

Comparison of 10 Hemostatic Dressings in a Groin Transection Model in Swine

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Background: Major improvements have been made in the development of novel dressings with hemostatic properties to control heavy bleeding in noncompressible areas. To test the relative efficacy of different formulations in bleeding control, recently manufactured products need to be compared using a severe injury model.

Methods: Ten hemostatic dressings and the standard gauze bandage were tested in anesthetized Yorkshire pigs hemorrhaged by full transection of the femoral vasculature at the level of the groin. Application of these dressings with a 5-minute compression period (at ~200 mm Hg) was followed with a subsequent infusion of colloid for a period of 30 minutes. Primary outcomes were survival and amount and incidence of bleeding after dressing application. Vital signs and wound temperature were continuously recorded throughout the 3-hour experimental observation.

Results: These findings indicated that four dressings were effective in improving bleeding control and superior to the standard gauze bandage. This also correlated with increased survival rates. Absorbent property, flexibility, and the hemostatic agent itself were identified as the critical factors in controlling bleeding on a noncompressible transected vascular and tissue injury.

Conclusions: Celox, QuikClot ACS⁺, WoundStat, and X-Sponge ranked superior in terms of low incidence of rebleeding, volume of blood loss, maintenance of mean arterial pressure >40 mm Hg, and survival.

Key Words: Bleeding, Hemostasis, Uncontrolled hemorrhage, Noncompressible wound.

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Mortality from hemorrhagic shock caused by massive bleeding in a wound is preventable. With proper dressing (bandage and compression) of the injured site for bleeding arrest, timely fluid resuscitation for hemodynamics restoration, and definitive hospital management, complications such as compartment syndrome, limb loss, or death can be minimized. Thus, early intervention is paramount to increased chances of survival, and this is the core focus of military and civilian trauma care.^{1,2}

There are several factors that contribute to differences in the response strategies for trauma in the civilian and combat situation. In the civilian setting, rapid response may be more easily obtained from rescue teams commissioned to answer emergency calls from police officers or even bystanders. Well located across the country, hospitals and other medical facilities provide first-line treatment and facilitate transfer to a more specialized center when needed. In the combat setting, on the other hand, evacuation and definitive care can be delayed due to ongoing combat, bad environmental conditions, or distance to the treatment facility. First-line treatment can also be challenging with the limited materials available in the field. Ideally, hemorrhage should be controlled within minutes after the injury by the victim or first responders. Direct pressure remains a very effective method to arrest bleeding. Tourniquets are proven effective in compressible areas such as the extremities but may endanger a limb even when the life is saved.³ Blind clamping in deep wounds is usually time-consuming and uncertain. When a severe wound is in a noncompressible area, each of the above treatments may prove impractical and ineffective for hemorrhage control.

A growing number of novel, commercially available hemostatic dressings have been presented and advertised to have hemostatic properties, offering promising solutions in noncompressible areas such as neck, peritoneum, or groin.^{4–9}

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Effective hemostatic dressings could supplement or serve as a substitute for the standard gauze. The US Army and Navy have started testing several local hemostatic agents intended for use in the acute hemorrhage setting.^{4,8,10–15} Even as the search for the most efficient dressing continues, hemostatic products such as HemCon and QuikClot have already been deployed in the battlefield.^{4,9,16–18} QuikClot is being used by the US Marine Corps in the battlefields of Iraq and Afghanistan.^{5,6,18} There has been no serious complication reported using either of the bandages except for a significant elevation in the wound temperature that occurs with the use of QuikClot because of the exothermic reaction in the agent's water adsorption mechanism.^{4,5,18–20} This temperature elevation was resolved in a next-generation product, ACS⁺.^{11,21}

A severe vascular injury model, transection of femoral vessels developed for swine and adapted from the model by Alam and coworkers^{9,10} is used to evaluate different novel dressings. The objective of this study is to compare the efficacy of 10 dressings of different nature in controlling bleeding in the same injury model. The specific hypothesis of this project is that the new products have better efficacy than the standard dressing (SD) in terms of (1) arresting bleeding, (2) preventing additional bleeding, and (3) improving survival.

