INITIAL EVALUATION OF THE EFFICACY AND SAFETY OF IN-HOSPITAL EXPANDABLE HEMOSTATIC MINISPONGE USE IN PENETrATING TRAUMA

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**CONFLICT OF INTEREST**

The authors have no conflicts of interest or disclosures of funding to declare.
**Background:** Hemorrhage remains the leading cause of preventable death after trauma. The XSTAT® expandable minisponge hemostatic device was developed for the control of severe, life-threatening bleeding from junctional wounds not amenable to tourniquet application. This is an initial report of the clinical use of this novel method of hemorrhage control for civilian penetrating injury.

**Methods:** A review of trauma admissions at a high volume level 1 trauma center was carried out from July 2016 to November 2017. All patients sustaining penetrating trauma with active hemorrhage were evaluated for XSTAT® use. Ten device deployments occurred during this time. Each deployment was reviewed in detail, capturing patient and injury data, efficacy of hemorrhage control, and evaluation of any potential device or treatment related complications.

**Results:** 6,363 trauma admissions were reviewed with 22.1% sustaining a penetrating mechanism of injury. XSTAT® was deployed in 10 (0.7%) penetrating trauma admissions with a mean age of 38.3 (range 16 – 59) years, SBP of 126.7 (range 74 – 194) mmHg, GCS 14.5 (range 13 – 15) and NISS of 9.5 (range 1 – 27). Eight patients had an identifiable arterial injury; the remainder had vein or soft tissue bleeding. Overall, half were junctional injuries. XSTAT® was able to stop bleeding in nine of ten patients on the first deployment, with the remaining patient requiring one repeat injection. Dwell times ranged from 1 to 40 hours (median = 15 h). There were no technical device failures or embolic complications. Retained sponges were identified in two patients on initial post removal x-rays following wound exploration for definitive hemorrhage control and sponge removal. No patient died during the study period.
Conclusions: XSTAT® use appears safe. It is rapid, reliable, and provides a high degree of hemorrhage control on first deployment. Sponge removal should always be followed by radiographic clearance. For patients with hemorrhage from cavitary wounds not amenable to tourniquet placement, this device was effective. Further study is warranted as XSTAT® use becomes more widespread.

Level of Evidence: V

Study Type: Case series

Keywords: topical hemostatic; balloon tamponade; junctional hemorrhage; minisponge dressing; XSTAT®
CASE DISCUSSION

A 20-year-old female presented to our level 1 trauma center as a top tier trauma activation in hemorrhagic shock. She had sustained multiple gunshot wounds with large volume blood loss reported at the scene and arrived with a blood pressure of 88/77 mmHg and heart rate of 148 bpm. Physical exam revealed two injuries to her right lower quadrant as well as an injury to her right groin. The junctional wound had a large underlying hematoma and active bleeding. This was controlled with direct pressure, a plain radiograph of the abdomen was obtained, and the patient was transported immediately to the operating room for definitive hemorrhage control. In order for the laparotomy to be safely performed, temporary groin hemorrhage control was necessary. The location of the injury was not amenable to tourniquet placement, and attempts at Foley catheter balloon tamponade were unsuccessful due to balloon extrusion. One XSTAT® 30 device was then deployed into the wound, resulting in immediate hemorrhage control allowing for completion of the abdominal exploration [Figure 1]. The laparotomy demonstrated no source of hemorrhage and the blood loss was attributed to the junctional wound. Attention was then returned to this area. At this point, after the infusion of 5 units of packed red blood cells and 1 unit of plasma, the patient’s hemodynamics were normalizing. A plain radiograph was obtained to rule out an associated fracture and the groin was explored. The wound was extended, the XSTAT® sponges removed and a complete transection of the right profunda femoris artery just beyond the common femoral bifurcation [Figure 2] was found. This was ligated. Repeat intraoperative radiograph was obtained to ensure complete removal of the sponges [Figure 3]. Hemodynamics continued to improve and the patient was transferred to the ICU and ultimately discharged home.
INTRODUCTION

This case highlights the challenge of effective jugntional or other non-compressible hemorrhage control where a tourniquet cannot be used and other means are unsuccessful. The importance of immediate hemorrhage control cannot be overstated, as hemorrhage remains the leading cause of preventable death, accounting for 30-40% of trauma related mortality.\textsuperscript{1} With any visible external bleeding, achieving immediate hemorrhage control is the priority.\textsuperscript{2,3}

