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Biosurgical Hemostasis in Thoracic and Cardiac Surgery: A Practical Approach

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Abstract

Patients undergoing cardiothoracic surgery, especially open cardiac procedures requiring cardiopulmonary bypass, are exposed to several alterations in primary and secondary hemostasis. These derangements are associated with increased microvascular bleeding that is refractory to conventional surgical maneuvers aimed at achieving hemostasis. This poses a technical problem for the surgeon and exposes the patient to increased morbidity from uncontrolled bleeding and any associated transfusion of blood products. Use of biosurgical hemostatic agents, specifically in patients undergoing cardiac surgery, have been shown to be safe and effective in reducing time to hemostasis, decreasing transfusion of blood products, and improving patient outcomes. Despite their merits, selection of a topical hemostat is frequently based on anecdotal experience and limited knowledge of the available agents. The prepared surgeon is familiar with these agents and can anticipate opportunities for their deployment in the setting of coagulopathy.

Keywords: cardiothoracic surgery, biosurgical agents, topical hemostatic agents, surgical hemostasis, blood conservation

1. Introduction

In the United States, national data has shown that cardiac surgical procedures utilize somewhere between 10 and 15% of the approximately 15 million units of packed red blood cells received by surgical patients annually [1]. To this point, the Society of Thoracic Surgeons (STS) published a series of blood conservation guidelines in 2007 and 2011 aimed at cardiac surgery procedures [2, 3]. These guidelines developed a risk profile of factors associated with increased post-operative blood transfusion such as: advanced age, reduced preoperative red blood cell volume, utilization of antiplatelet or antithrombotic drugs, procedural factors (including the complexity, urgency, or re-operative nature of the surgery), and non-cardiac patient comorbidities. With these high risk factors identified, a set of evidence-based blood conservation guidelines were established to include: utilization of medications to increase preoperative blood volume (eg, erythropoietin) or decrease post-operative blood loss (eg, anti-fibrinolytics), intra-operative blood salvage or sparing techniques, autologous pre-donation to reduce stress upon the patient's own blood, transfusion algorithms and recommendations for a multimodality approach that utilizes all of the above. The subsequently revised guidelines in 2011 included: pre-operative management of dual-antiplatelet therapy,

utilization of drugs that augment blood volume or limit blood loss, use of blood derivatives (eg, fresh frozen plasma, coagulation factor concentrates, etc.), updates in the management of blood salvage techniques, consideration for minimally invasive techniques to limit blood loss or transfusion, recommendations for blood conservation in conjunction with extra-corporeal membrane oxygenation and cardiopulmonary bypass, and implementation of topical hemostatic agents. Despite these measures, there has been an increase in blood product utilization by patients undergoing cardiac surgery procedures over the last decade. The reasons likely being multifactorial but include a rise in number of patients undergoing complex, multiple component cardiac surgeries (e.g., CABG and valve procedure), increased number of patients exposed to clopidogrel or similar strong anti-platelet medications, and removal of aprotinin from the US market in 2007. Aprotinin is an anti-fibrinolytic serine protease that has been shown to decrease blood product transfusion in CABG patients by nearly 39% [4]. However, further research demonstrated increased patient morbidity and mortality and it was subsequently removed from the market. Subsequent studies have shown increased transfusion requirements in cardiac surgery patients since its removal [5].

The effect of blood product transfusion on cardiac surgery patients has been well studied in the literature and associated with incremental morbidity as defined by renal failure, prolonged ventilator support, serious infection, cardiac complications or neurologic events for each unit transfused [6]. Recent data investigating patients undergoing coronary surgery associated intra-operative transfusion with a more than three-fold increase in 30-day mortality [7]. By comparison, less has been written about blood product transfusion in general thoracic procedures. However, the available data echoes much of what has been described in cardiac surgery. A large retrospective study by Ferraris, et al. analyzed 8728 patients undergoing non-vascular thoracic procedures. The study found an adverse, dose-dependent relationship between intra-operative blood transfusions and morbidity, pulmonary complications, sepsis, wound complications, and length of stay [8]. Given the increased utilization of blood products in cardiac patients and the associated risks of transfusion, it is important to identify patients at risk for bleeding complications following cardiac surgery.

Bleeding is a significant complication of open cardiac surgery, with an incidence ranging from approximately 5–15%. Cardiac surgery procedures are associated with significant alterations in physiology compared to non-cardiac thoracic surgery. Cardiopulmonary bypass (CPB) and exposure of the patient's blood to a non-endothelialized circuit has been associated with stimulation of both intrinsic and extrinsic coagulation pathways. To counteract this, patients are systemically heparinized. Cardiopulmonary bypass is likewise associated with platelet dysfunction and consumption secondary to platelet adhesion to surfaces, hemodilution, and platelet aggregation. CPB associated thrombocytopenia is further exacerbated by the process of intra-operative red blood cell salvage. After blood is aspirated from the surgical field, it is collected in a sterile reservoir and processed. The process of centrifugation separates red blood cells from platelets and plasma which are both removed as waste. The isolated red blood cells are then washed of debris in anticipation of reinfusion and therefore without a component of plasma or platelets. Following initiation of CPB, cardioplegia is achieved and patients are cooled for the cardioprotective effects of hypothermia which impair the enzymatic reactions of the coagulation cascade. In a recent study, aortic procedures were associated with the highest bleeding complication rate (15.0%) and isolated CABG with the lowest risk (5.1%). Complications from bleeding were associated with increased LOS and critical care utilization. Patients undergoing re-exploration for bleeding demonstrate larger increases in both LOS and days spent in critical care [9]. Naturally, the significant consumption of health-care resources following these complications translates to an incremental economic burden on both the patient and the healthcare system. In adult cardiac surgery