MATERIALS AND METHODS

Hemostatic Dressings

The products used for this study and their abbreviations are listed in Table 1. The 10 hemostatic products and the standard compressed gauze bandage (SD) (H&H compressed gauze, H&H associates, Bena, VA) were categorized accord-

TABLE 1. List of Test Hemostatic Products in Alphabetical Order Used in This Study and Categorized by Form and Type: The Abbreviations for Each Product are Given

Test Products	Abbreviation	Description
Powder/granular agents		
ACS ⁺	ACS ⁺	Mineral Al/Si Zeolite with attenuated exothermic reaction
Celox	CEL	Chitosan based granules
Instaclot	IC	Proprietary composition powder
WoundStat	WS	Polymer/mineral Al/Si granules
Solid (flexible) agents		
Alpha bandage	AB	4 inch × 4 inch interwoven fabric, bamboo, and fiberglass
BloodStop	BLS	Coated deoxidized cellulose based gauze
X-sponge	XS	4 inch × 4 inch gauze coated with proprietary hemostatic formulation
Solid (rigid) agents		
Chitoflex	CHI	3 inch × 28 inch roll made of chitosan
HemCon	HC	4 inch × 4 inch pad made of chitosan
Polymem FP-21	FP-21	3-layer Dextran/chitosan based 4 inch × 4 inch wafer

ing to nature, form, and composition. Hemostatic dressings were made of a wide range of material from mineral-based products made of zeolite, smectite, and kaolin to biologically based products made of chitin. This gives a total of 10 test agents and 1 control SD (11 groups in total). A more detailed description of each of the products is provided in Appendix.

Animal Model

The study adhered to the principles stated in the Guide for the Care and Use of Laboratory Animals, (National Research Council, 1996 Edition). The study was approved by the Naval Medical Research Center/Walter Reed Army Institute of Research Institutional Animal Care and Use Committee and Uniformed Services University of the Health Science. All procedures were performed in accordance to the Animal Welfare Act and in an animal facility approved by the Association for Assessment and Accreditation for Laboratory Animal Care International.

Yorkshire swine (weight range, 25 kg–35 kg, Animal Biotech Industry; Danboro, PA) were refrained from food the night before the experiment, but they had free access to water. Anesthesia was induced with intramuscular injection of ketamine HCl (30 mg/kg) and inhalation of isoflurane 3% to 4%. Atropine (0.05 mg/kg) was used to reduce mucous secretion. After the placement of the endotracheal tube, isoflurane concentration was reduced to 2% to 3% until initiation of injury. The animals were allowed to breathe spontaneously unless the end-tidal CO₂ and respiration rate fell outside normal values, in which case necessary mechanical ventilation was provided [mixture of oxygen and air was administered through a Narkomed M or Narkomed 2B Ventilator (North American Dräger Telford, PA)]. An 18G–20G angio-catheter was placed in the right carotid artery using the open technique to acquire blood pressure and withdraw blood samples. The right external jugular vein was also cannulated with a 7F or 9F Introfex introducer (Schein Care Corp., Irvine, CA; Edwards Life Sciences, Irvine, CA) for fluid administration. The catheters were connected to sensors (Transpac IV, Trifurcated Monitoring Kit, Hospira, Lake Forest, IL) attached to a hemodynamic monitoring system (Hewlett Packard, Palo Alto, CA) to allow for continuous monitoring and recording of vital signs. All catheters were continuously flushed with 0.9% saline solution (5 mL/h) to maintain patency. Pulse oximetry (Data-Omedex/V3301, SurgiVet, Waukesaha, NJ) was obtained from the tongue, tail, or ear.

Transection Model

The skin at the right inguinal area of the thigh was incised ~10 cm long to expose the groin area. The femoral vein and artery were exposed. Invasive dissection of the femoral vessels was avoided to prevent any vessel constriction or spasm. After a brief period of stabilization and recording of baseline vital parameters, the injury was made by transecting the femoral blood vessels and the adjacent muscles to produce uncontrolled hemorrhage, Time 0 (T0). This resulted in the immediate gush of both arterial and venous blood. Blood was suctioned into a vacuum canister with aspiration directed on the blood accumulating in the

groin cavity but not directly from the injured area to avoid dislodging formed clots. This aspirated blood was continuously weighed and recorded as pretreatment blood loss.