While manual compression and tourniquets are effective for the distal extremity, junctional injuries are challenging. These locations, including the neck, axilla, groin and perineum, are not amenable to standard tourniquet placement, and direct pressure can be difficult to apply and maintain.\textsuperscript{4} Although several Food and Drug Administration approved devices for junctional hemorrhage control have been developed, they are bulky and most EMS agencies and hospitals do not have access to them. The clinical efficacy of these devices and indications for their use also remain unclear.\textsuperscript{5} Junctional trauma remains a significant clinical challenge and cause of preventable mortality.\textsuperscript{6,7}

Balloon tamponade deployed within penetrating cavitary wounds has also been described.\textsuperscript{8,9} Typically, Foley catheter balloons or similar devices are inflated within the wound in an attempt to gain hemorrhage control. Although we use this technique routinely at our center, it requires a wound that will accommodate catheter entry, without balloon extrusion, with a balloon diameter that is adequate for effective tamponade. In the case presented, the wound cavity was extremely large and the skin incision would have required suturing even if a sufficiently large balloon were available. Additionally, in the prehospital transport setting, there
is the potential for the balloon to be accidentally pulled out because the catheter extends out of the wound, making the use of balloon catheters suboptimal.

The XSTAT® non-absorbable, expandable, hemostatic sponge dressing (RevMedx, Inc. Wilsonville, OR) is a novel FDA approved device developed for temporarily controlling hemorrhage from these difficult wounds. Although initially developed for wounds sustained in military combat, the FDA approved the device for use in the civilian sector in April 2014. The XSTAT® hemostatic device consists of multiple highly compressed rapidly expanding cellulose minisponges contained within a small (XSTAT® 12) or large (XSTAT® 30) syringe-like deployment device [Figure 4]. The smaller device contains approximately 38 minisponges with a maximum external diameter of 13 mm, while the larger device is able to accommodate approximately 92 minisponges for injection with a diameter of 30 mm. These non-absorbable minisponges containing a radiopaque marker are injected into the wound cavity where they rapidly expand when contacting blood or fluid, creating a tamponade effect and providing hemostatic pressure from within the wound. In compressed form, each sponge has a diameter of approximately 1 cm, with variable length. Per the manufacturer, the sponges are safe to leave in place for up to 4 hours, until definitive surgical hemorrhage control can be achieved.

At our institution, this device was first introduced into practice in July 2016. Here we present our first ten in-hospital deployments of XSTAT® in penetrating civilian trauma.
METHODS

All trauma admissions from July 2016 to November 2017 were reviewed. During this period, all patients with penetrating traumatic injury and active hemorrhage were evaluated for XSTAT® use. Deployment was at the discretion of the attending trauma surgeon on call, and was only utilized for injuries with active hemorrhage not amenable to tourniquet placement or those not adequately controlled by other means. The choice of a small or large deployment device was dictated by the size of the external wound. The small device has a maximum external diameter of approximately 13 mm and the large of 30 mm. A single device was used initially in all cases, and hemorrhage control assessed. If unsuccessful, additional device deployment was again at the discretion of the attending trauma surgeon. These sponges were used either as a temporary bridge to definitive operative hemorrhage control or as packing would be for non-operatively managed wounds at the discretion of the attending trauma surgeon. Sponge removal was performed manually and the injured area underwent plain radiograph evaluation to ensure no retained sponges remained within the surrounding soft tissue [Figure 5]. All radiographs were reviewed with an attending radiologist.

As part of the quality improvement process, with each deployment the indication for use, hemostatic efficacy, time of deployment and time of removal were recorded in real time. Each deployment was then reviewed in detail, capturing demographic data, arrival vital signs, new injury severity score, mechanism and location of injury. The efficacy of bleeding control was evaluated including type of device utilized, number of devices required, and dwell times from deployment to removal. The source of bleeding, including injured vessels, was then defined and all operative procedures for hemorrhage control were reviewed in detail. Plain films were
reviewed to assure adequate imaging was obtained to rule out retained foreign bodies. Finally, mortality data, hospital and ICU length of stay, as well as complications potentially attributable to device use were reviewed.

RESULTS

Over the 17-month study period, 6,363 trauma admissions were reviewed, including 1,236 top tier trauma activations. Of these, 1,409 (22.1%) patients sustained a penetrating injury. XSTAT® was deployed in 10 (0.7%) penetrating trauma admissions with a mean age of 38.3 (range 16 – 59) years, SBP of 126.7 (range 74 – 194) mmHg, GCS 14.5 (range 13 – 15) and NISS of 9.5 (range 1 – 27). Of these, eight patients had an identifiable arterial injury; the remainder had vein or soft tissue bleeding. Overall, half were junctional injuries. XSTAT® was able to stop bleeding in nine of ten patients on the first deployment, with the remaining patient requiring one repeat injection. Dwell times ranged from 1 to 40 hours (median = 15 h). There were no technical device failures or embolic complications. Retained sponges were identified in two patients on initial post removal x-rays following wound exploration for removal. In all cases, the retained sponges were found and successfully removed. No patient died during the study period. Individual patient data, injury details and complications are displayed in Table 1.

