Extrapolation of Battlefield Resuscitative Care to the Civilian Setting

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Experiences in treating wartime casualties in Iraq and Afghanistan have already led to changes in civilian trauma care practices. While advances in the care of civilian musculoskeletal injuries are likely as a result of ongoing military basic and clinical research, major advances in resuscitative care have already been realized. Early liberal use of tourniquets to control bleeding from combat-associated extremity trauma has led to decreased mortality. Military experience has demonstrated that use of temporary intravascular shunts is effective for mitigating ischemic injury from vascular trauma until definitive repair can be accomplished. Hemostatic dressings have improved the surgeon’s hemorrhage control armamentarium. Clinical experience with hypotensive resuscitation has led to refinement and improvement in the technique. Use of recombinant factor VIIa has improved hemorrhage control in the context of brain injury and coagulopathy and increasing the ratio of plasma to red cells during early shock resuscitation has improved survival. (Journal of Surgical Orthopaedic Advances 19(1):62–69, 2010)

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Many concepts in orthopaedic trauma are developed in the civilian sector before further evolving in a combat environment. With lessons learned from military use, these concepts are reintroduced to the civilian medical community, having been subjected to vigorous frontline testing, often in extreme situations well beyond the scope of the community provider. Out of necessity, US combat operations in Iraq and Afghanistan have furthered the advancement of a number of orthopaedic trauma techniques and devices. With the modern protective equipment worn by the 21st century American soldier, along with advances in vehicle armor, soldiers may be able to survive significant injuries, with a resultant increase in high-energy extremity wounds requiring aggressive measures to maximize survival and limb salvage. Some of the tools in the armamentarium of the military orthopaedic trauma surgeon can be parlayed back into the context of civilian orthopaedic care. While many advances in fracture treatment, wound management, and tissue engineering are likely to become clear as time progresses and research currently underway is completed, many important advances in patient resuscitation, hemorrhage control, and treatment of the dysvascular limb have already become apparent. These include the use of tourniquets, temporary vascular shunts, hemostatic dressings, and novel resuscitative techniques.

**Tourniquets**

Clearly one of the most efficacious changes in the treatment of battlefield injury associated with extremity wound hemorrhage has been the early and liberal use of tourniquets to achieve immediate hemostasis. The data demonstrating the efficacy of early tourniquet application have been so compelling that adoption of similar algorithms for trauma care in the civilian setting seems warranted (1).

A large portion of both civilian and military acute trauma mortality results from uncontrolled hemorrhage (2, 3). Although it is likely that a large percentage of those deaths that result from hemorrhage are associated with acute truncal injury, studies have estimated that as many as 9% of preventable deaths may have been related to bleeding from extremity wounds during the Vietnam conflict (4). Autopsy results from the current conflict confirmed that extremity hemorrhage continues to represent an important cause of preventable death (5).
Reports from previous conflicts had indicated that properly applied tourniquets can be lifesaving and that their use is associated with low morbidity (6, 7). As a result, teaching combat medics to achieve prehospital extremity hemorrhage control became a major priority for leaders in military medicine, and in approximately 2004, standard-ized tourniquets were deployed to US combat personnel throughout Iraq and Afghanistan (8). In 2005, effectiveness of self-applied tourniquets in volunteers was demonstrated and subsequently policies were developed and enforced that provided appropriate equipment and training to facilitate tourniquet self-application for US combat personnel (9).

Since that time, several studies have reported the results of early tourniquet use in a combat environment (1, 8, 10). The results of these studies have been consistent. First, early self-application of tourniquets by nonmedical personnel in a combat environment is feasible and efficacious. Second, it is apparent that in the context of extremity hemorrhage second to battlefield injury, early tourniquet application can be lifesaving. Third, in the context of hemorrhage from extremity injury, prehospital tourniquet application is more efficacious than emergency department application, and application before onset of shock is more efficacious than application after onset of shock. All of these findings seem to make sense. If someone is bleeding to death from a wound on an extremity, applying a tourniquet in a fashion that causes the bleeding to stop is a good idea and, the earlier that can be accomplished, the better.