Treatment and Monitoring

The animals were randomly assigned to 1 of the 11 bandage regimens ($n = 8$ per group). Rectal temperature was monitored and maintained between 37°C and 39°C using a Bair Hugger device (Model 505, Bair Hugger, MN). A temperature probe (Type K, Thermo-Couple Thermometer/Model BAT12, Physitemp, Clifton, NJ) was placed on the cavity created through the dissection to monitor for any change in temperature. After uncontrolled bleeding for 2 minutes (T2), the treatment consisted of placement of the test dressing on the injured site with a SD placed over it. The test dressings were applied based on the manufacturer's directions for use. A second dressing (SD, standard compressed gauze bandage) was necessary to remedy the small size of some dressings. A constant pressure of 175 mm Hg $\pm$ 28 mm Hg (measured by HM 28 pressure monitor, Dwyer, CA) was applied over the wound with the dressings for 5 minutes. The pressure was then released (T7) and the skin apposed over the dressing. This would leave a residual pressure of 30 mm Hg $\pm$ 5 mm Hg. At 15 minutes, T15, resuscitation was initiated by administration of 500 mL of isotonic colloid intravenously (Hextend, Biotime, Abbott, Abbott park, IL) through the external jugular vein over 30 minutes (T15–T45) using a pump set (Masterflex, Cole Parmer or Flo-Gard 6201, Baxter, Deerfield, IL). This volume corresponded to $\sim$ 15 mL/kg body weight. No additional fluid was administered regardless of the mean arterial pressure (MAP) or the blood loss. The dressings remained in place on the wound and untouched for the remainder of the experiment. All animals were monitored until the end of the 3rd hour (T180) at which time the dressings were removed and the injured site inspected for presence of clots. Death before the end of the observation period is defined as no recordable blood pressure or apnea and unappreciable heart sounds for 5 minutes. For the pigs who survive until the 3rd hour, Euthasol solution (0.3 mL/kg) was injected to kill the animal.

Recording and Data Acquisition

Shed blood volume was collected in a sealed container (2L MediVac, CardinalHealth) and continuously weighed on a top-loading scale (Mettler, PS 5100). Rectal and wound temperature (at the interface of blood and dressing) were continuously recorded using temperature probes (BAT 12). Blood pressure (MAP, diastolic, and systolic) and heart rate were continuously measured on a blood pressure analyzer (Micro-Med, Louisville, KY). CO₂, Isoflurane level, respiration rate, and oxygen saturation were recorded manually every 5 minutes for the first 45 minutes and every 15 minutes thereafter. Data were organized in a Microsoft Excel spreadsheet for further analysis.

Arterial and mixed venous samples were taken at different time points: T0, T5, T15, T45, T60, T120, and T180. Blood samples were subjected for complete blood count and analyzed for blood gas using the ABL 750 (Radiometer,

Copenhagen) or Nova Stat Profile Ultra (Nova Biomedical, Waltham, MA).

Volume blood loss (mL) was calculated from the weight (g) as: weight (g)/1.056 g/mL. Estimated blood volume (EBV) was calculated as: animal weight (kg) $\times$ 65 mL/kg. Percent blood loss is defined as the volume of blood loss divided by the EBV of the pig. Blood loss was divided into pretreatment (injury and initial hemorrhage to 2 minutes; T0 to T2) and posttreatment (from T2 to end point). Aspirated shed blood was continuously recorded, and total posttreatment blood loss was calculated as measured shed blood, blood absorbed in test dressing, and blood absorbed in the second dressing (SD), each weighed at the end of the experiment.

Recurrence of bleeding was recorded to assess each product for bleeding control after release of the 5-minute manual compression and/or when MAP reached 40 mm Hg. Recurrence of bleeding was accounted for as determined by incidence of aspiration (i.e., no bleeding or bleeding retained in the dressing versus blood clearly seen oozing from the dressings and requiring aspiration).

Histologic examination was also performed on a number of samples for each treatment group. The distal tissue (including muscle, vessel, and nerve) was collected after the dressing was removed. The tissue was fixed in 10% formalin, embedded in paraffin, microtomed (6 μ m), and stained with hematoxylin and eosin (H&E). Tissues were examined with light microscopy by a board-certified veterinary pathologist who was blinded to treatment group. The following parameters were noted: presence of edema, presence of fibrin or thrombi, potential for burn injury, necrosis, cellular influx, and neutrophil influx. Global scoring was an average of scores assigned to observations, graded as mild (1), moderate (2), and severe (3) and characterized as focal (1), multifocal (2), and diffused (3).

Retention of blood in the dressing (absorption) was measured by in vitro weight after pouring 10 mL or 20 mL of blood on the top of 20 mg of the product. Clotting was assessed in a test tube with 2-mL blood recalcified with CaCl₂ to which 1 mg of product was added. Clotting time was measured by tilting the tube 45 degrees every 30 seconds until firm clotting was detected.

Statistical Analysis

The original design of the study was to evaluate each dressing on eight animals. Analysis of variance, Mann-Whitney, Kruskal-Wallis, Fisher's exact, and χ^2 tests were performed (Statistix, Tallahassee, FL; SAS Institute, Cary, NC). Data are presented as mean $\pm$ standard deviation, and $p \leq 0.05$ was considered significant. The dressings were initially ranked according to survival, as survival of the animals across the 3-hour experiment will directly affect quantitative blood loss and bleeding arrest, which is also outcome for this evaluation.