The location of injury and source of hemorrhage varied widely. Overall, half were junctional. The bleed was from an identifiable artery or branch in eight, vein in one and soft tissue in one. Specific named arteries included the vertebral artery, profunda femoris artery, as well as branches of the profunda femoris and inferior epigastric artery.
In all but one case, the initial deployment of XSTAT® was adequate for hemorrhage control, demonstrating initial efficacy in nine of ten cases. In the failed case, initial deployment was not effective. This was a large perineal wound caused by an unknown object during an assault. The initial large device deployment slowed the bleeding, however was insufficient, prompting deployment of a second device. This effectively controlled external hemorrhage. The patient was taken to the angiography suite and the ongoing internal bleeding was localized to multiple arterial pelvic branches and treated with left internal iliac artery embolization followed by wound exploration and sponge removal.

Sponge dwell times ranged from 1 hour to 40 hours (median = 15 h). There were no technical device failures or embolic complications. After application and removal, plain radiographs were utilized to ensure complete sponge evacuation. Solitary retained sponges were identified in two of ten cases on initial post removal x-rays following wound exploration. These were removed and repeat radiographs used to clear the site.

Complications attributable to XSTAT® use and sponge removal were identified in a single patient. In this case, sponge retrieval required a 2-3 cm extension of the wound in order to remove sponges from a deep cavity caused by a stab wound. This patient also developed rhabdomyolysis secondary to muscle necrosis requiring subsequent debridement. This was followed by the development of acute kidney injury. The sponges were in place for a 40-hour dwell time as the patient required significant resuscitation before stabilizing sufficiently to undergo wound exploration. The presence of the sponges, while effective for hemorrhage control, may have contributed to the myonecrosis and acute kidney injury.
DISCUSSION

Hemorrhage remains the leading cause of preventable mortality after injury, highlighting the importance of immediate hemorrhage control, ideally at the point of injury. Junctional hemorrhage, specifically, remains a difficult problem to address, particularly in the prehospital setting. In one evaluation of military combat casualties, 21% of potentially preventable prehospital deaths resulted from junctional hemorrhage. Although tourniquet placement has demonstrated excellent safety and efficacy in both military and civilian settings for extremity injury, they cannot be applied to proximal extremity or junctional injuries. The development of this rapidly expanding minisponge hemostatic dressing presents a potential solution to this problem, as well as that of non-compressible hemorrhage not adequately controlled with other means.

The underlying hemostatic mechanism of XSTAT® is very rudimentary, relying on simple expansion and internal compression of the bleeding source. The tamponade effect is exerted as blood is absorbed, causing the sponge to expand, naturally filling penetrating or cavitary wounds and compressing the surrounding tissue. This conformability allows equal distribution of pressure uniformly throughout the defect, ensuring application of pressure at the point of injury, without the need for any diagnostics or knowledge of the underlying vascular injury. This proof of concept has been verified in a penetrating wound model study by Kragh, demonstrating improved maintenance of pressure at both the side and bottom of the wound as measured by manometry when compared to standard gauze dressing. XSTAT® expanded evenly with a balanced distribution of pressure, as opposed to the asymmetrical pressure distribution of packed gauze. Additionally, time to application strongly favored XSTAT® with
an eight-fold reduction, as well as an absence of mechanical wound shear which was seen with gauze packing.

In the preclinical evaluation of XSTAT®, swine femoral artery injuries (6.0 mm arteriotomy) were controlled in 100% of cases, with a decrease in wound packing time from 4.6 to 1.1 minutes as compared to standard gauze packing. An additional analysis of swine subclavian artery and vein transection demonstrated hemorrhage control in 87.5% of injuries, with a solitary failure related to the loss of an applicator tip within the wound, preventing sponges from accessing the point of bleeding. Applicator tips are now secured to the device with glue to remedy this problem.