A major concern expressed in association with discussions about liberal prehospital use of tourniquets is that complications of their use will exceed their potential benefit. In the context of bleeding that could have been potentially controlled with less aggressive means, such as direct pressure, tourniquet application has the possibility of leading to nerve damage, muscle damage, and increased bleeding associated with incorrect application. To better understand the risk–benefit ratio associated with tourniquet application, several studies have examined complication rates associated with tourniquet application. Rates of nerve palsy at the level of the tourniquet in each study have been low (<2%), with most such injuries being transient. Tourniquet application has been associated with increased survival, indicating that incorrect application is not likely widespread. Data suggest that muscle injury can be mitigated by the shock control that tourniquet application achieves rather than exacerbated by creation of a locally ischemic environment.

**Temporary Vascular Shunts**

Temporary vascular shunts are a means of immediately bypassing segmental vascular injuries not amenable to immediate repair. A shunt is a man-made conduit that can be interposed between the two ends of the severed vessels. Devices exist that are specifically designed for this purpose, but if needed, any sterile tubular structure can be used, including pediatric feeding tubes, intravenous tubing, and Foley catheters.

The first description of the use of vascular shunts appears to be by Sir George Henry Makins in 1919 (11). Describing his experiences with World War I vascular injuries, he included accounts of using paraffin-coated silver tubes that were used to bridge segments of arterial deficiencies. These tubes were allowed to slowly thrombose over approximately 4 days. They were then removed and the vessels were ligated. Limb salvage was possible in a small number of soldiers, ostensibly due to the ability of the limb to gradually accommodate to the decreasing blood flow. Obviously, it is difficult to assess whether or not these shunts had any impact on this patient population.

More than 50 years later, Eger et al. published their experience with temporary intravascular shunts (TIVS) using a simple polyethylene tube to bridge arterial injuries during the Israel–Egypt border war (12). They reported an 8% amputation rate, including only one out of eight popliteal artery injuries. Their indications for TIVS included multiple severe injuries to an artery, multiple arterial injuries, and replantation of severed limbs. These indications are still appropriate today (13).

There are several uses for TIVS in the hands of the orthopaedic surgeon. The first is in the setting of the rural or austere environment. Placement of TIVS is a simple procedure in the hands of a trained extremity surgeon, much more so than vein grafting or other similar procedures. In a rural hospital, without a vascular surgeon or a surgeon trained in revascularization techniques, a shunt can be placed expeditiously prior to transport to a higher level of care. This allows reperfusion of the extremity until definitive treatment can be performed. There are numerous reports of this from the ongoing combat operations in Iraq and Afghanistan. Taller et al. reported on the placement of 23 vascular shunts over a span of about 6 months at a small Echelon II surgical unit in Iraq (14). Likewise, Chambers et al. presented their results on the use of 27 vascular shunts used over 6 months at another mobile forward surgical hospital (15). Rasmussen et al. presented their results on the use of 27 vascular shunts used over 6 months at another mobile forward surgical hospital (15).

Another use for TIVS is in the setting of damage control. In the polytrauma patient with critical physiology, a complex vascular reconstruction may be poorly tolerated...
and ill-advise. Just as the concept of damage control applies to immobilization of fractures via external fixation, skeletal traction, and splinting, so too does it apply to reconstruction of irreparable vascular injuries, specifically by intravascular shunting, with definitive reconstruction performed during a separate trip to the operating room. In a review of their 10-year experience with TIVS, Subramanian et al. found that damage control was the most common indication for this procedure, with an incidence of 44% (13). In this patient population with peripheral vascular injuries requiring TIVS, no patients required amputation provided there were no associated fractures. However, the presence of a Gustillo IIIC fracture in the damage control group led to a 38% amputation rate, despite having better base deficits and lower Injury Severity Score (ISS) \( p = .02 \). This is likely in part due to a 62% prevalence of popliteal vessel injuries requiring TIVS in the Gustillo IIIC fracture group compared to 8% in the nonfracture group \( p = .006 \).

