, and reported survival has been excellent with an acceptable complication frequency [42]. The feasibility of ECMO treatment has improved with the recent availability of quite small ECMO units, which has broadened possible applications to include even prehospital uses, such as in nontraumatic cardiac arrest [43, 44]. The need and eventual implementation of prehospital ECMO in trauma EVTM patients remain to be explored.

16.9 Coagulation

Bleeding patients often present with coagulopathy, and risk factors, among others, include acidosis, hypothermia, and high extents of shock and injury severity [45]. Obviously, trauma REBOA patients are at risk of developing a traumatic

coagulopathy since many of these risk factors apply. Cohort studies of trauma REBOA patients clearly show that they present with deranged coagulation, hypothermia, and acidosis, which are further compromised by the use of REBOA [15, 17, 31]. Monitoring includes repeated arterial blood gas analyses, and early and repeated coagulation tests using conventional laboratory screens and/or a viscoelastic method [30, 46]. Coagulation management includes hemostatic resuscitation with goal-directed recommended red blood cell and plasma ratios, platelets, fibrinogen, maintained calcium levels, tranexamic acid, and steps to avoid and correct hypothermia [30].

Bleeding management is complicated in patients, especially the elderly, who may be on daily treatment with drugs that inhibit the plasmatic and/or the cellular components of the coagulation systems, which require certain measures to be taken [30, 47]. The influence of antiplatelet therapy on platelet function is not easily detected using viscoelastic methods. Therefore, specific platelet function tests that use various receptor-targeted proaggregatory stimulators have been developed and implemented in clinical use [48]. In bleeding patients on antiplatelet therapy, platelet transfusion may be an option, but its efficacy in a related condition has lately been questioned [49]. The anticoagulant effects of warfarin are detected by routine coagulation tests, using international normalized ratio, and are rapidly reversible by K-vitamin-dependent coagulation factor treatment (prothrombin complex concentrates) [50]. In patients taking new direct oral anticoagulants, inhibitors of activated factor X or the direct thrombin inhibitor, the plasma levels of the drugs can be measured. Only dabigatran can be reversed specifically [51], and a combination of prothrombin complex concentrates and tranexamic acid may be the only reversal option until more specific antidotes are developed [30].

Following bleeding, a hypercoagulable state arises, which in addition to immobilization, warrants prophylactic anticoagulation to avoid thromboembolic events, especially in patients with existing mechanical valves or stents, or newly implanted stents or endografts as part of the EVTM concept. Prophylactic treatment of venous thromboembolism in trauma patients is recommended within 24 h after bleeding control, preferably with a combination of pharmacological and mechanical methods [30, 52, 53]. In extensive endovascular surgery with stent implantation in the aorta and its branches, low molecular weight heparin is often restarted between 6 and 12 h after surgery, when clinical detected bleeding can be ruled out. A summary of periprocedural antithrombotic regimens in percutaneous cardiovascular interventions, including also cardiac stents, has been published [54]. If there is a need for a powerful antiplatelet inhibiting drug, as in a situation where a coronary stent has been acutely placed, the use of cangrelor, a new and high-affinity inhibitor of the P2Y12 receptor, with a very short elimination half-life (3–6 min), can be used instead of the long-acting clopidogrel or ticagrelor [55]. If needed, viscoelastic methods with and without added heparinase detect residual unfractionated, and to a partial extent also fractionated, heparin effects, which are reversable by protamine administration. In patients in need of anticoagulation where bleeding might be a problem, a fully neutralizable anticoagulation may be considered, such as heparin with protamine.

In a trauma patient with newly implanted or pre-existing grafts, the balance between the risk of bleeding and the risk of graft thrombosis is probably

delicate, and prophylactic dosing and timing of initiation must be thoroughly considered in each individual case. General recommendations based on evidence cannot be stated.

16.10 Gastrointestinal Tract and Nutrition

Gastrointestinal function is monitored through clinical symptoms and signs; no biochemical marker is in clinical use. Recently, a grading system for acute gastrointestinal injury in critically ill patients was published [56], and its feasibility and validity in intensive care patients have been proven [57]. The intravesical pressure—a substitute for the intra-abdominal pressure—should be liberally monitored in trauma REBOA patients, since trauma itself and aortic occlusion are both risk factors for abdominal compartment syndrome [58, 59]. In addition, clinical awareness of mesenteric ischemia must be high, since it has been reported as a complication in trauma REBOA patients [19, 20].

The integrity of the gastrointestinal tract is at risk in REBOA patients, since hypoperfusion and ischemia-reperfusion injury of the gastrointestinal tract cause damage to the epithelial cell barrier, resulting in bacterial translocation and inflammation. This has two important implications for the care of REBOA patients.

First, the epithelial cells are crucial for the uptake of water, electrolytes, and nutrients from the intestinal lumen, and there is a risk of intestinal paralysis. In general, the early start of enteral feeding within 24–48 h in intensive care patients is recommended, and the energy requirements should preferably be measured using indirect calorimetry [60]. In critically ill patients with an increased risk of feeding intolerance, the evidence for early enteral feeding is low. Nonetheless, societal guidelines recommend deliberate and carefully monitored early enteral feeding in resuscitated trauma patients, even in those with abdominal trauma if continuity of the gastrointestinal tract is confirmed/restored [61]. In conditions that may include those of REBOA patients, the start of enteral feeding must be delayed until resolved; these include uncontrolled shock, uncontrolled acidosis or hypoxemia, inadequate tissue perfusion, increased intraabdominal pressure during enteral feeding, abdominal compartment syndrome, overt bowel ischemia, mechanical ileus, uncontrolled gastrointestinal bleeding, and a gastric aspirate volume of >500 mL per 6 h [61].