RESULTS

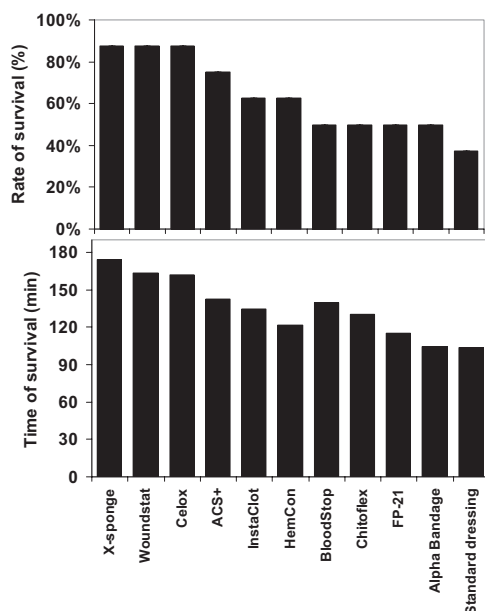
Baseline Data

A total of 96 pigs were used in the study. Eight pigs died because of severe hemorrhagic shock within 20 minutes

TABLE 2. Baseline Parameters Among the Test Groups at T0 and T2

	Parameter	Mean $\pm$ SD
Preinjury	Weight (kg)	29.8 $\pm$ 3.1
	Rectal temperature ($^{\circ}$ C)	38.2 $\pm$ 3.3
	Initial MAP (mm Hg)	71.9 $\pm$ 11.9
Pretreatment	Rate of loss (mL/min)	508 $\pm$ 175
	Blood loss at T2 (% of EBV)	35.0 $\pm$ 10.1
	MAP at T2 (mm Hg)	19.2 $\pm$ 10.0

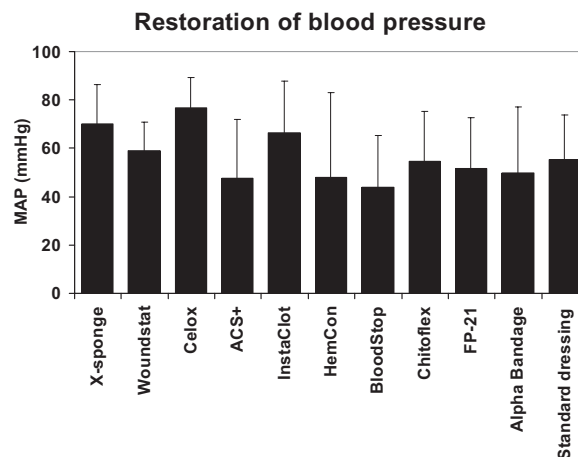
T0, time 0; T2, time 2 hours; MAP, mean arterial pressure; EBV, estimated blood volume; SD, standard deviation.

**Figure 1.** Rate of survival and duration of survival across all dressings.

and were not included in the analysis. A total of 88 pigs were included for analysis. There was no difference among the treatment groups preinjury at T0 in terms of the weight, initial temperature, and initial MAP (analysis of variance). At pretreatment, after injury, there was no difference in blood loss (average 35.0% $\pm$ 10.1% EBV) or MAP at 2 minutes posthemorrhage (reduced from baseline to 19.2 mm Hg $\pm$ 10.0 mm Hg). These data are summarized in Table 2.

Survival

Products were ranked according to survival rate (Fig. 1). There was no significant difference for survival rate (contingency analysis) or for survival time (χ^2 analysis) among all products. When ranked according to survival rate at the end of the 3-hour observation period, the four first dressings—XS, CEL, WS, and ACS⁺—exhibited an average survival rate and time (84.4% $\pm$ 6.2%, 160 minutes $\pm$ 13 minutes) that was greater than the four last dressings—BLS, CHI, FP-21, and AB—i.e., those with the lowest survival rate

**Figure 2.** Restoration of blood pressure: The highest MAP achieved after fluid resuscitation across all groups during the 3-hour experiment time (mean $\pm$ standard deviation).

and time (50% $\pm$ 0% and 114 minutes $\pm$ 75 minutes, $\chi^2 p < 0.01$). IC and HEM showed intermediary survival rates, not different from the four first or the four last dressings. All animals treated with the test dressings had better survival than SD-treated animals (37%, 104 minutes $\pm$ 72 minutes; $p < 0.05$).