TIVS can also be used to temporarily address vascular injuries while addressing concomitant osseous or soft tissue injuries, with definitive reconstruction performed at the end of the same operative procedure. This allows rapid reperfusion of the extremity, which allows better assessment of tissue viability during debridement and can allow the orthopaedic surgeon the time to properly address other injuries without sacrificing technique to minimize warm ischemia time. Conversely, the definitive vascular repair need not be rushed in order to allow orthopaedic intervention to rapidly ensue, thus decreasing the risk of failure due to a suboptimal repair. TIVS can even be used to reperfuse a limb after a critically long period of ischemia while the graft is harvested and prepped for reconstruction. Finally, TIVS allow the time to seek intraoperative consultation from other orthopaedic or plastic surgeons regarding the advisability of limb salvage, possibly decreasing the need for secondary amputations at a later date (13). There is literature supporting immediate vascular repair without TIVS prior to orthopaedic intervention, with the suggestion that a good vascular repair can endure the stress of orthopaedic manipulation (17). However, not all orthopaedic manipulations are the same, and the final limb length may be in question prior to fixation, as in the settings of fracture shortening or segmental bone loss. Primary skeletal stabilization thus may make subsequent vascular reconstruction simpler with more predictable results (18, 19).

In order to maximize potential for success with TIVS, some technical points should be observed. Resuscitation should be initiated prior to placing the shunt. Peripheral vascular resistance increases with hypovolemia, which decreases flow through the shunt. There is some evidence from animal studies that profound hypotension may lead to increased shunt thrombosis (20). Basic concepts of vascular control and repair apply: The vessel ends should be well visualized to minimize intimal injury with shunt placement and thrombectomy performed with a Fogarty or similar catheter. Local flushing with heparin is frequently performed, using from 5 to 100 U/mL. The shunt should be as large a caliber as possible and limited in its intraluminal length to prevent inadvertent entry into a side vessel or close apposition to a vessel wall, both of which may increase the chance of thrombosis (15, 20). If possible, an associated vein injury should be repaired or shunted as well. Clamping or ligation of a major vein, in the setting of restored arterial flow, has been suggested as a risk factor for tissue ischemia and bleeding (16) as well as compartment syndrome (18).

Upon insertion of the shunt, the overlying vessel ends must be secured to the conduit. In-line shunts require the use of heavy silk ties or rubber vessel loops, while many looped shunts either have built-in occlusion devices or require special vascular tourniquets. Once secured, it is imperative that the limb be immobilized with as little bend in the shunt as possible. While shunts have proven themselves to be well functioning after patient transport and even prolonged delay before reconstruction, shunt thrombosis has been attributed to repositioning of the limb after the procedure. Fasciotomy should be performed in virtually all patients after revascularization, especially with injuries involving both artery and vein or with prolonged ischemia. There does not appear to be a need for systemic anticoagulation with TIVS, even when using nonheparinized conduits (21).

The outcomes with TIVS have been very good, particularly with shunting of proximal vessels. Subramanian et al. published their results with TIVS over a 10-year span. Sixty-six patients were treated with a total of 99 shunts. Seventy percent were placed in arteries and the rest in veins. Sixty patients had vascular injuries to the extremities, necessitating 93 shunts. Approximately half the patients left the operating room with at least one shunt in place, with an average shunt “dwell” time of 23.5 hours prior to reconstruction. Only one thrombosis occurred in the extremities and no thrombosis occurred in any shunt placed in a proximal vessel, despite the absence of anticoagulation. There were 10 secondary amputations, nine of which were performed in patients with associated fractures. One amputation was due to a thrombosed shunt, with five others due to complications with the final vessel reconstruction. The overall limb salvage rate was 74% (13).

Rasmussen et al. presented 12 months of experience with TIVS at an Echelon III facility in Iraq. Thirty temporary shunts were placed, including 22 that were proximal to the antecubital or popliteal fossa, and eight that were in the tibial arteries or antebrachium. The proximal shunts had an 86% patency rate with an average.
An ideal hemostatic dressing has several qualities (25, 26). It should be able to rapidly stop severe arterial and venous bleeding, even when applied to actively bleeding vessels or in a pool of blood, and should do so without adverse side effects. It should be easily stored and ready to use at room temperature without premixing. Minimal to no training should be needed, and it should be easily administered by a first responder or by the patient. Finally, it should be relatively inexpensive.