In the current data set, the first reported clinical application of XSTAT® in penetrating civilian trauma, the initial deployment efficacy was 90%. Temporary hemorrhage control was achieved, even in the setting of significant arterial bleeding. The solitary failure ultimately required embolization of the left internal iliac artery for definitive control of bleeding from multiple pelvic branches caused by a deep perineal laceration. Tamponade was difficult to achieve due to the size of the cavity and the large wound opening, which allowed spillage of injected sponges, rather than expansion within a contained cavity. These large cavitary wounds are potentially ideal for XSTAT® use, but highlight the need for a penetrating skin wound smaller than the underlying cavity, accommodating sponge insertion but preventing unwanted extrusion. In these cases, skin suturing may be required. For patients where the initial deployment is ineffective, a second injection remains an option, which in this case was effective.
XSTAT® placement was found to be straightforward. The syringe type deployment device is intuitive and no diagnostics are necessary prior to use. Determination of the exact nature and location of the injured blood vessel is not necessary. In a user evaluation of XSTAT® device and applicator use, controlled application was performed in under 90 seconds in all first attempts by civilian EMS or military medics, with a mean application time of 50.1 seconds.\textsuperscript{10} The device itself is portable, lightweight, and may be stored at room temperature. The self-sustaining nature of tamponade with XSTAT® use would allow rescuers to focus on other tasks during extrication or transport to definitive care. These qualities make it ideal for prehospital application.

Although application is straightforward and rapid, the removal of hemostatic material is more difficult and time intensive when compared to simple gauze packing. In the previously discussed wound model study by Kragh, the mean time of sponge removal required a 22-fold increase when compared to a continuous standard gauze roll.\textsuperscript{19} Animal data supports a 5-fold increase in time required for removal.\textsuperscript{10} In addition, within this case series, extension of the skin incision to enlarge the wound was required in one case for complete sponge evacuation.

Retained sponges were identified in 2 of 10 cases after attempted removal. This highlights the importance of obtaining imaging at the time of sponge retrieval to ensure the absence of retained foreign bodies. In practice, even when adequate wound exploration appears to have been completed, sponges may be overlooked and could result in potentially serious complications if left undetected. While attempts at localizing all sponges based on number per applicator would be ideal, in practice, sponges are often lost due to wound extrusion, incomplete
syringe evacuation, or many other variables. Additionally, the manufacturer states each applicator contains an approximate rather than exact number of sponges, further invalidating this practice. For these reasons, post-evacuation radiography is mandatory.

The development of rhabdomyolysis potentially related to prolonged dwell time highlights the importance of this device as a temporary method of hemorrhage control, bridging the patient to definitive care. It is important to note that this complication developed in the setting of a 40-hour sponge dwell time, as the patient was unable to tolerate an operative procedure prior to this. While the recommended safe dwell time is 4 hours, as demonstrated in this case series, longer dwell times may be required, and should be dictated by the patient’s clinical condition. Unfortunately, the maximum safe dwell time has yet to be established. However, because complications due to local tissue ischemia are possible, as soon as the patient is able to tolerate it, sponge removal and definitive hemorrhage control should be obtained.

CONCLUSION

Junctional and non-compressible hemorrhage control remains a challenge, particularly in the prehospital setting. XSTAT® is a rapid, reliable and hands free device for achieving control of hemorrhage within wounds not amenable to tourniquet placement or other simple methods. While there is a high rate of bleeding control with initial deployment, repeat injection may be required. The sponges should be used as a temporary bridge to definitive hemorrhage control. Removal should be followed by radiographic confirmation. Further evaluation of this product is warranted as its use expands.
AUTHOR CONTRIBUTION

ZW and KI provided the conceptual study design. ZW and KI participated in the literature search. LL, KM, EB, AS, DD and KI performed surgical procedures. ZW, KM, AS and KI participated in the data collection. ZW, LL, EB and KI performed the data analysis. ZW, LL, KM, EB, AS, DD and KI performed the data interpretation. All authors participated in writing and critically reviewing the final manuscript.
REFERENCES


FIGURE LEGENDS

Figure 1: Application of XSTAT® 30 within a penetrating groin wound. External compression of wound with evidence of expanding hematoma [A]. Insertion of XSTAT® 30 applicator into penetrating wound [B] followed by deployment of sponges into cavity [C]. Final evaluation of hemostasis at level of tissue injury [D].

Figure 2: Complete transection of right profunda femoris artery after XSTAT® evacuation and vessel control.

Figure 3: Intraoperative radiograph demonstrating complete evacuation of retained sponges. Radiopaque ‘X’ on deployed sponges are visible ex vivo after spillage during evacuation [dotted line], compared to surgical clips [solid square].

Figure 4: XSTAT® hemostatic device for junctional wounds. The larger XSTAT® 30 [A] as compared to the smaller XSTAT® 12 [B] device, used based on size of wound opening. The ejected radiopaque sponges are visible in their compressed [C] and fully expanded [D] form.

Figure 5: Plain radiography demonstrating indwelling radiopaque sponges [A], followed by intraoperative radiography demonstrating absence of retained foreign body after exploration and removal [B].
Figure 4