Restoration of Blood Pressure

Before the start of fluid resuscitation at T15, posttreatment MAP increased to an average of 33.5 mm Hg $\pm$ 17.2 mm Hg from the lowest MAP after injury and initial bleeding (19.2 mm Hg $\pm$ 10 mm Hg) and was not different among treatment groups. The highest blood pressure was recorded for each individual treatment during the entire experimental period and is presented in Figure 2. After fluid resuscitation and with bandages still in place with a residual compression pressure of 30 mm Hg $\pm$ 5 mm Hg, the MAP was restored to an average of 56.6 mm Hg $\pm$ 22.9 mm Hg with levels above 60 mm Hg for CEL, XS, and IC; there were no significant differences among these levels. In all other dressings including SD, blood pressure was restored between 60 mm Hg and 40 mm Hg.

Incidence of Rebleeding

The incidence of rebleeding refers to the occasion when the dressing fails to achieve hemostasis after the release of compression pressure at T7 or when MAP increased to 40 mm Hg. As illustrated in Figure 3, the dressings with the least incidence of rebleeding were XS, WS, CEL, and IC, which did not exceed a 40% rate at either time point. All fared similarly and were not significantly different from ACS⁺, a dressing currently in deployed use by US military. Rebleeding rates were greater with HC, FP-21, CHI, and BLS; all showing significantly greater incidence than the top group ($\chi^2 p < 0.005$).

Posttreatment Blood Loss

Posttreatment blood loss is another measure of the ability of the dressing to control bleeding. This value is the

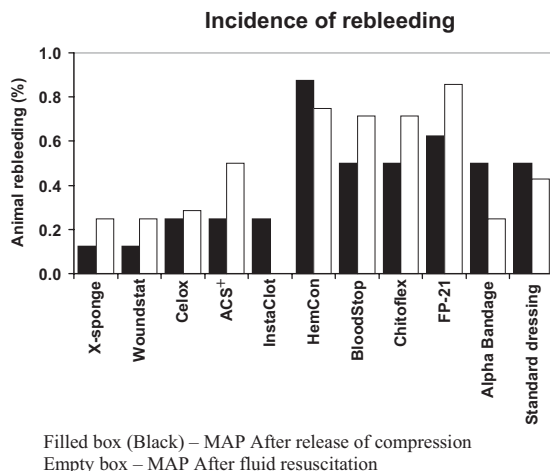


Figure 3. Incidence of rebleeding after release of compression and with restoration of MAP. Animals were scored as 0 (no rebleeding) or 1 (rebleeding requiring aspiration).

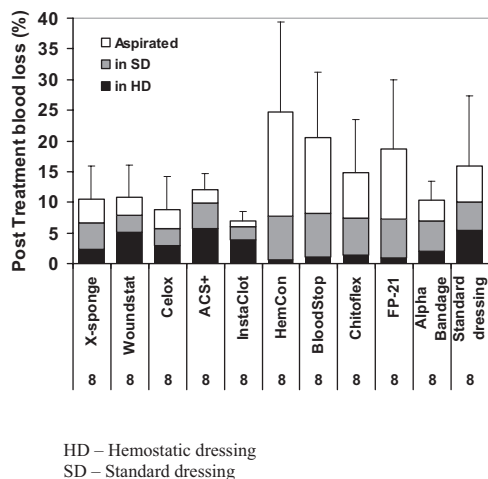


Figure 4. The posttreatment blood loss broken down as blood in the test dressing, blood in the standard dressing, and aspirated blood.

sum of the amount of blood absorbed by both test and SDs, and the amount of aspirated blood after the bandages were applied. As illustrated in Figure 4, IC, CEL, XS, and WS had the least amount of blood loss, whereas HC, BS, FP-21, and CHI had the most (>15% EBV). The difference in the average of the highest ranked and lowest ranked groups was statistically significant ($p < 0.05$). Note that as more blood is absorbed by the test dressing, the amount of aspirated blood tends to be less. This is true across all bandages except for the SD.

Change in Wound Temperature

The temperature recorded at the interface of the product and the inguinal muscles did not change significantly after application of the dressings, except for ACS⁺. ACS⁺ caused a rise of $7.2^{\circ}\text{C} \pm 8.7^{\circ}\text{C}$ between 2 minutes and 4 minutes

TABLE 3. Absorptive Capacity and Clotting Time for the Hemostatic Dressings

Products	Absorption Factor* (g/g)	In Vitro Clotting Time† (s)
ACS ⁺	0.52	180
AB	2.66	230
BLS	8.23	N/A
CEL	10.41	320
CHI	2.11	310
FP-21	4.91	205
HC	1.46	200
IC	4.13	220
WS	5.15	128
XS	2.66	129

Products are listed by alphabetic order.