Second, initiation of prophylactic antibiotics must be considered due to the use of REBOA and the resultant bacterial translocation, but robust evidence is lacking. Guidelines on acute mesenteric ischemia, where bacterial translocation is massive, trauma laparotomies and penetrating abdominal trauma suggest use of broad-spectrum antibiotics with anaerobic coverage [62, 63]. The prophylactic antibiotic regimen should be started within 1 h of the start of intervention and be stopped within 24 h [64]. Obviously, the initiation of antibiotics in trauma patients is common for various reasons [65]. Before a definitive antibiotic treatment is started beyond the 24 h of prophylaxis, bacterial cultures must be secured from blood, urine, and the respiratory system as well as from specific wound sites.

16.11 Renal Function

In intensive care, renal function is monitored by hourly measurements of diuresis, at least daily measurements of plasma/serum creatinine and/or cystatin C levels, and documentation of fluid balance. Research is being performed on novel markers and on clinical prediction models [66], but these are not currently being used in regular clinical practice.

Several mechanisms contribute to acute kidney injury (AKI) in an EVTM patient [67, 68], in particular, the usage of REBOA causes renal ischemia-reperfusion injury and acute tubular necrosis [69]. Consistently, cases of AKI have been reported in trauma REBOA patient cohorts [17, 18]. In severe trauma patients, the incidence of AKI is 20–25% [66, 67], and probably even higher in REBOA patients, but long-term survivors after trauma usually do not need chronic renal replacement therapy [67]. Pharmacological renal protection strategies are, in general, not supported by the evidence, and not recommended [69, 70].

Supportive treatment of kidney function in a REBOA patient consists of controlled volume resuscitation with avoidance of volume overload using cardiovascular monitoring. For the euvolemic patient without chronic hypertension, there is a target mean arterial pressure of 65–70 mmHg, while a higher or individualized target should be used for patients with preexisting chronic hypertension, achieved preferably by norepinephrine infusion. Loop diuretics may be used to treat volume overload, but not for renal protection purposes [71].

In REBOA patients, continuous renal replacement therapy (CRRT) may be indicated for several reasons, including acidemia, hyperkalemia, and fluid removal/volume control due to anuria. The timing of initiation of CRRT in an AKI patient must depend on clinical judgment if there is no life-threatening indication [70]. Volume correction by CRRT in the AKI patient may facilitate weaning from the ventilator [72]. One retrospective study found that early initiation of CRRT in trauma patients with AKI was associated with lower mortality [73]. In patients at risk of bleeding, regional anticoagulation with citrate is recommended in CRRT [70].

Conclusions

Resuscitation and trauma management according to EVTM introduce novel aspects of critical care, including the postreperfusion physiologic effects using REBOA, expected complications, and anticoagulation. Thus, high clinical suspicion of detrimental complications is warranted, certain monitoring should be used, and sound clinical judgment is necessary. Future work should aim to find markers of organ damage to guide the critical care of the EVTM patient, investigate the frequency of complications related to REBOA usage compared to standard management, and explore optimal treatment of EVTM/REBOA-related complications.

Expert's Comments by Andrew Kirkpatrick

Doctors Nilsson and Axelsson have written an excellent and focused review of what is currently known concerning the physiology and pathophysiology of patients surviving EndoVascular resuscitation and Trauma Management (EVTM). As the authors

acknowledge, there is much still to be learned as utilizing Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) is a relatively new practice in most centers. There is more experience with Endovascular aneurysmal repair (EVAR) in which aortic occlusion, coagulopathy, and massive transfusion clearly associate with severe intra-abdominal hypertension (IAH) and the abdominal compartment syndrome (ACS) [59]. Survivors of REBOA deployment will be critically ill with all the expected complications of catastrophic trauma and from technical aspects of major arterial access, but also with additional critical visceral concerns related to the unique physiology of aortic occlusion. Specifically, such patients display markedly increased rates of mesenteric ischemia, renal failure, and severe IAH. Further, the effects of IAH/ACS will not be limited to the abdomen but will be systemic due to elaborated biomediators propagating multiorgan dysfunction syndrome/multisystem organ failure and/or through polycompartmental pressure interactions [74, 75]. It is likely that post EVTM, patients will be especially susceptible to what Malbrain has termed the Acute Intestinal Distress Syndrome. This is a postresuscitation syndrome in which a first "hit" such as severe trauma/shock induces bowel ischemia-reperfusion injury, releasing proinflammatory mediators into the peritoneum and systemic circulation, leading to neutrophil priming, increased intestinal permeability, extravasation of fluid into the bowel wall and mesentery, translocation of intestinal bacteria, and absorption of bacterial endotoxin. Subsequently, with massive resuscitation and aortic occlusion as a second severe "hit," visceral edema leads to severe IAH, compressing intra-abdominal lymphatics, further decreasing visceral perfusion thus escalating the increased permeability and driving further bacterial translocation/endotoxin absorption and generation of proinflammatory mediators [74, 76–79]. Intra-abdominal pressure monitoring will thus be imperative for post EVTM patients, for whom aggressive IAH management will be required [80], including decompressive laparotomy if necessary. Obviously, a less invasive solution to trauma that ultimately requires a maximally invasive solution to consequences of that first solution is far from ideal. Progress in medicine is rife with challenges that led to innovative solutions as scientific understanding and technique progress, and post EVTM critical care management will hopefully be one of those areas.

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Complications of Endovascular and Hybrid Surgery

17

Jeniann Yi and Charles J. Fox

17.1 Access Site Complications

Initial forays into endovascular and hybrid surgeries utilized open exposure of the vessels to obtain access. Technical advances now allow for safe, percutaneous access as the preferred approach [1]. Access site complications occur in 1–9% of percutaneous interventions, with reduced rates of complications when using routine imaging guidance [2]. Percutaneous closure devices are also used with increasing frequency to aid in hemostasis of the access site. The most commonly used site for access is the femoral artery; less frequent sites include radial, brachial, axillary, and pedal arteries [3, 4]. Risk factors for access site complications include anatomic location, female gender, advanced age, anticoagulation, sheath size, and lack of closure device [5]. Complications incurred at the access site include hematoma, pseudoaneurysm, and acquired arteriovenous fistula.