QuikClot (Z-Medica, Wallingford, CT) is a commercially produced mineral zeolite hemostatic dressing that works by acting like a “molecular sieve” and preferentially adsorbing water, thus concentrating platelets and clotting factors and thus promoting rapid clot formation while creating an exothermic reaction (27). It is packaged as a powder, which allows it to conform to the surface of complex wounds, but also makes it more easily displaced in wounds with brisk arterial bleeding. There is a bagged form of this dressing called QuikClot ACS (Advanced Clotting Sponge). The zeolite is identical in chemical nature, but formed into round beads instead of in its granular form and is packaged in mesh bags. This form of application may keep the zeolite granules from dispersing in the face of high-pressure bleeding (28). QuikClot costs approximately $10 per packet and has been associated with significant elevation of local tissue temperatures during the course of the exothermic reaction.

Some hemostatic dressings are derived from naturally occurring polysaccharides. Poly-N-acetyl glucosamine (P-NAG) is a compound derived from algae. When deacetylated more than 70%, it is termed “chitosan” (27, 29). HemCon (HemCon, Tigard, OR) and CELOX (SAM Medical Products, Newport, OR) are chitosan dressings designed to control hemorrhage. The former is a stiff wafer that appears to work via mucoadhesion with sealing of the bleeding vessels. The latter is a finely granulated agent that creates hemostasis by interacting with local erythrocytes and platelets to facilitate cross-linked clot formation (30). Given the relatively inflexible nature of HemCon, it can be difficult to get it to conform to deep and irregular wounds (29), but it has performed well in combat operations (25). CELOX may have similar hemostatic performance to HemCon but, given its granular structure, may perform better in narrow, deep, or irregular wounds (32). HemCon costs approximately approximately $100 a dressing while CELOX costs approximately $25 for a 35-g packet. Both products are FDA approved.

Rapid Deployment Hemostat (RDH; Marine Polymer Technologies, Danvers, MA) is a chitin-based dressing that appears to work via activation of platelets, causing release of vasoconstriction mediators, as well as triggering and enhancing the intrinsic coagulation cascade. The hemostatic mechanism of RDH is related to its tight crystalline structure, in contradistinction to chitosan products, which are less organized and less biologically active (31). This product has undergone several permutations, to include addition of a surgical gauze backing and an increase of the active ingredient, fully acetylated poly-N-acetyl glucosamine from 5 mg/cm² to 16 mg/cm² via lyophilization (32). The approximate cost of the newest version of this dressing, modified RDH (MRDH or RDH-3), is $300 per dressing (26).

The dry fibrin sealant dressing (DFSD; American Red Cross Laboratory, Rockville, MD) is designed to deliver the coagulation-promoting properties of fibrinogen and...
thrombin without the difficulties of applying a liquid compound into an actively bleeding wound or having to mix the components prior to administration (33). The dressing is absorbable, stable at room temperature, and immediately available for use. However, there are some concerns regarding relative fragility of the device, and its cost of $500 to $1000 per dressing, which is considerably more than other hemostatic options (26).

All of these dressings have been tested in large animal models, although the methodology of these studies have been variable, with models being applicable to either arterial or venous bleeding, or a combination of the two. Arterial bleeding is usually modeled with swine aortotomy or femoral arteriotomy (26). Arteriotomy, rather than frank arterial transection, allows for continued high-flow bleeding without the hemostatic effect of arterial retraction. In this type of high-flow model, QuikClot was found to be ineffective in controlling hemorrhage and did not yield survival times longer than with the use of a standard gauze bandage. This was due to the rapid dispersion of the granular zeolite away from the source of bleeding, with resultant inability to form a clot (25). QuikClot ACS may prove more effective in this scenario, given its larger bead size and mesh bag (28). HemeCon has shown promise in the setting of high-flow bleeding, significantly increasing hemostasis from 0% to 70%, albeit for less than 2 hours, compared to a standard gauze dressing in an aortotomy model (34). The DFSD was very effective in this same study, conferring 100% hemostasis lasting 4 days in five of the six subjects. The RDH-3 dressing was shown to decrease the number of 1-minute compressions necessary to induce hemostasis in a swine model involving a 1-cm longitudinal incision in the aorta (35).