* Weight of blood absorbed/weight of dressing.

† Clotting time (s) determined with 2-mL blood at 37°C.

after application without visible burn injury in the wound or other macroscopic complications.

Histology Studies

We looked for pathologies at the interface of the dressing and cellular boundaries for possible abnormalities because of attachment of the dressings. Most sections were observed to have myofiber edema and necrosis; we attributed this to the cut injury, which crossed the muscles. Among all the bandages, ACS⁺ was the one noted to have more edema-like changes with the greatest depth in the muscle layer that could be attributed to a mild burn injury. Some dressings such as IC, WS, and CEL clearly had refringent material attached to the connective tissues. No deposition of material was observed in the large vessels that could have induced disruption of the endothelium.

In Vitro Characteristics

Absorbent properties and clotting time for the different hemostatic dressings were also evaluated. Results are summarized in Table 3. CEL, WS, and BS, in decreasing order, had the greatest absorbent capacity, whereas ACS⁺, HC, and CHI, in increasing order, had the least.

DISCUSSION

The baseline averages show that the pigs included in the study were similar in terms of their weight and MAP. The transection model used in this study created a substantial vascular and tissue injury to cause at least a class III hemorrhagic shock, a 30% to 40% loss of total blood volume and subsequent decrease in the average MAP by 75% from baseline.²² This simulates one type of combat injury that occurs when warfighters are wounded in the extremities causing multiple vessel injury and massive bleed before first aid or surgical attention. The MAP values after uncontrolled bleeding and subsequent bandage treatment increased because of the ability of the animal to compensate. The restoration of MAP to baseline level can be attributed, in part, to the efficacy of the dressing and to this transection model

where the retraction and constriction of the vessels played a major role in controlling bleeding.

Blood loss and survival of animals treated with SD were compared well with previous results.²⁰ It is important to point out that the SD performed rather well because the incidence and amount of bleeding in that group approximated the average for all the dressings. Without the hemostatic material, the performance of gauze was limited to passive compression and its absorbing capacity, as supported by *in vitro* measurement of blood absorption by the gauze. However, absence of coagulation caused blood to saturate this nonhemostatic dressing, yielding continuous bleeding and low survival. With this study, we were able to identify dressings that were more efficacious than SD in terms of absorbing and clotting blood.

Overall, there was no statistically significant difference in survival rate and time for all products in this model. When ranked by survival, the best four dressings (CEL, WS, XS, and ACS⁺) were also the most efficient in terms of controlling bleeding. They showed superior bleeding arrest by maintaining a low incidence of rebleeding and low volume blood loss with MAP >50 mm Hg. Except for XS, all of them are, at least partially, in powder form. Celox is composed of Chitosan granules, which give the product its good absorptive property. The gel formed by the interaction of the granules with blood promotes blood clotting. WoundStat is made of an aluminum silicate mineral clay containing cations that swell and form plastic clay after absorbing water. ACS⁺ is also an aluminum silicate product with beads that absorb water from blood and hold water molecules in pores. X-sponge, which is synthetic gauze, has clotting ability attributed to the Kaolin coating of the fabric material. Kaolin is an aluminum silicate (compare WS and ACS⁺) that acts as a surface activator, giving this dressing an edge over the other gauze dressings in its potent coagulating property.

Two dressings, HC and IC, exhibited slightly lower, intermediate responses (five of eight animals surviving). HC is effective in stopping bleeding when there was sufficient adherence of the dressing to the wound, preventing blood from escaping. When sealed successfully, the blood trapped underneath the dressing has a greater tendency to form a clot. However, when the seal failed, massive bleeding occurred. In contrast, IC showed relatively little rebleeding during the experiments and when it occurred, it was after release of compression and led to early death. There may be several causes for the low volume of aspirated blood in surviving animals. It could be due to the ability of the patch to stop bleeding by creating a physical seal (as with HC) or to the additional effect of partial compression pressure from the dressing (as a pressure adjunct) while it is packed in the wound. The shape and size of the IC patch filled the whole space in the wound, and the SD on top may have created adjunct compression preventing blood loss. These observations with HC and IC suggest that the mechanism for bleeding control may be mechanical, creating a seal and affording a better wound environment for natural clotting.