17.1.1 Hematoma

Hematoma results from failure of hemostasis at the puncture site. The clinical significance of a hematoma varies greatly. Kwok et al. performed a meta-analysis of percutaneous coronary intervention (PCI) studies and found the rate of major access site bleeding to be 11.2% with associated mortality rate of 2.8% in these patients

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[6]. Small, minimally symptomatic hematomas are typically observed without consequence, whereas large and/or expanding hematomas are more likely to require intervention. Furthermore, hematomas can dissect into contiguous anatomic spaces, such as the retroperitoneum, inguinal canal, or associated nerve sheaths. Large hematomas can also result in skin necrosis, anemia, and hypotension. Once diagnosed, hematoma management includes frequent observation, correction of underlying coagulopathy, and supportive care. Additional pressure at the access site may aid in controlling the expansion of the hematoma with improved hemostasis. Transfusions and blood pressure management are indicated for symptomatic patients. Imaging via computed tomography or duplex ultrasonography may be helpful to diagnose the hematoma extent, presence of active bleeding, and possible associated pseudoaneurysm. Operative exploration of a hematoma is warranted with associated nerve compression, skin necrosis, persistent hypotension or anemia, and uncontrolled pain.

17.1.2 Pseudoaneurysm

A pseudoaneurysm following percutaneous access indicates a failure to seal the vessel puncture site, resulting in a contained area of bleeding where the space is in communication with the vessel lumen. Examination typically reveals a pulsatile mass associated with tenderness. Duplex ultrasonography demonstrates a pulsatile sac communicating to the vessel via the neck of the pseudoaneurysm with turbulent flow, sometimes referred to as the "yin-yang sign." Small (<2.5 cm) pseudoaneurysms may thrombose off without intervention and can be observed [7, 8]. Directed external pressure on the neck of the pseudoaneurysm with ultrasound guidance may be attempted to shut down flow into the pseudoaneurysm. For amenable pseudoaneurysms, ultrasound-guided thrombin injection into the neck can also be used to induce thrombosis. Khoury et al. reported a success rate of 96% in their series of 131 patients [8]. However, intervention on pseudoaneurysms with short, fat necks are less likely to be successful with potential complications such as intra-arterial injection with distal embolization. If these interventions are unsuccessful, open exploration may ultimately be required to primarily repair the pseudoaneurysm.

17.1.3 Acquired Arteriovenous Fistula

An arteriovenous fistula following percutaneous access (Fig. 17.1) represents an aberrant communication between the artery and vein. It is quite rare as compared to other access site complications, with an incidence of 0.017–0.86% following arterial catheterization [9]. Causes include simultaneous ipsilateral vein and artery access as well as inadvertent access of the vein when attempting arterial access or vice versa. Symptomatically, patients may complain of pain, limb swelling, or congestive heart failure. Examination findings of a pulsatile mass with palpable thrill or

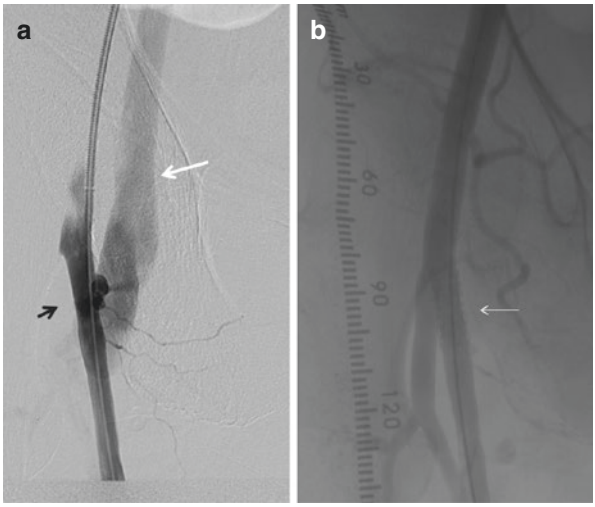

Fig. 17.1 Digital subtraction angiogram (**a**) of the right superficial femoral artery depicts a pseudoaneurysm (black arrow) associated with an arteriovenous fistula (white arrow) after percutaneous transfemoral cardiac catheterization. A fluoroscopic image (**b**) shows the endovascular management of the pseudoaneurysm and resolution of rapid venous filling after placement of a 6 × 22 mm iCAST stent (white arrow), post-dilated to 8 mm. (Atrium Medical Corporation, Hudson, NH)

audible bruit are suggestive of an arteriovenous fistula. Diagnosis can be confirmed with imaging, such as duplex ultrasonography demonstrating an arterialized waveform in the vein and low resistance flow in the artery. Up to 38% of acquired arteriovenous fistulae will spontaneously resolve within 1 year [10]. When persistent, treatment options include endovascular therapy and open surgery. Embolization of the fistulous connection can be accomplished using coils or vascular plugs. Placement of a stent graft to provide coverage of the arterial component has also been performed successfully, though stent fracture and long-term patency are potential concerns depending on the location of the fistula [11]. Failure of less invasive methods with persistent symptomatology, increasing size, rupture, infection, or mass effect are all indications for open surgical repair.

17.2 Intervention Complications

Endovascular procedures require luminal access using wires, catheters, sheaths, balloons, and other devices to provide therapeutic interventions. This places the vessels at risk of damage, particularly in calcified, atherosclerotic vessels. Potential complications from endoluminal manipulation include dissection, thrombosis, embolization, and rupture.