patients undergoing re-exploration for bleeding, a meta-analysis by Biancari, et al. sought to characterize sources of bleeding identified at the time of re-exploration. They collected data from 18 different studies, a total of 51497 patients where 2455 had undergone reoperation for bleeding/tamponade. Of these patients, surgical sources of bleeding were identified in 65.7% of patients in comparison to diffuse bleeding which can be more troublesome. Bleeding was further delineated as cardiac/bypass graft (40.9%) or mediastinal (pericardial, sternal, etc.) (27.0%). The predominant sites identified were: the body of the graft (20.2%), the sternum (17.0%), vascular suture lines (12.5%), the internal mammary harvest site (13.0%) and anastomoses (9.9%) [10]. Alternatively, diffuse bleeding, often attributed to coagulopathy secondary to anti-thrombotic agents can represent a significant challenge in achieving hemostasis with increased risk for residual blood loss and transfusion of blood products. Biancari et al., suggest that re-exploration for bleeding in cardiac surgery patients may be a preventable event with systematic evaluation of these areas and meticulous hemostasis prior to closure. Biosurgical hemostatic agents may serve as valuable adjuncts in this process and in the reduction of bleeding complications.

Topical hemostatic agents are useful adjuncts to reducing operative and post-operative bleeding and play an essential role in cardiothoracic surgery procedures. Patients presenting for cardiac surgery, as opposed to non-cardiac thoracic surgery, have likely been exposed to antiplatelet agents such as aspirin, clopidogrel, ticagrelor, apciximab or systemic anticoagulation agents such as warfarin or heparin (including intra-operative bolus dosing and subsequent reversal with protamine). Furthermore, patients undergoing cardiac procedures utilizing cardiopulmonary bypass are even more prone to bleeding and blood product transfusion [11]. In patients undergoing cardiothoracic surgery, non-surgical bleeding, defined as microvascular bleeding secondary to coagulopathy or capillary oozing can limit the utility of conventional surgical maneuvers in achieving hemostasis such as suture ligation, electrocautery, and surgical clips. The presence of non-surgical bleeding due to coagulopathy should be primarily directed at correction of the underlying abnormality but also presents an opportunity for the utilization of biosurgical hemostatic agents which can serve as useful adjuncts in gaining adequate hemostasis.

Selection of a hemostatic agent is often anecdotal and the following review seeks to clarify the available agents, their mechanisms, efficacy, and potential risks associated with their use. Conceptually, biosurgical hemostatic agents can be broadly classified as active, non-active, or a combination of both. A hemostatic agent is considered active if it contains agents directly involved in the clotting cascade such as thrombin in isolation or combined with a mechanical agent. In contrast, non-active agents contain no clotting factors, rather they provide a mechanical or synthetic seal to aid in achieving hemostasis. Lastly, there are a few available agents which utilize elements of both major categories that are known as flowable hemostatic agents.

2. Thrombin with or without gelatin carrier (Thrombin JMI®, Evithrom®, and Recothrom®)

Thrombin is an endogenous serum protease formed from its precursor prothrombin during activation of the intrinsic and extrinsic coagulation pathways. Thrombin is involved in the cleavage of fibrinogen to fibrin which polymerizes to serve as the basis of a hemostatic clot. Thrombin concurrently activates factor XIII which aids in fibrin crosslinking and strengthening the polymerized fibrin mesh to complete the clot atop the platelet plug, thereby achieving hemostasis. Historically, thrombin was isolated from bovine plasma with well documented reports of producing clinically significant antibody responses and hemorrhagic complications (excessive

post-operative bleeding and re-operation for bleeding) following patient exposure. Typically, patients develop antibodies to bovine factor V and Va, with more than half of patients producing auto-antibodies to human coagulation proteins, specifically factor V which can produce life-threatening bleeding [12]. In response to these concerns, both human derived and recombinant human thrombin have been developed. An unpublished phase III, prospective randomized controlled double-blinded study demonstrated that human-derived thrombin was as effective as bovine-derived thrombin in providing effective hemostasis. In this study, human-derived thrombin was applied to a gelatin sponge and produced effective hemostasis in 93.6% of cardiovascular surgery patients within 6 minutes and 61.7% within 3 minutes when applied to oozing or bleeding of mild intensity that could not be controlled with other surgical techniques [13]. Recombinant human thrombin was examined in a similar study that did not include cardiovascular surgery patients, but did include vascular surgery procedures and demonstrated comparable results regarding efficacy [14]. Both human and recombinant thrombin boast reduced immunologic response compared to bovine thrombin. Recombinant thrombin has the added benefit of minimizing the theoretical risk of viral transmission compared to human thrombin that has been pooled from donor plasma.