BLS, CHI, FP-21, and AB, the bandages that performed poorly in controlling bleeding and promoting survival, were

all made from materials such as chitosan and cellulose, but none of them were in powder/granular form. In experiments performed in this study, one unit (as defined by manufacturer) of each dressing was applied. It should be stated that the five 4 inch × 4 inch pieces in the BLS package (i.e., one unit) might not have been a sufficient material in this model. FP-21 demonstrated impressive clotting properties; however, this bandage material did not conform well to the wound surface on application. Thus, the rigid dressing might not allow complete or immediate contact with the wound, resulting in less clotting/more bleeding. Although conformation may occur gradually as the dressing becomes increasingly pliable with time (because of saturation with blood), this delay may result in the occurrence of rebleeding at an earlier time point. On the other hand, AB provided good contact in the wound because of its flexibility. However, the initial blood loss arrest could not be executed rapidly enough with this product, possibly due to a slower rate of absorption. Overall, these dressings had a greater hemostatic capability in comparison with their absorption capacity.

Dressings that were more absorbent exhibited a lower volume of aspirated blood. This suggests that absorption may be an important, although not necessarily sufficient, criterion for effective control of bleeding. For example, despite its good absorption properties, SD did not support survival. It is possible that because of its relatively large size, SD absorbed a large volume of blood without arresting the bleeding itself. However, with test dressings like XS or WS that also absorbed relatively large amounts of blood, their additional hemostatic properties promoted blood clotting, reduced post-treatment blood loss, and increased survival. Given the likely importance of both absorption and hemostatic properties, it is important that these dressings be seen as pressure adjuncts. Dressing failures could occur when they are inaccurately perceived as having properties that obviate the rescuer from needing to apply pressure.

It is worth mentioning that in this swine model of transection injury, the laceration of the femoral artery, vein, and surrounding soft tissues including muscles tried to simulate a particular type of multiple injury seen in the battlefield.^{4,5} However, this model has limitations. The inguinal injury created (10 cm–12 cm) is limited to a particular site and size that may be better in accommodating dressings of a particular configuration.⁹ This reinforces the fact that dressings that did not perform well in this model might excel in others. However, it seems logical to state that for the more random and unexpected type of injuries, the dressings should be flexible enough to conform to the shape and site of any wound. It should also be noted that we evaluated the test dressings as applied with the SD, and therefore performance reported here is a combination of both. Moreover, the limited fluid resuscitation and other relevant physiologic factors not examined in this study could change the animals' outcomes. Foremost of these is the effect of patient movement (as the patient is transported from one place to another) on the efficacy of the dressing in terms of controlling bleeding. We experimented with a "leg shake" at the end of the procedure on surviving animals but not consistently, and we did not

report results. Our approximation of the time elements mentioned earlier may vary greatly in the real world, and this could also significantly affect the amount of bleeding and subsequently the efficacy of the dressings and survival of the animal. To illustrate, the first 2 minutes of uncontrolled bleeding was supposed to coincide with the time wounded warfighters can reach their first aid kit and control the bleeding by themselves, using the bandage that they have.^{3,22} T15 or the time at which the fluids were given is the approximate time that vascular access might be established for the injured warfighter such that fluids could be started if the warfighter is in the immediate vicinity of a first aid unit. These are only approximations, at best.

Finally, it is important to take into account the ease of application of the dressing in the combat setting, where injured warfighters may be alone and under hostile fire. Several other factors such as cube size (weight and volume), environmental stability, ease of removal for surgical repair, and cost should also be considered in the selection process.

CONCLUSION

Ten types of hemostatic dressings, used as pressure adjuncts, were tested together with standard compressed gauze dressing in a transection injury on the groin of a swine causing a mixed vascular and soft tissue bleeding injury. It was found that three new types of hemostatic dressings, namely Celox, WoundStat, and X-Sponge, and a currently deployed product, ACS⁺, performed better than standard gauze in controlling bleeding and improving survival in pigs during a 3-hour observation period. The improved performance in bleeding control and prevention of rebleeding was attributed to the composition and form of dressings. The active hemostatic properties, in addition to their absorption ability and pliability, provided further advantage for bleeding control in actively bleeding wounds. In general, it seems apparent that products with high absorption and hemostatic capacity performed well in this model.

APPENDIX

Standard Dressing

Standard dressing (SD, Compressed gauze, H&H associates, Bena, VA) is a standard cellulose loosely woven compressed gauze with high absorption shown to absorb 15 times its weight in blood and conforms to uneven cavities of the wound.