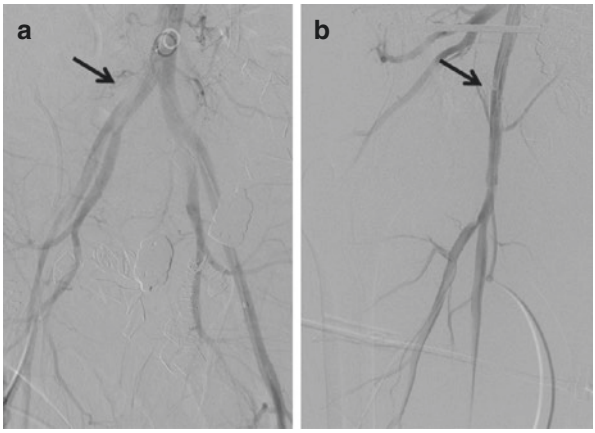

Fig. 17.2 Hemorrhagic and neurogenic shock from a combined spinal cord injury with open pelvic ring disruption was managed with Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA), pre-peritoneal pelvic packing, and external fixation. A digital subtraction angiogram demonstrated a filling defect (arrow) compatible with thrombus in the right common and external iliac arteries (**a**) and extensive clot with right femoral artery dissection (**b**, arrow) that resulted in transfemoral amputation

17.2.1 Dissection

Dissection following endovascular intervention (Fig. 17.2) is especially common, with incidences of 7.4–53% reported in the literature [12]. Treatment of stenosis by disrupting plaque, such as with balloon angioplasty, is likely to cause a degree of dissection. This may be clinically irrelevant, unless the dissection flap propagates distally or with overdistention in a normal vessel. The passage of wires, catheters, or other devices can also result in intimal dissection. Small dissections that are not flow-limiting may be observed. Clinically significant dissections must be addressed, but usually can be treated endovascularly with stent graft placement across the dissected portion [13].

17.2.2 Thrombosis/Embolization

A prothrombotic state is created during endovascular interventions due to disruption of the endothelium and introduction of foreign bodies. Arterial thrombosis following endovascular procedures can result in distal ischemia, and venous thrombosis can result in limb swelling with potential for venous embolism [9]. Thrombolytics can be attempted in patients without contraindications, but mechanical thrombectomy may ultimately be necessary. This can be performed either open or endovascularly to successfully remove the thrombus [4].

Distal embolization during revascularization is a potential life- and limb-threatening complication. In a series of 388 patients undergoing superficial femoral

revascularization, 2.3% had distal arterial embolization [14]. Factors associated with distal embolization included longer lesions and chronic total occlusions. McKinsey et al. compared distal embolization rates with and without embolic protection devices and found no difference. However, the authors did comment on preferential use of these devices in patients with longer, more stenotic, and heavily calcified lesions [15]. Small emboli may not be hemodynamically significant and can be observed. When intervention is indicated, an endovascular approach via thrombectomy or angioplasty may be successful. Rarely, open embolectomy may be required to restore blood flow.

17.2.3 Rupture

One of the most worrisome procedural complications is vessel rupture (Fig. 17.3). Overdistention with balloon angioplasty or extraluminal wire placement can result in vessel rupture. Thankfully, it is relatively rare with one multicenter series reporting 0.9% incidence among 587 iliac artery treatments [16]. Once identified, inflation of a balloon for tamponade can temporize the injury. Placement of a stent graft across the rupture can achieve hemostasis and resolve the injury. If unsuccessful, open repair is mandated [17].

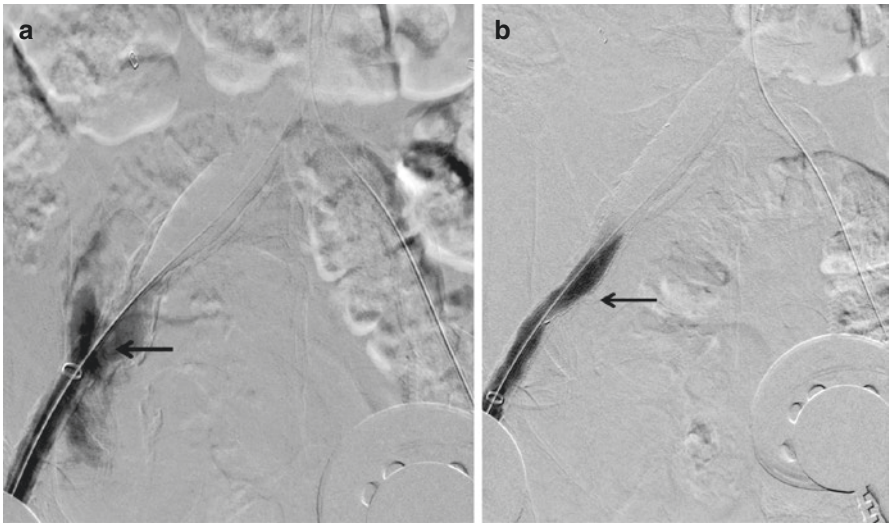

Fig. 17.3 Sudden hemorrhage, loss of blood pressure, and brief period of cardiac arrest resulted from a ruptured right common iliac artery (**a**, arrow) during the large diameter sheath placement for elective endovascular aneurysm repair (EVAR). A proximal aortic balloon occlusion (Cook Medical Inc., Bloomington, IN) allowed for expeditious sizing and deployment of a 16 × 12 mm Excluder limb (**b**, arrow) and extended with a 13 mm Viabahn endoprosthesis (WL Gore & Associates, Inc. Flagstaff, AZ) to successfully manage the complication and complete the repair of the abdominal aortic aneurysm (**c**, image courtesy of David Kuwayama, MD)

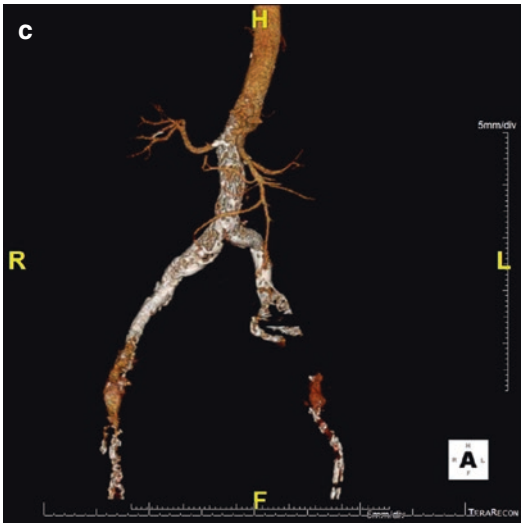

Fig. 17.3 (continued)