An active hemostatic agent such as thrombin is particularly useful in cardiac surgery patients where innate coagulation is impaired secondary to systemic heparinization while on cardiopulmonary bypass. It should be considered for mild to moderate non-surgical bleeding (not amenable to suture ligation or electrocautery) or in a surgically inaccessible area such as the dome of the left atrium or raw myocardial edges from a deep intra-myocardial coronary following bypass grafting [15]. In non-cardiac procedures, instillation of thrombin, complexed with fibrinogen, has also been described as an efficacious hemostatic therapy in the management of severe hemoptysis (>150 cc/12 hrs) [16]. Although bronchial artery embolization (BAE) is the treatment of choice in these patients, this therapy may be unavailable and endoscopic fibrinogen-thrombin instillation can serve as a bridge to embolization or as primary therapy in its absence.

Thrombin can be delivered alone via a spray applicator, with an inert carrier such as a gelatin sponge, or in combination with fibrinogen (fibrin glue). When paired with a gelatin component, the sponge is capable of absorbing 45 times its own weight, expanding to nearly 200% of its initial volume and facilitating concentration of coagulation factors in the area of concern. Like bovine derived thrombin, the gelatin is derived from porcine or bovine sources and carries with it a theoretical risk of antigenicity [17]. Caution should be used in applying gelatin sponge based thrombin products to open arterial bleeding due to potential risk for embolization. Of note, thrombin spray is contraindicated in treating massive or arterial bleeding and caution should be exercised to avoid entry into large blood vessels as it can produce severe intravascular clotting.

An essential consideration in using thrombin as a topical hemostat, depending on its source, is its proper preparation and storage. Both bovine derived and recombinant thrombin are available in powder form meaning they require mixing with saline to reconstitute into solution for application. They should be stored at room temperature [18, 19]. Conversely, human thrombin is packaged in solution and stored frozen. It may be left refrigerated for up to 30 days and can be stored at room temperature for no more than 24 hours per the manufacturer.

Products such as FloSeal deliver human thrombin (previously bovine) in a gelatin-based matrix consisting of collagen microgranules to produce swelling and tamponade upon contact with blood. Compared to other fibrin sealants, it requires blood as a source of fibrinogen. Similar to standalone pooled human thrombin, a theoretical risk of viral transmission exists with utilization of FloSeal despite

manufacturer efforts to reduce viral load during production. Regarding efficacy, a prospective randomized study compared FloSeal with Gelfoam thrombin after conventional surgical methods failed to control bleeding and demonstrated that FloSeal had superior hemostatic efficacy with a comparable safety profile to Gelfoam thrombin [20]. The aforementioned study group consisted of patients undergoing cardiac surgery and demonstrated that FloSeal achieved hemostasis in 94% of patients compared to 60% in the Gelfoam thrombin control group within 10 minutes. This difference was even more pronounced at 3 minutes where hemostasis was successful in 72% of the FloSeal group compared to 23% of the control. Similarly, a prospective randomized study by Nasso, et al. compared FloSeal to a control group of Surgicel or Gelfoam and included patients undergoing cardiac and thoracic aortic procedures. They demonstrated statistically higher rates of successful hemostasis, shorter times to hemostasis, and lower rates of post-operative transfusion of blood products, in the FloSeal group [21]. Common sites of cardiac bleeding treated in the study included coronary bypass anastomoses, cardiectomy sites, and anastomotic sites involving a prosthesis. The trial likewise found that FloSeal was associated with a statistically significant higher rate of successful hemostasis and shorter time to hemostasis when compared to the control group. Lower rates of blood product transfusion, incidence of re-exploration, and shorter ICU LOS were also appreciated in the group treated with FloSeal, although not statistically significant.

3. Fibrin sealants (Tisseel®)

Fibrin sealants first gained FDA approval in 1989 with the commercial release of Tisseel. Fibrin sealants generally contain separated components of freeze dried coagulation proteins, mainly fibrinogen and thrombin but also fibronectin. They are typically supplied in a dual syringe system that admix the two agents immediately prior to application. Fibrinogen, of course if a precursor to fibrin, the very foundation of the clot and is activated by thrombin, which serves as a catalyst when delivered simultaneously. Fibronectin on the other hand, is a high molecular weight, extracellular matrix glycoprotein that is physiologically deposited at the site of injury along with fibrin and serves as a sealant to aid in wound healing [22]. The mechanical strength of the sealant is driven by the concentration of fibrinogen and the relative concentration of thrombin determines the rate of clot formation [23]. By understanding the individual components of fibrin sealants, it is relatively easy to understand how these products mimic the final stages of wound healing and can be especially useful in patients with coagulopathies from systemic heparinization or other anticoagulants. One prospective randomized clinical trial of fibrin sealant versus more conventional hemostatic agents in cardiac surgery patients undergoing re-sternotomy or re-exploration identified significant shorter time to hemostasis and decreased post-operative blood loss compared to patients in the control group [24]. A randomized controlled trial in pediatric patients undergoing cardiac surgery with known significant coagulopathy demonstrated intraoperative use of fibrin sealant significantly reduced the amount of bleeding and transfusion of blood/blood products but also decreased the time to hemostasis [25]. Caution should be used with fibrin sealants, especially in coronary artery bypass grafting where they have been reported to be associated with increased risk of myocardial injury when applied intra-operatively. Lamm, et al., describe several cases of acute occlusion of coronary bypass grafts after administration of a fibrin sealant near anastomotic sites [26]. In each reported case, embolectomy at that time demonstrated fresh fibrin clot within the graft. The aforementioned study specifically examined Tissucol (Baxter) in aortocoronary bypass operations.