Mixed arterial and venous injury models may represent the most realistic model of vascular injury (36). QuikClot has been shown efficacious in a complex mixed-vascular groin injury model, with a reduction of 3-hour mortality rate from 100% to 0% compared to no treatment ($p = .02$) and a trend toward improvement over the 57.4% mortality rate achieved with a standard gauze dressing ($p = .07$) (37). In the same study, the HemCon dressings were very inconsistent in performance. The dressings produced “superb hemorrhage control” in five of seven swine, with all five animals surviving the trial. The other two swine experienced rapid failure of the dressing with poor adherence and subsequent death of the animals. The authors believed the mixed results to be due to manufacturing variability.

CELOX was compared to HemCon and QuikClot in another mixed-vessel swine groin injury model. The three agents all showed improvement of survival compared to a standard compression dressing, with only CELOX being statistically better than the standard dressing with a survival rate of 100% compared to 50% ($p = .018$). QuikClot subject survival trended toward significance with 11 out of 12 or 92% surviving ($p = .072$). Adherence to the vessels appeared to be the determinant of success with these dressings. The CELOX dressing had a 0% rebleed rate. The HemCon wafer was found to work well if it remained adherent. Once dislodged, death ensued rapidly. The single death in the QuikClot group occurred when the dressing migrated into a soft tissue void next to the injured vessels (30). There have been no animal studies of RDH-3 in mixed-vessel injuries, but a prior version of this dressing, RDH-2, was shown to be ineffective in lowering the mortality rate or blood loss in a complex groin injury swine model (37). The DFSD was used in a high-energy proximal femoral ballistic injury goat model and significantly reduced blood loss while increasing mean arterial pressure despite lack of resuscitation (36).

Combat experience with these dressings has yielded positive results. A series of 103 uses of QuikClot, 69 of which were performed by military surgeons in Iraq, yielded a 92% efficacy rate, with eight cases failing in massively injured coagulopathic patients (38). Since QuikClot works by concentrating coagulation factors, the authors were not surprised to see a decrease in performance in these patients. Of note, there was only one serious complication in this series. A patient developed scar formation around the ureter, causing ureteral obstruction 2 months after application of QuikClot around a gunshot in the iliac vein. This paucity of thermal injuries raises questions about the actual risks of exothermic damage in the clinical use of this product. Another series reviewed 64 uses of HemCon during combat operations in Iraq and Afghanistan (24). The bandage was successful in 62 cases (97%), with two failures involving blind placement into large cavitation wounds.

It is difficult to determine which dressing is the best for hemorrhage uncontrolled by standard pressure dressings. The DFSD is efficacious in all relevant models of bleeding, but it is not FDA approved and is very expensive. QuikClot has been shown to perform well in mixed-vessel and severe vessel bleeding, but its granular nature prohibits its use in brisk arterial bleeding. Newer forms of the dressing, including QuickClot ACS, may be better suited for these high-flow environments. Attempts have been made to alter the chemical composition of the zeolite in order to decrease its exothermic properties (28), with some decrease in efficacy, but clinical experience suggests that the risk of serious injury from thermal injury remains mostly theoretical. HemCon performs very well in severe venous injuries, with some efficacy in mixed-vessel and arterial injuries. The main drawback of this dressing is its stiff composition, making it difficult to use in narrow or irregular wounds. There is evidence that CELOX may combine the function of a chitosan dressing with the form
of a granular dressing, making it more easily applied, although it is possible that it would be less suited for arterial injuries, for the same reason as the granular form of QuikClot. CELOX, however, has not been studied as extensively as HemeCon, because it is a relatively new product in comparison. Based on existing literature, RDH-3 has not yet been demonstrated to be an effective treatment for uncontrolled traumatic hemorrhage.