17.3 Post-procedure Complications

17.3.1 Infection

Infection at the access site following intervention usually involves skin flora, such as *Staphylococcus epidermidis* and *Staphylococcus aureus* [4]. A prospective series of 164 patients undergoing percutaneous femoral access noted only one infectious complication [18]. Use of percutaneous closure devices may increase this risk, with an infection rate of up to 9% in one series [19]. Treatment may require open exploration with debridement of all infected tissue as well as repair of the infected vessel. Insertion of devices such as stent grafts can also be complicated by infection. While systemic antibiotics can be used, ultimately explantation of the infected graft may be required. Fortunately, rates of stent graft infection are low; for example, the incidence of aortic endograft infection ranges from 0.3% to 4.8% with slightly higher rates reported for thoracic grafts, perhaps owing to the larger size [20].

17.3.2 Contrast-Induced Nephropathy

Administration of contrast media can result in contrast-induced nephropathy (CIN). It is generally defined as a rise in serum creatinine of 0.5 mg/dL or >25% of baseline within 48 h of contrast administration. The incidence is believed to be low overall, though rates have been reported ranging from 1% to 25% [21]. Predisposing factors include diabetes mellitus, renal insufficiency, critical illness, hypotension, and advanced age [21, 22]. Multiple pharmacologic measures to prevent CIN have been suggested, such as sodium bicarbonate, *N*-acetylcysteine, intravenous fluid,

dopamine, theophylline, vitamin C, vitamin E, and statins. Of these, the best supported interventions are volume expansion with normal saline or sodium bicarbonate [21]. Serum creatinine levels typically return to baseline within 1–3 weeks. However, CIN was associated with increased morbidity and need for renal replacement therapy among critically ill patients; thus, its impact can be quite significant [23].

17.3.3 Contrast Media Allergy

Allergic response to iodinated contrast media in patients can complicate the use of endovascular techniques. Contrast media reactions are defined as immediate (≤1 h after exposure) or nonimmediate (>1 h after exposure), and can include cutaneous, respiratory, and cardiovascular symptoms. Fortunately, true hypersensitivity reactions are rare and only 0.02–0.04% of all contrast media administrations result in major hypersensitivity reactions [24]. This has also improved with the introduction of iso-osmolar contrast media. Allergy skin testing to confirm hypersensitivity is variably useful, with most benefit in patients with severe immediate reactions. This suggests that IgE-mediated pathways are only partially responsible for contrast reactions and thus not a "true" allergy. Treatment of a patient having an acute allergic response is supportive care and treatment of the anaphylactic reaction. Premedication to minimize the response to contrast media can be performed, typically involving corticosteroid, and antihistamine medications. A review by Tramer et al. found that pre-medication reduced the incidence of respiratory symptoms in patients from 1.4% to 0.4% [25]. However, the best treatment is prevention; imaging modalities without contrast media when clinically equivalent can be utilized as well as alternative forms of contrasted imaging, such as carbon dioxide or gadolinium.

Conclusion

Endovascular and hybrid approaches have revolutionized the potential for vascular intervention through minimally invasive techniques. Unfortunately, this technology comes with its own set of complications. Thankfully, these remain relatively rare overall. As in many areas of surgery, the best treatment of a complication is prevention; thus, knowledge of the predisposing factors that increase such risks can minimize their occurrence overall.

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Endovascular Resuscitation and Trauma Management: Education and Simulation

18

Yosuke Matsumura, Mikkel Taudorf, Edmund Søvik, and Lars Lönn

18.1 The Necessity of Education and Simulation

Trauma surgery, according to the European Union of Medical Specialists (UEMS), covers all aspects of trauma, including musculoskeletal damage in prehospital management, emergency room (ER) responsibilities, intensive care management, and rehabilitation. Major trauma is the leading cause of death and disability in people under 40 years of age, due to traffic accidents and interpersonal violence [1]. However, with the aging population growing in many countries, older people are likely to make up a larger proportion of the trauma cohort in the future [2].

The goals of all team members in the ER are the same, but their skillsets differ. Activities in an acute setting may, for a person without professional or specialized knowledge in the field, give the impression of controlled chaos. There is no single, valid, routine procedure in trauma care and endovascular surgery, so education and

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training in the immediate environment constantly present a challenge. The principles of Advanced Trauma Life Support (ATLS) [3] are used in most facilities worldwide, and procedures such as EndoVascular resuscitation and Trauma Management (EVTM) need to find their place in current algorithms. The implementation of EVTM [4] is, therefore, a task that is currently subject to competition.

18.2 The Bridge and Synergies Between Open Surgery and the Endovascular Approach

The education of front-line practitioners is a challenge within EVTM. Virtual-reality simulation and porcine-, cadaver-, and cath-lab training outside the ER provide structured practical experiences of clinically crucial but uncommon procedures. In particular, an innovative approach with simulators represents a paradigm shift in the way to learn high-risk procedures. Note that the curriculum is crucial at all stages of the learning process. Metric-based simulation training outside the ER may supplant parts of the learning curve for endovascular procedures.

An endovascular procedure is an acutely time-sensitive intervention in a trauma context [5], one that is identical to damage control used in traditional surgery. The benefits of Resuscitative Endovascular Balloon Occlusion of the Aorta (REBOA) [6], or of a hybrid approach, are well-established, but the educational and logistic aspects are not. At tertiary centers there are multiple specialties: trauma and vascular/endovascular surgery, emergency medicine (EM), interventional radiology (IR), and critical care. In some regions, there is currently a shortage of endovascular physicians involved in trauma. Additionally, there are differing opinions regarding appropriate qualifications and board certification in the endovascular field.