Applications in general thoracic surgery include intra-operative application of fibrin glue for the prevention of prolonged air leak in patients undergoing pulmonary resection. Air leak can arise from pulmonary parenchyma secondary to surgical manipulation or stapling. Generally, these parenchymal air leaks resolve spontaneously in a few days. Prolonged air leak (greater than 7 days) is associated with increased length of stay and may ultimately require further intervention. Studies exploring the efficacy of fibrin glue in the prevention of post-operative air leak have yielded mixed results to support their routine use [27, 28, 29].

4. Progel™

Progel (Bard) is a pleural air leak sealant consisting of polyethylene glycol and human serum albumin. It is the only FDA approved product to treat pleural air leaks in open thoracotomy, video-assisted, and robotic-assisted thoracic surgery. It is delivered in an adjustable syringe applicator providing either a stream for focal application to suture/staple lines or as a spray for increased surface area application. Progel's intrinsic elasticity makes it an attractive option for application to the pleural surface of the lung with an ability to tolerate re-expansion within 2 minutes of use [30]. A multicenter, prospective, randomized control trial demonstrated that intra-operative application of Progel resulted in fewer post-operative air leaks compared to the control group (65% vs. 86%, respectively) and shorter median length of stay (6 vs. 7 days, respectively) [31].

5. Evarrest®

Evarrest (Ethicon), is a fibrin sealant patch made of oxidized regenerated cellulose covered with thrombin (human derived) and fibrinogen. Contact of the powdery, active side of the patch with bleeding tissue causes thrombin to activate fibrinogen to fibrin and form a stable clot. The newly formed clot subsequently integrates with the patch's matrix design to assist in achieving hemostasis [32]. Advantages of Evarrest include that it is ready to use and bio-absorbable in about eight weeks. Contraindications to its use are comparable to other topical active agents in that it should not be applied to control bleeding from large vascular defects or intravascularly. Like most thrombin containing products, there is also risk of reaction to human blood products.

Evarrest has been successfully described in the control of major vascular injury during robotic assisted lobectomy and segmentectomy [33]. In the vignette provided by Gharagozloo et al., pulmonary artery/vein bleeding was controlled with direct pressure aided by a tightly rolled gauze sponge wrapped with an Evarrest fibrin sealant patch for 3 minutes while seeking to obtain proximal control. Should conversion to thoracotomy be required, pressure should continue to be held with a non-robotic instrument through the assistant port and allowing for complete removal of the robot from the field.

6. BioGlue®

BioGlue is a bovine serum albumin and glutaraldehyde tissue adhesive originally developed as an adjunct for hemostasis in cardiovascular surgery, gaining FDA approval in 2001. Similar to fibrin sealants, BioGlue's components are provided in two separate vials and delivered via a two-chambered syringe. The two agents are

mixed within the applicator tip immediately prior to application. When applied to tissue, the glutaraldehyde and albumin form strong covalent crosslinking with each other and the tissue at the site. The mechanical seal is not only independent of the patient's intrinsic clotting mechanisms but polymerizes rapidly and adheres to synthetic graft materials, making it an attractive option for controlling anastomotic bleeding in cardiac and vascular surgery when utilizing synthetic (eg Dacron®, Gore-tex®, and polyurethane) grafts or patches. BioGlue requires a bloodless field to adhere unlike some other agents, limiting its utility for active bleeding. It is generally applied to an anastomotic site in a thin layer prior to unclamping and restoration of perfusion [34]. Specific applications in cardiothoracic surgery include [35]:

Repair of type A aortic dissections. Specifically, the re-approximation of dissected aortic arch layers.

Aortic root reconstruction. Bovine albumin-glutaraldehyde may be used to seal the proximal anastomosis of the LVOT and replaced aortic root. This can be a particularly difficult suture line to place repair sutures.

Left ventricular apical cannulation. BioGlue can be applied when sewing a left ventricular assist device cannula cuff to the apex of the left ventricle, an area known to be especially prone to bleeding. Sealing this area with bovine albumin-glutaraldehyde is particularly useful as it will be under the stress of systolic left ventricular pressures and constant motion.

Right/left ventricular tear or rupture repair. BioGlue can be used in conjunction with patches of oxidized regenerated cellulose (Surgicel) to support fragile repairs of the right ventricle. It can also be used in traumatic ruptures of the left ventricle with bovine pericardium instead of Surgicel.