Powder/Granular Agents

Advanced clotting sponge (ACS⁺, Z-Medica, Wallingford, CT) is a Food and Drug Administration (FDA)-approved nonexothermic mineral Al/Si Zeolite. Each unit is a package of 100 g of porous Zeolite beads encapsulated in conjoined medical mesh bags (4 inch × 4 inch × 2 inch). It is a poor absorbent and can absorb 0.5 times its weight of blood, and its clotting ability is average. According to the manufacturer, it concentrates plasma and blood cells on the surface of the beads to accelerate coagulation. It should be used rapidly after opening of the external aluminum pouch, as the product is moisture sensitive.

Celox (CEL, Sam Medical Products, Newport, OR) is FDA-approved Chitosan-based granules (from shellfish). A unit is presented as one (35 g) package of loose powder. Chitosan powder has a negative charge that gives it adherent properties and forms a gel in contact with hydrous substances. Blood cells (red cells and platelets) could become trapped in this gel. Celox can absorb 11 times its weight of blood volume. Its clotting ability is poor. The manufacturer indicates that its clotting property is dependent on blood flow, wound size, wound type, and the size of the subject. It is stable after opening the external pouch.

Instaclot (IC, Emergency Medical Devices, Loxahatchee, FL) is a fine mineral powder of proprietary formula, covered by a dissolvable membrane that should be in contact with the wound. Each unit is configured as a 3 inch × 6 inch patch of 100 g. It should be sufficient to cover a 10-cm wound. Its clotting ability is average. According to the manufacturer, it can absorb blood up to 12 times its own weight in 2 minutes.

Woundstat (WS, TraumaCure, Bethesda, MD) is a polymer/mineral composite bandage FDA-approved for severe bleeding treatment. One package (165 g) is one unit. It is made of smectite, an aluminum silicate mineral clay containing cations such as iron, calcium, and magnesium. This is a hydrous material that swells after absorbing water and forms a plastic clay with strong adhesiveness. It can absorb five times its weight of blood volume and clotting ability is above average. It is stable after opening the external pouch.

Solid (Rigid) Agents

Chitoflex (CHI, HemCon Medical Technologies, Portland, OR) is a 3 inch × 28 inch roll made of chitosan. Each package of one roll is considered one unit. Chitoflex does not have the rigid backbone of HemCon and is therefore flexible. Also, unlike HC, CHI offers two sides for adhesion. It is also mucoadhesive once in contact with blood. It does not absorb blood more than twice its weight and has a poor clotting ability.

HemCon (HC, HemCon Medical Technologies, Portland, OR) is a 4 inch × 4 inch pad made of chitosan. Each vacuum pack contains one 4 inch × 4 inch enhanced Hemcon bandage (one unit). It is not flexible and tends to break when pushed in the wound. It does not absorb blood more than twice its weight and has a poor clotting ability. Once in contact with blood, it becomes a mucoadhesive and seals the wound very tightly.

Polymem FP-21 (FP-21, Ferris Manufacturing Corp, Burr Ridge, IL) is a 4 inch × 4 inch wafer of Dextran/chitosan. It dissolves when in contact with blood and combines with blood to form a gel. This gel can contain as much as five times the weight of blood, but it has average clotting promotion.

Solid (Flexible) Agents

Alphabandage (AB, Entegron, NC) is a 4 inch × 4 inch woven fabric of bamboo and fiberglass. One unit contains four Alphabandage pieces. It is FDA approved as Stasilon/fr. It is a woven mixture of fibers selected for their ability to activate blood platelets and promotes coagulation

proteins as per manufacturer's information. For severe wounds involving arterial/venous transections, it is recommended that two of the 4 inch × 4 inch pads be placed side by side directly at the site of uncontrolled bleeding. Then, back up these pads with the two additional 4 inch × 4 inch pads. It is a poor absorbent and has average clotting properties.

BloodStop (BLS, Life Science) is a nonwoven gauze made of oxidized cellulose. One unit consists of five 4 inch × 4 inch pieces. The manufacturer reports that when it comes into contact with blood, BloodStop speeds coagulation and expands to a gel that adheres to the surface and applies pressure because it seals the wound. It is used primarily in obstetric and surgical bleeds.

X-Sponge (XS, Z-Medica, Wallingford, CT) is a nonwoven coated gauze. Each sponge is a four-ply 4 inch × 4 inch synthetic rayon/polyester coated with kaolin. Kaolin is an aluminum silicate, a very potent coagulation initiator that acts as a surface activator. Each package of five X-Sponge gauze pads is considered one unit. It is stable after opening the external aluminum envelope, and each sponge can be used individually at a later time. Its absorption capacity is no more than three times its weight of blood, and it has good clotting ability.

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