18.3 EVTM Practitioners: Who Are the Educational Targets?

The structure of trauma care differs between regions and countries. The operator involved in elective endovascular cases on a regular basis is the expert with regard to skills and knowledge in an endovascular context. A life-threatening trauma situation often involves hemodynamic instability, coagulopathy, a combination of procedures or a change to surgery, time-sensitive procedures, and permissive nonselective embolization. However, hospital structures and logistics may not allow endovascular experts to be involved in acute emergent situations [5].

Trauma surgeons or emergency physicians have overall responsibility for trauma patients, and are involved in initial resuscitation as well as in setting and implementing emergency strategies. Based on hospital logistics and familiarity with endovascular procedures, these "first responders" can be good candidates for the practice of EVTM. First responders may initiate endovascular procedures immediately, provided they have endovascular experience. A curriculum with a strict structure is essential when EVTM procedures are being trained away from the job. The curricular idea of mastery through learning/proficiency-based progression training (PBP)

involves acquisition of the essential knowledge and skills needed to meet predetermined achievement standards. In a simulated setting, workshops should have a defined standard level to be reached in the education, training, and credentialing of endovascular operators. This should be implemented into the educational curricula for trauma. A PBP training curriculum and protocol, with the use of a simulator and previously validated metrics, has been shown to produce skills superior to those generated using traditional simulation-enhanced methods [7].

18.4 Nontechnical Skills in EVTM Education

Top-class trauma care requires the careful planning and management of resources. In an actively bleeding patient, the time taken to stop the hemorrhage affects the outcome. Therefore, halting an ongoing endovascular procedure and switching to open surgery is a delicate matter.

There are several alternative ways of implementing the EVTM concept globally. For IR physicians or endovascular surgeons to cover emergency cases 24/7, continuously and with seamless collaboration, require close multidisciplinary reliability. Teaching basic endovascular tasks for the achievement of time-sensitive responses for hemodynamically unstable patients is one option. The first responder, if proficient in endovascular procedures, will initiate the endovascular task promptly and, at the same time, request the presence of an IR physician.

18.5 Technical Skills in EVTM: Achievable Goals of EVTM Education and Simulation

First, traditional surgical skills require the use of the senses to be able to see, touch, and smell as maneuvers are adopted. However, endovascular intervention robs the surgeon of the ability to see in three dimensions and make use of direct tactile feedback, known as haptics. Two-dimensional fluoroscopy replaces sensing of the open wound, and interventional haptic feedback is miniscule by comparison. Thus, interventional psychomotor skills cannot be regarded as interchangeable with open surgical skills or laparoscopic ones.

Second, procedural skills (Table 18.1) represent the ability to closely follow a given protocol. In essence, the protocol gives the ordered steps needed to perform REBOA. Table 18.2 gives an example of a step-by-step procedure. In most in-hospital cases, REBOA will be performed using both an ultrasound-guided puncture and fluoroscopy to visualize the position of the balloon. However, there are situations, either in a pre-hospital setting or even in an in-hospital location without fluoroscopy, where REBOA will be performed without fluoroscopy [8–10]. It is essential to know how far the balloon can be inserted into the arterial system; it is also important to use a balloon with a low risk of rupturing the aorta, by using either a non-compliant balloon with a limited diameter or a very compliant soft balloon. Due to the nature of interventional techniques, the methodical introduction of

Table 18.1 Essential techniques and knowledge requirements in EVTM education

Essential techniques and knowledge requirements in EVTM education
Ultrasound guided femoral arterial access US image, puncture, guidewire, dilator, sheath placement
The vascular anatomy of femoral artery and aorta The bifurcation of common femoral artery (CFA), possible malposition into small branches
The confirmation of the guidewire in the aorta US, X-ray, fluoroscopy
Realizing the difficulty in the elderly tortuous aorta Tortuosity, stenosis, calcification
The balloon position in REBOA The risk of ischemia in Zone 1 and potential benefit of partial occlusion
Utilization of computed tomography (CT) image Avoid any unnecessary injection to reduce the procedure time
Appropriate choice of embolic agent and embolic range Consider hemodynamic instability and coagulopathy

Table 18.2 Suggested step-by-step procedure for REBOA

1.	Select appropriate side of puncture (right/left groin)
2.	Prepare for aseptic puncture. Apply sterile drape
3.	Insert local anesthetics if there is time
4.	Insert the introducer needle in the common femoral artery (preferably ultrasound guided, depending on operator experience and patient pulse) using the Seldinger technique
5.	Aspirate and make sure you are in the arterial vessel lumen
6.	Insert guidewire. J-tip first, to Aortic Zone 1. If fluoroscopy is not available, insert wire approximately 60 cm. If you feel resistance, stop and re-evaluate. To confirm the guidewire in the aorta with US or X-ray is highly recommended even without fluoroscopy
7.	Remove introducer needle
8.	Insert introducer sheath fully. If you feel resistance, stop and re-evaluate. Make sure that aspiration of blood is possible. If easy aspiration of blood is impossible, stop procedure. Do not insert the balloon. When you have decided not to use REBOA, but require the femoral arterial access, you may choose a smaller (4 or 5Fr) arterial sheath as a first access instead of a REBOA sheath (7–12 Fr)
9.	Insert the balloon catheter over the guidewire. If fluoroscopy is not available, insert the balloon catheter 30–35 cm for Zone III occlusion or 55 cm for Zone 1 occlusion
10.	Inflate sterile physiological saline or contrast according to the balloon specifications. If contrast is used, high viscosity will increase inflation pressure and inflation/deflation time
11.	Blood pressure shall increase rapidly after balloon inflation
12.	To avoid migration of the balloon, make sure the balloon catheter is fastened and secured in place, either by holding manually or by the use of suture or another fixation device
13.	Lack of blood pressure response may indicate misplaced balloon (wrong vessel or below bleeding focus), malfunctioning balloon or insufficient balloon diameter
14.	Balloon inflation time must follow good clinical practice. It is recommended to deflate the balloon slowly for approximately 1 minute every 5–10 minutes, with great caution in case of a rapid fall in blood pressure
15.	Before final deflation and removal of the balloon, the source of the bleeding must be under control and taken care of. Deflate the balloon completely by aspirating all fluid, and pull catheter and wire gently out of the introducer. If resistance is felt, try rotating slowly while pulling gently on the catheter
16.	Remove the introducer. Maintain adequate hemostasis either by manual compression or choice of vascular closure device
17.	Always check distal arterial status with Doppler or ultrasound. If not available check peripheral arterial pulse

equipment according to protocol is essential to successful intervention. Failure to follow protocol may result in minutes of preparatory work becoming meaningless if the necessary instruments cannot be handled properly, and may even give rise to the procedure being abandoned. Literally speaking, there is no room for error.