Post-infarction ventricular septal defect repair. BioGlue can be used to seal the overlapping Dacron patches of the repair together.

Ensuring hemostasis of suture lines. Particularly when applied to aortic aneurysm repairs, coronary anastomoses, and arteriotomies.

Criticism of BioGlue includes its low viscosity and difficulty controlling its application. This can be mitigated by injecting slowly and allowing the glue to partially set prior to completely expelling the mixture from the applicator tip. Various reports of adverse events have described early failure of coronary artery bypass grafts, leaking of glue through needle holes causing embolization, and anastomotic stricture impairing aortic growth [36, 37, 38].

7. Bone wax and Ostene ®

Median sternotomy is the most common approach in cardiac surgery. It can also be used in non-cardiac thoracic surgery to access the lower trachea, mainstem bronchi, tumors of the anterior mediastinum, and retrosternal goiters. The sternum is primarily made of spongy, cancellous bone encased in a rim of cortical bone. Its high surface area to volume ratio make it no surprise that it is highly vascular and prone to osseous hemorrhage. Bleeding from the median sternotomy of a heparinized patient can be challenging to control. Mechanical hemostatic devices such as bone wax can greatly aid in providing an impenetrable barrier. The most classic formulation described by Sir Victor Horsley in 1885 consisted of beeswax, almond oil and salicylic acid [39]. In current use, most surgeons know medical grade bone wax as a non-absorbable mixture of sterilized beeswax and a softening agent such as Vaseline or paraffin with isopropyl palmitate. In use, bone wax is quite malleable and can be worked to any desired consistency before application either manually or via submersion in warm, sterile solution before removing from the packaging. Despite its relative ease of use, there are several significant complications that one should consider.

First and foremost, experimental studies have demonstrated that bone wax significantly reduces the number of bacteria needed to initiate infection [40, 41]. For this reason, bone wax should never be utilized in a contaminated field. Secondly, bone wax is relatively inert, having been identified as remotely as 10 years following initial application. Histological studies have confirmed these suspicions on autopsy showing chronic granulomatous inflammation and foreign body reaction [42]. Given the above findings, it is understandable how bone wax could complicate healing of the sternum following median sternotomy by not only increasing risk of mediastinitis and osteomyelitis but impairing sternal edge apposition and inducing chronic inflammation.

Ostene, like bone wax, readily provides hemostasis without impairing bone healing. It was originally described in 2001 as an absorbable alternative to bone wax. Ostene is water-soluble and composed of hydrophilic alkylene oxide copolymers and is eliminated from the bone surface within 24–48 hours of application [43]. Several studies have compared Ostene to bone wax regarding sternal healing and favor its use to reduce sternal dehiscence and chronic inflammation [44, 45].

8. Surgicel®

The Surgicel family of products utilize oxidized, regenerated cellulose delivered in a loosely knit sheet, fibrillar sheet, or powder to aid in providing local hemostasis from capillary or minor venous bleeding. They are non-active mechanical hemostatic agents, meaning they do not contain specific coagulation factors and are best served in patients with intact innate coagulation (ie not on cardiopulmonary bypass). Once saturated with blood, Surgicel swells in to a brown-black gelatinous mass because of the decreased local pH initiating red cell lysis. It then serves as a scaffold for platelet aggregation and is generally absorbed completely within 4–6 weeks [46]. Surgicel has the added advantage of being bacteriostatic with some activity against MRSA reported [47, 48]. One underestimated feature of Surgicel is its ease of handling and non-adherence to instruments. However, like most hemostatic agents, caution should be exercised with its use. A key disadvantage of Surgicel is that by lowering the local pH, other active hemostatic agents may be rendered ineffective, namely thrombin [49]. Other authors have reported Surgicel remnants being misdiagnosed as an abscess, even mimicking mediastinitis that may be difficult or impossible to distinguish on imaging [50].

Surgicel is commonly applied in video-assisted thorascopic surgery during lymphadenectomy. In general, bleeding from lymphadenectomy can be avoided with careful dissection in avascular planes. However, occasional entry into the lymph node capsule introduces troublesome but non-life threatening bleeding that can easily be controlled using direct pressure with a topical hemostat such as Surgicel [51]. Typically bleeding improves following lymph node removal, but Surgicel may be left in the lymph node basin for any mild persistent bleeding.