Regardless of the type of dressing chosen, similar guidelines do exist. Other, more conventional attempts at hemostasis, including the use of a conventional pressure dressing and tourniquet if possible, should be made prior to using a hemostatic dressing. Vigorous resuscitation should be ongoing while awaiting hemostasis, because hypovolemia compounds the effects of the hemorrhage and may prevent the dressing from working as effectively. It is imperative that these dressings are applied as directly to the source of bleeding as possible, and the application of prolonged pressure to the dressings is also necessary to ensure proper positioning and to facilitate their function. Finally, efforts must be made to limit motion at the wound, as this may dislodge the dressing and lead to rapid exsanguination and death.

**Novel Resuscitative Techniques**

**Fluid Resuscitation Strategy**

A concept that was already appreciated at the start of the war — and quickly reinforced — was the importance of deliberate hypotension in early resuscitation, while the patient is still actively bleeding. Increases in blood pressure lead to increased hemorrhage from open vessels and rebleeding from those that have transiently clotted. This leads to a vicious cycle of hypotension–fluid–increased bleeding–more hypotension that increases mortality. An important (and oft-forgotten) lesson of prior wars was the limitation of fluid therapy early in the course of care, until the time of definitive surgical control of active bleeding. Physicians in the present conflict were more likely to recognize this theory at the start of the war because of a large amount of animal research into uncontrolled hemorrhage in the 1980s and 1990s (39) and the results of two human trials in civilian trauma patients (40, 41). Management of a patient with deliberate hypotension still requires coordination in the early going and improves with practical experience. Further, as the war has progressed, the emphasis in both military practice and large civilian centers has shifted from hypotension through fluid restriction to hypotension through anesthesia, with appropriate fluid loading. This concept has not been tested scientifically but makes intuitive sense (vasodilatation seeming preferable to vasoconstriction in the shocked patient) and is a common practice among experienced providers (42).

**Factor VIIa**

One significant impediment to good resuscitation early in the war was the lack of clotting factors in military hospitals. Plasma and platelets require complex logistical efforts to get to the bedside, more so than packed red blood cells, and were often in short supply. This led to a number of casualties suffering from — and dying of — the coagulopathy of trauma, despite anatomically amenable injuries. Recombinant human clotting factor VIIa (FVIIa) became available in civilian trauma practice just prior to the war, and use in military hospitals helped drive initial enthusiasm for it as a “universal hemostatic.” Hundreds of casualties received FVIIa during the first years of the war for management of coagulopathy, and doubtless a large number benefited. Not surprisingly with a new therapy, however, there was a backlash when complications were observed. While the actual rate of adverse thromboembolic events is relatively low (43) and hard to discern from the background incidence in severely injured patients (44), a few widely publicized thrombotic events led to diminished use of FVIIa in recent years, down to a relatively low steady state today. The need for FVIIa was also diminished by improved resuscitation techniques and the greater availability of plasma and platelets. At present FVIIa is recognized as an available tool in the armamentarium, one which may have a favorable risk–benefit ratio in some patients in hemorrhagic shock and in some brain-injured patients with coagulopathy and the need for an urgent procedure (45).

**Early Support of Coagulation**

One of the most important lessons learned from the present war is the importance of early support of the coagulation system. Although hinted at by the experience of major trauma centers in the 1990s (46), the initial evidence supporting a higher ratio of plasma to red cells during early resuscitation came directly from the US Army in Baghdad (47). In the rapidly bleeding, hemodynamically unstable patient, retrospective evidence showed that a ratio of red blood cells to plasma to platelets of 1:1:1 was associated with the greatest survival. This initial military report has subsequently been confirmed by both single-center and multicenter civilian studies, and a prospective civilian trial of this therapy is now underway. Army-wide adaptation of a 1:1:1 resuscitation policy occurred in the summer of 2007 and has since been associated with improved outcomes in a number of further papers. This approach
is now the central piece of “damage control resuscitation,” a resuscitation regimen tailored to facilitate early hemostasis in bleeding patients.

Conclusion

Experience gained in early resuscitation of wounded warriors has led to improvements in delivery of trauma care that have increased survival in both the military and civilian sectors. Liberal use of tourniquets has improved surgeons’ ability to control life-threatening bleeding. Techniques for resuscitation of shock have dramatically improved. Thus while war has resulted in countless casualties with associated pain and suffering, positive developments such as these will likely contribute to saving many more lives in the future.

References