The team should train and become familiar with a standardized REBOA kit. A standardized set of tools must, as a minimum, contain a puncture needle, a guide wire, an arterial introducer, and the balloon actually needed for the procedure, as well as the sterile draping, swabs, syringes, and equipment needed to secure the balloon and prevent it from moving. These items can make up a menu with different suppliers, but there are also complete menu kits available on the market. REBOA is a procedure performed in a very stressful situation, and the time spent finding necessary and compatible equipment should be kept to a minimum [11, 12].

Third, cognitive behavior denotes how people react, based on their inherent body of knowledge, when they encounter the unexpected. Simply stated, cognitive skills come into play when surgical difficulties or complications present themselves.

Therefore, it is obvious that a workshop alone will not transform students into proficient operators or experts. Educational courses or workshops, however, give both faculties and students the opportunity to share knowledge, experience, and skills.

18.6 What Resources Can We Use for Away-from-the-Job Simulation in EVTM Education?

18.6.1 Simulators

A medical simulator should be a common and basic training resource in all healthcare education. The benefit, among others, is the possibility to repeat exercises with opportunity for discussion. As part of a curriculum, exposure to a variety of simulation-based scenarios is a useful part of REBOA training. Simulators should be included in the building of a curriculum as a natural part of a quest for excellence. Currently, Mentice and Simbionix offer REBOA software programs and also provide vital signs response in terms of heart rate and blood pressure. Additionally, both simulators have a function for training embolization procedures, including material such as coils, plugs, gelatin sponge, and particles.

Access to the common femoral artery is the first challenging step in the REBOA procedure, especially if the groin is pulseless. Ultrasound-guided access simulators are available to train the vascular access. Examples of simulators are given in Figs. 18.1, 18.2, 18.3, and 18.4.

18.6.2 Porcine Models

Endovascular research and training courses using anesthetized animals are available in both military and civil settings. The adult swine vascular tree approximates human vessels despite anatomical incongruence and there is a lack of human

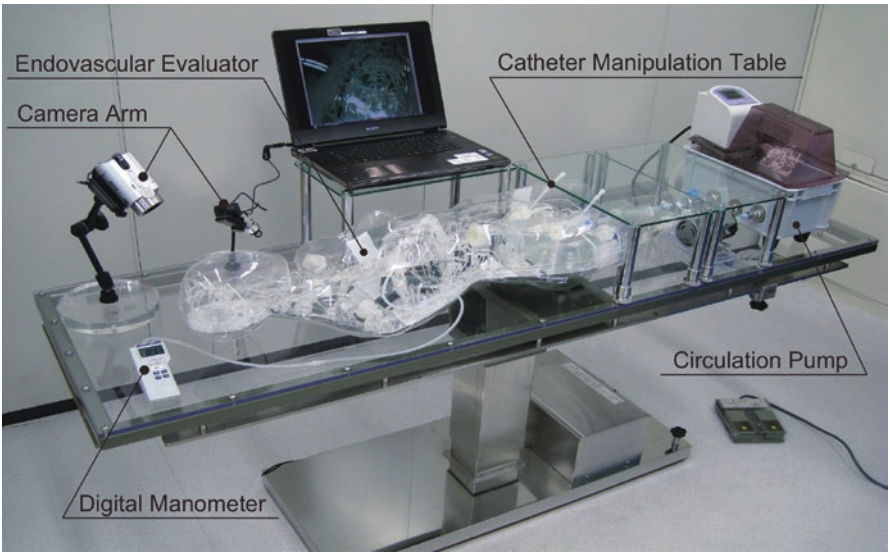

Fig. 18.1 Endo Vascular Evaluator (EVE, FAIN-Biomedical Inc. Aichi, Japan). The endovascular surgery simulator EVE precisely reconstructs human vascular lumen. The circulatory system may be adjusted with the fluid control unit. Simulation quality may be enhanced by using EVE inside a fluoroscope, providing compatibility with a wide range of X-ray imaging techniques. (Photo: Courtesy of FAIN-Biomedical Inc. http://fain-biomedical.com/. http://www.brbiomedicals.com/endo_vascular_evaluator.html)

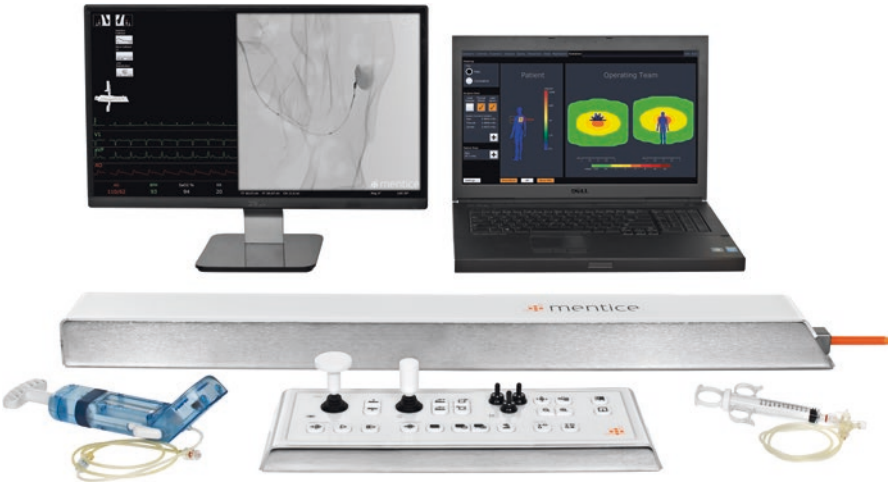

Fig. 18.2 The Mentice VIST® G5 Simulator (Mentice, Gothenburg, Sweden). The modules include a wide variety of training scenarios to challenge the learner's technical skills, clinical decision-making abilities, and procedural proficiency. Flexible and intuitive to set up and use. Small footprint, robust, and lightweight. (Photo: Courtesy of Mentice AB. http://www.mentice.com/vist-g5)