9. Microporous polysaccharide hemospheres (Arista™ Absorbable Hemostat)

Arista AH (Bard) is a microporous polysaccharide hemosphere (MPH) powder derived from purified plant starch with FDA approval for not only cardiothoracic but vascular, gynecological, urology, orthopedic, general, plastic and ENT surgeries as well. Notably, Arista has been FDA approved as a cell saver, or autologous blood salvage circuit, compatible hemostat. Arista rapidly dehydrates blood, causing the

MPH particles to swell and concentrate blood solids such as platelets, RBCs, and coagulation proteins to form a gelled matrix [52]. This gelatinous matrix creates a scaffold for formation of the fibrin clot and provides a mechanical barrier to continued blood loss regardless of the patient's coagulation status. Arista is typically enzymatically degraded by serum amylases and cleared from the body within 24–48 hours per the manufacturer. To apply, the area of concern should have as much excess blood removed as possible, Arista should be liberally applied to the site of bleeding, wound-appropriate pressure should be held, and excess Arista should be removed by irrigation. Like most hemostatic agents, it should not be placed in blood vessels or when there may be risk of embolization. A retrospective study by Bruckner, et al., compared the application of topical Arista to historical agents including FloSeal, Gelfoam thrombin, or Surgicel in cardiothoracic procedures. They found a decreased time to hemostasis, decreased post-operative blood loss, and reduced blood product transfusion requirement within the first 48 hours post-operatively without any identified adverse events.

10. Conclusion

Bleeding in the cardiothoracic surgery patient is well studied. Specifically, cardiac surgery patients are frequently subject to systemic heparinization and potentially multiple antiplatelet medications. Thus, significantly increasing their risk for nonspecific bleeding refractory to traditional surgical hemostatic maneuvers. Complications from uncontrolled bleeding are both costly to the patient in terms of outcomes and economically to the healthcare system as well. Selection of the proper hemostatic adjunct can reduce time to hemostasis, blood product transfusion, and improve patient outcomes. Frequently, selection of a hemostatic agent has been constrained by anecdotal experience and limited knowledge of the diverse array of agents presently available. Choosing a hemostatic adjunct relies on understanding of its mechanism of action, indications for use, and knowledge of potential complications surrounding its use. In addition, many topical hemostats have also found novel uses in non-cardiac thoracic surgery to reduce post-operative air leaks and length of stay following pulmonary resection. The prepared surgeon has familiarized themselves with these agents and can anticipate opportunities for their deployment.

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References

- [1] Robich MP, Koch CG, Johnston DR, et al. Trends in blood utilization in United States cardiac surgical patients. *Transfusion*. 2015;55(4):805-814. doi:10.1111/trf.12903
- [2] Society of Thoracic Surgeons Blood Conservation Guideline Task Force, Ferraris VA, Ferraris SP, et al. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. *Ann Thorac Surg*. 2007;83(5 Suppl):S27-S86. doi:10.1016/j.athoracsur.2007.02.099
- [3] Society of Thoracic Surgeons Blood Conservation Guideline Task Force, Ferraris VA, Brown JR, et al. 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. *Ann Thorac Surg*. 2011;91(3):944-982. doi:10.1016/j.athoracsur.2010.11.078
- [4] Sedrakyan A, Treasure T, Elefteriades JA. Effect of aprotinin on clinical outcomes in coronary artery bypass graft surgery: a systematic review and meta-analysis of randomized clinical trials. *J Thorac Cardiovasc Surg*. 2004;128(3):442-448. doi:10.1016/j.jtcvs.2004.03.041
- [5] Walkden GJ, Verheyden V, Goudie R, Murphy GJ. Increased perioperative mortality following aprotinin withdrawal: a real-world analysis of blood management strategies in adult cardiac surgery. *Intensive Care Med*. 2013;39(10):1808-1817. doi:10.1007/s00134-013-3020-y
- [6] Koch CG, Li L, Duncan AI, et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. *Crit Care Med*. 2006;34(6):1608-1616. doi:10.1097/01.CCM.0000217920.48559.D8
- [7] Vlot EA, Verwijmeren L, van de Garde EMW, Kloppenburg GTL, van Dongen EPA, Noordzij PG. Intra-operative red blood cell transfusion and mortality after cardiac surgery. *BMC Anesthesiol*. 2019;19(1):65. Published 2019 May 4. doi:10.1186/s12871-019-0738-2
- [8] Ferraris VA, Davenport DL, Saha SP, Bernard A, Austin PC, Zwischenberger JB. Intraoperative transfusion of small amounts of blood heralds worse postoperative outcome in patients having noncardiac thoracic operations. *Ann Thorac Surg*. 2011 Jun;91(6):1674-80; discussion 1680. doi: 10.1016/j.athoracsur.2011.01.025. Epub 2011 Apr 23. PMID: 21514923.
- [9] Al-Attar N, Johnston S, Jamous N, et al. Impact of bleeding complications on length of stay and critical care utilization in cardiac surgery patients in England. *J Cardiothorac Surg*. 2019;14(1):64. Published 2019 Apr 2. doi:10.1186/s13019-019-0881-3
- [10] Biancari F, Kinnunen EM, Kiviniemi T, et al. Meta-analysis of the Sources of Bleeding after Adult Cardiac Surgery. *J Cardiothorac Vasc Anesth*. 2018;32(4):1618-1624. doi:10.1053/j.jvca.2017.12.024
- [11] Barnard J, Millner R. A review of topical hemostatic agents for use in cardiac surgery. *Ann Thorac Surg*. 2009;88(4):1377-1383. doi:10.1016/j.athoracsur.2009.02.092
- [12] Ortel TL, Mercer MC, Thames EH, Moore KD, Lawson JH. Immunologic impact and clinical outcomes after surgical exposure to bovine thrombin. *Ann Surg*. 2001;233(1):88-96. doi:10.1097/00000658-200101000-00014

- [13] Ethicon. Prescribing information: Evithrom; 2007.
- [14] Chapman WC, Singla N, Genyk Y, et al. A phase 3, randomized, double-blind comparative study of the efficacy and safety of topical recombinant human thrombin and bovine thrombin in surgical hemostasis. *J Am Coll Surg*. 2007;205(2):256-265. doi:10.1016/j.jamcollsurg.2007.03.020
- [15] Bracey A, Shander A, Aronson S, et al. The Use of Topical Hemostatic Agents in Cardiothoracic Surgery. *Ann Thorac Surg*. 2017;104(1):353-360. doi:10.1016/j.athoracsur.2017.01.096
- [16] de Gracia J, de la Rosa D, Catalán E, Alvarez A, Bravo C, Morell F. Use of endoscopic fibrinogen-thrombin in the treatment of severe hemoptysis. *Respir Med*. 2003 Jul;97(7):790-5. doi: 10.1016/s0954-6111(03)00032-5. PMID: 12854628.
- [17] Ham SW, Lew WK, Weaver FA. Thrombin use in surgery: an evidence-based review of its clinical use. *J Blood Med*. 2010;1:135-142. doi:10.2147/JBM.S6622
- [18] Pfizer Inc. Prescribing information: Thrombin-JMI, 2019.
- [19] Baxter. Prescribing information: Recothrom, 2019.
- [20] Oz MC, Cosgrove DM 3rd, Badduke BR, et al. Controlled clinical trial of a novel hemostatic agent in cardiac surgery. The Fusion Matrix Study Group. *Ann Thorac Surg*. 2000;69(5):1376-1382. doi:10.1016/s0003-4975(00)01194-2
- [21] Nasso G, Piancone F, Bonifazi R, et al. Prospective, randomized clinical trial of the FloSeal matrix sealant in cardiac surgery. *Ann Thorac Surg*. 2009;88(5):1520-1526. doi:10.1016/j.athoracsur.2009.07.014
- [22] Pankov R, Yamada KM. Fibronectin at a glance. *J Cell Sci*. 2002;115(Pt 20):3861-3863. doi:10.1242/jcs.00059
- [23] Achneck HE, Sileshi B, Jamiolkowski RM, Albala DM, Shapiro ML, Lawson JH. A comprehensive review of topical hemostatic agents: efficacy and recommendations for use. *Ann Surg*. 2010;251(2):217-228. doi:10.1097/SLA.0b013e3181c3bcca
- [24] Rousou J, Levitsky S, Gonzalez-Lavin L, et al. Randomized clinical trial of fibrin sealant in patients undergoing resternotomy or reoperation after cardiac operations. A multicenter study. *J Thorac Cardiovasc Surg*. 1989;97(2):194-203.
- [25] Codispoti M, Mankad PS. Significant merits of a fibrin sealant in the presence of coagulopathy following paediatric cardiac surgery: randomised controlled trial. *Eur J Cardiothorac Surg*. 2002;22(2):200-205. doi:10.1016/s1010-7940(02)00271-3
- [26] Lamm P, Adelhard K, Juchem G, et al. Fibrin glue in coronary artery bypass grafting operations: casting out the Devil with Beelzebub?. *Eur J Cardiothorac Surg*. 2007;32(4):567-572. doi:10.1016/j.ejcts.2007.07.020
- [27] Fleisher AG, Evans KG, Nelems B, Finley RJ. Effect of routine fibrin glue use on the duration of air leaks after lobectomy. *Ann Thorac Surg*. 1990 Jan;49(1):133-4. doi: 10.1016/0003-4975(90)90371-c. PMID: 2297261.
- [28] Fabian T, Federico JA, Ponn RB. Fibrin glue in pulmonary resection: a prospective, randomized, blinded study. *Ann Thorac Surg*. 2003 May;75(5):1587-92. doi: 10.1016/s0003-4975(02)04994-9. PMID: 12735583.
- [29] Gagarine A, Urschel JD, Miller JD, Bennett WF, Young JE. Effect of fibrin glue on air leak and length of hospital