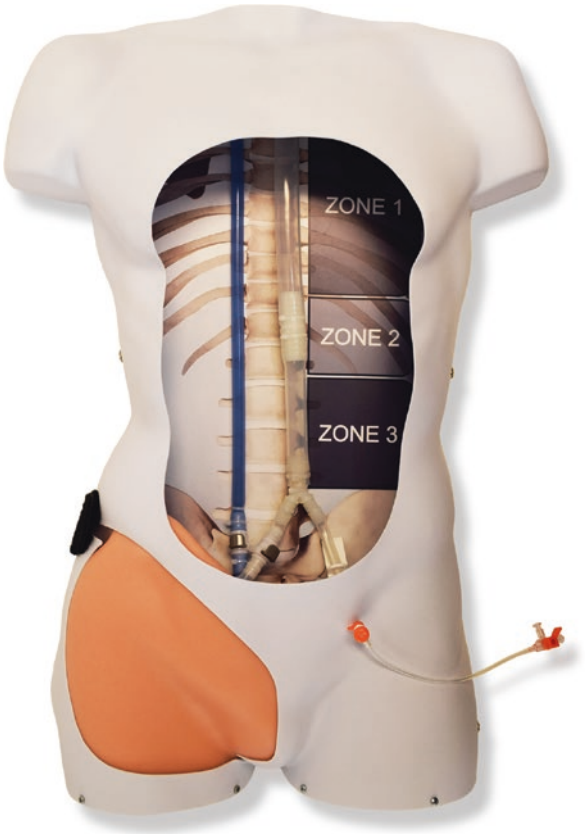

Fig. 18.3 REBOA Access Task Trainer (RATT) Pulsatile Simulator (Prytime Medical Devices, Inc., TX, USA). Simulated tissue access patch, replaceable arteries facilitate multiple trainings. Contains artery, vein and bony landmarks. Ultrasound compatible. Reusable and replaceable. (Photo: Courtesy of Prytime Medical Devices, Inc., The REBOA Company™. http://prytimemedical.com/wp-content/uploads/2017/08/RATT-Brochure-Digital-1.pdf)

pathology. The benefit of animal models lies in their physiology, with a "wet-lab" that contrasts with "dry-lab" simulators. Having a live-animal vascular-injury response attracts students and has educational merits. Endovascular damage control can be combined with open surgery. The ethical drawback of using animals for training is obvious. The 3R's principle must always be observed when using animals in education [13, 14]. The use of a porcine laboratory to train endovascular surgical skills, given its undocumented efficacy in improving endovascular skills and its higher financial cost, is an ethical and financial concern given that virtual-reality simulators are available.

18.6.3 Cadaver

The anatomy and diversity of individuals are used didactically in cadaver workshops. Vessel calcification, stenosis, tortuosity of the arteries, and other challenges can be addressed in order for students to become proficient operators.

Fig. 18.4 ANGIO Mentor from 3D Systems (Simbionix 3D Systems, Airport City, Israel). Hands-on practice of endovascular procedures performed under fluoroscopy in the cath lab, interventional suite, or an OR, in an extensive and complete virtual reality simulated environment. (Photo: Courtesy of Simbionix 3D Systems. https://www.3dsystems.com/medical-simulators/simbionix-angio-mentor)

A central pressurized cadaver model for REBOA simulation [15] was originally reported being used in the Basic Endovascular Skills for Trauma (BEST) course in Maryland [11]. REBOA sessions in Advanced Surgical Skills for Exposure in Trauma (ASSET) courses [16] use pressurized cadaver models that give the experience of "wet-lab" changes in proximal blood pressure during aortic occlusions. The catheterization of the artery is also reported being performed in cadavers [17]. Although the compliance in use of cadavers differs in each institute or region, a cadaver lab can be utilized in surgical and endovascular education [18].

18.6.4 Cath-Lab Training

All endovascular specialists are familiar with the Seldinger technique for gaining access to the common femoral artery. Collaboration is key to transferring hands-on knowledge to other clinical specialists. With basic training on simulators, physicians not familiar with the Seldinger technique will become better prepared to engage in basic endovascular activities.

18.7 Summary

There are several endovascular initiatives and workshops around the world: Diagnostic and Interventional Radiology in Emergency, Critical Care, and Trauma (DIRECT, Japan 2011, see [12]); Basic Endovascular Skills for Trauma (BEST, USA, 2013, see [11]); Endovascular Skills for Trauma & Resuscitative Surgery (ESTARS, USA, 2014, see [19]); EndoVascular resuscitation and Trauma Management (EVTM, Sweden, 2015); Prehospital and Emergency Department Endovascular Resuscitation (PEER, UK, 2016); and more.

The necessity of providing simulation education in trauma is widely recognized. The training also bridges the gap between different specialists working in a trauma context. Simulators, porcine and cadaver work, and cath-lab training are important elements in technical, cognitive, and communication-skills education. Proficiency-based progression training (PBP) to acquire essential knowledge and skills up to predetermined achievement standards is fundamental in this context. Sharing the simulation experience will accelerate improvement in EVTM approaches and practices [7].

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