- stay after pulmonary lobectomy. *J Cardiovasc Surg (Torino)*. 2003 Dec;44(6):771-3. PMID: 14994744.
- [30] C.R. Bard. Prescribing information: Progel, 2018.
- [31] Allen MS, Wood DE, Hawkinson RW, Harpole DH, McKenna RJ, Walsh GL, Vallieres E, Miller DL, Nichols FC 3rd, Smythe WR, Davis RD; 3M Surgical Sealant Study Group. Prospective randomized study evaluating a biodegradable polymeric sealant for sealing intraoperative air leaks that occur during pulmonary resection. *Ann Thorac Surg*. 2004 May;77(5):1792-801. doi: 10.1016/j.athoracsur.2003.10.049. PMID: 15111188.
- [32] Ethicon. Prescribing information: Evarrest, 2018.
- [33] Gharagozloo F, Meyer M. Technique of robotic lobectomy III: control of major vascular injury, the 5 “P”s. *Mini-invasive Surg* 2020;4:57. <http://dx.doi.org/10.20517/2574-1225.2020.44>
- [34] Bhamidipati CM, Coselli JS, LeMaire SA. BioGlue in 2011: what is its role in cardiac surgery?. *J Extra Corpor Technol*. 2012;44(1):P6-P12.
- [35] Zehr KJ. Use of bovine albumin-glutaraldehyde glue in cardiovascular surgery. *Ann Thorac Surg*. 2007;84(3):1048-1052. doi:10.1016/j.athoracsur.2007.01.012
- [36] Khan H, Chaubey S, Desai J. Early failure of coronary artery bypass grafts: an albumin cross-linked glutaraldehyde (BioGlue) related complication. *J Card Surg*. 2011;26(3):264-266. doi:10.1111/j.1540-8191.2011.01208.x
- [37] LeMaire SA, Carter SA, Won T, Wang X, Conklin LD, Coselli JS. The threat of adhesive embolization: BioGlue leaks through needle holes in aortic tissue and prosthetic grafts. *Ann Thorac Surg*. 2005;80(1):106-111. doi:10.1016/j.athoracsur.2005.02.004
- [38] LeMaire SA, Schmittling ZC, Coselli JS, et al. BioGlue surgical adhesive impairs aortic growth and causes anastomotic strictures. *Ann Thorac Surg*. 2002;73(5):1500-1506. doi:10.1016/s0003-4975(02)03512-9
- [39] Zhou H, Ge J, Bai Y, Liang C, Yang L. Translation of bone wax and its substitutes: History, clinical status and future directions. *J Orthop Translat*. 2019;17:64-72. Published 2019 Apr 11. doi:10.1016/j.jot.2019.03.005
- [40] Nelson DR, Buxton TB, Luu QN, Rissing JP. The promotional effect of bone wax on experimental *Staphylococcus aureus* osteomyelitis. *J Thorac Cardiovasc Surg*. 1990;99(6):977-980.
- [41] Johnson P, Fromm D. Effects of bone wax on bacterial clearance. *Surgery*. 1981;89(2):206-209.
- [42] Sudmann B, Bang G, Sudmann E. Histologically verified bone wax (beeswax) granuloma after median sternotomy in 17 of 18 autopsy cases. *Pathology*. 2006;38(2):138-141. doi:10.1080/00313020600561732
- [43] Ostene Bone Hemostasis Material [instructions for use]. Los Angeles, Calif: Ceremed Inc. PN-26 CF607 Rev. H 2011.
- [44] Vestergaard RF, Jensen H, Vind-Kezunovic S, Jakobsen T, Søballe K, Hasenkam JM. Bone healing after median sternotomy: a comparison of two hemostatic devices. *J Cardiothorac Surg*. 2010;5:117. Published 2010 Nov 24. doi:10.1186/1749-8090-5-117
- [45] Vestergaard RF, Nielsen PH, Terp KA, Søballe K, Andersen G, Hasenkam JM. Effect of hemostatic material on sternal healing after

cardiac surgery. *Ann Thorac Surg*. 2014;97(1):153-160. doi:10.1016/j.athoracsur.2013.08.030

[46] Frantz VK. Absorbable cotton, paper and gauze: (oxidized cellulose). *Ann Surg*. 1943;118(1):116-126. doi:10.1097/00000658-194311810-00010

[47] Scher KS, Coil JA Jr. Effects of oxidized cellulose and microfibrillar collagen on infection. *Surgery*. 1982;91(3):301-304.

[48] Spangler D, Rothenburger S, Nguyen K, Jampani H, Weiss S, Bhende S. In vitro antimicrobial activity of oxidized regenerated cellulose against antibiotic-resistant microorganisms. *Surg Infect (Larchmt)*. 2003;4(3):255-262. doi:10.1089/109629603322419599

[49] Achneck HE, Sileshi B, Jamiolkowski RM, Albala DM, Shapiro ML, Lawson JH. A comprehensive review of topical hemostatic agents: efficacy and recommendations for use. *Ann Surg*. 2010;251(2):217-228. doi:10.1097/SLA.0b013e3181c3bcca

[50] Kaneyuki D, Mogi K, Sakata T, Takahara Y. Surgicel® packing remnants mimicking mediastinitis after adult cardiac surgery. *Interact Cardiovasc Thorac Surg*. 2018;26(6):1035-1036. doi:10.1093/icvts/ivy006

[51] White A, Swanson SJ. How to deal with benign hilar or interlobar lymphadenopathy during video-assisted thoracic surgery lobectomy-case report series. *J Vis Surg*. 2016;2:22. Published 2016 Jan 27. doi:10.3978/j.issn.2221-2965.2016.01.04

[52] Arista AH Absorbable Hemostatic Particles: The latest generation in hemostasis from BD. https://www.crbard.com/CRBard/media/ProductAssets/DavolInc/PF10133/en-US/PF10133_AristaBrochure-2018.pdf. Accessed July 27, 2020.