

Review Article

Hemostasis in the Surgical Field

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Abstract: Hemostatic mechanisms are an integral part of the human physiology. Traditionally divided into intrinsic and extrinsic arms, the coagulation cascade converges, through the interactions of the many various factors, at a standard element—thrombin. As a consequence, variety of various agents is developed to supplement this common, critical step to assist surgical hemostasis. Intraoperative interventions most ordinarily include sutures and heat-generating cauterly devices; however, these methods are sometimes insufficient or inappropriate for a selected procedure or anatomic location, resulting in the event of other adjunctive therapies, including topical hemostats. Topical hemostatic agents generally act as active, passive, and combinations therapies, counting on their individual composition and mode of action. We offer a quick review of the traditional coagulation cascade, including critical points, followed by a discussion of surgical strategies and adjunctive therapies want to achieve surgical hemostasis and concluding with a discussion of topical thrombins.

Keywords: Hemostasis, thrombin, topical hemostat, coagulation.

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INTRODUCTION

Despite advances in surgical technique, excess bleeding remains a serious complication related to surgery and contributes to poor clinical outcomes. Risk factors for perioperative bleeding include those associated with patient variables, iatrogenic phenomena, primary complications, or the precise surgery or technique. For example, the danger of bleeding is increased in patients taking anticoagulants or antiplatelet agents, those with underlying intrinsic bleeding disorders, or those with specific comorbidities, including diabetic mellitus, hypertension, and renal insufficiency [1, 2] Further, primary complications of surgery, such as infection, can lead to the development of disseminated intravascular coagulation and widespread diffuse bleeding [1]. Iatrogenic factors, including poor surgical technique, hypothermia, acidosis, and hemodilution (infusion of huge volumes of plasma-poor fluids) also contribute to the risk of perioperative bleeding [1].

Surgical variables are prime determinants of the danger of intraoperative and perioperative bleeding [3]. Indeed, spinal surgeries and vascular procedures require the disruption of highly vascularized areas, and arteria coronary bypass grafting requires the utilization of cardiopulmonary bypass, which, by virtue

of heparinization, cannulation, and hemodilution, is related to high rates of bleeding. Anatomic and structural concerns also contribute to this specific risk of bleeding during surgery. Certain situations, such as friable tissue, reoperative adhesions, diffuse soft tissue bleeding, and bone bleeding are often not amenable to traditional surgical techniques (e.g., cauterly and suture ligation) used to control bleeding [3].

Intraoperative and perioperative bleeding are associated with poor outcomes. In one study, mortality rates increased from 8% for patients who experienced a blood loss of less than 500 ml during surgery to 42.9% for those who lost more than 2000 ml [4]. In addition to its effects on clinical outcomes, perioperative bleeding results in increased direct and indirect costs.⁵ These costs include those related to lost work productivity, obtaining blood products for transfusion, extended procedure times, prolonged length of hospital and intensive care unit stays, and significant requirements in terms of clinical and staff resources related to reoperation.

We provide a brief overview of intrinsic hemostatic mechanisms and selected interventions that can be used to promote and maintain hemostasis in the intraoperative and perioperative setting.

Table-1: Interventions to Minimize the Risk or Implications of Intraoperative and Perioperative Bleeding [1, 10–14]

| Type | Intervention |
|--|--|
| Preoperative measures | Administration of erythropoiesis-stimulating agents Autologous blood donations Consideration of individualized risk: benefit ratio for proceeding with surgical interventions Discontinuation of anticoagulants, including herbal medicines Establishment of evidence-based institution wide guidelines regarding optimal (lower) thresholds for red blood cell transfusions Minimization of blood sampling |
| Surgical techniques | Application of heat by using electric current through bipolar and monopolar electrosurgical devices (e.g., Liga Sure vessel-sealing system or vessel-welding systems). Application of heat by using ignition of gas (e.g., argon beam coagulator) Direct pressure. Mechanical devices such as endostaplers, hemoclips, and intracorporeal devices Suture ligation. Use of minimally invasive techniques such as endoscopic, laparoscopic, or percutaneous vascular procedures, or robotic-assisted procedures. Vessel coaptation through Harmonic frequency devices such as Harmonic shears or Harmonic scalpels. Vessel coaptation by ultrasonic cavitation with ultrasonic aspirator |
| Intraoperative and postoperative acidosis a measures | Correction of hypothermia Correction of |

Administration of systemic or topical hemostatic agents Transfusion of blood products with avoidance of hemodilution

Intrinsic Hemostatic Mechanisms

Hemostasis is a complex process that requires coordinated activation of platelets and plasma-clotting factors, ultimately to form a stable, cross-linked, platelet-fibrin clot [6]. This process can be separated into primary and secondary hemostasis. Primary hemostasis occurs in response to release of vasoactive and platelet-activating factors from injured blood vessels or other tissues. These substances cause temporary local contraction of vascular smooth muscle, also as platelet adherence and activation at the location of injury, to make a soft aggregate plug, followed by platelet activation.

In secondary hemostasis, activated platelets secrete serotonin, prostaglandin, and thromboxane to maintain local vasoconstriction, while activation of the coagulation cascade by tissue factor release from injured tissue ultimately results in fibrin formation, as well as cross-linking and stabilization of the platelet plug [6].

The coagulation cascade is dependent on sequential enzymatic reactions among circulating coagulation factors [6]. These factors are produced by the liver and circulate in an inactive form until the coagulation cascade is started. The central players within the coagulation cascade include activated factors X and V and thrombin (factor II) [7]. Factor V is situated at a particularly important point within the coagulation cascade—the convergence within the intrinsic and extrinsic coagulation pathways (Figure 1) [8]. Thus, the presence of any substance that could inhibit factor V can theoretically exert a profound effect on the generation of thrombin—the final protein within the coagulation cascade responsible for the generation

of fibrin. In fact, factor V inhibitors can cause inactivation or depletion of factor V; associated clinical sequelae, though rare, range from asymptomatic abnormalities in laboratory measures of coagulation to bleeding and coagulopathy [9].

Therapeutic Hemostatic Strategies

Several sorts of interventions are often used to promote hemostasis within the intraoperative and perioperative periods. These include preventive measures, technical considerations, transfusion of selected blood products, or administration of systemic or topical hemostatic agents (Table 1).1, [10-14].

Preventive Measures

Preoperative strategies that reduce the risk of bleeding are associated with improved outcomes in patients undergoing surgery. For patients engaging in elective procedures, use of antiplatelet agents, anticoagulants, and nonsteroidal antiinflammatory drugs should be discontinued well before the surgical date [10]. For those receiving these drugs on an ongoing basis who have more immediate needs for surgical intervention, consideration should be given to delaying the surgical procedure for several days to allow for discontinuation of these drugs and restoration of hemostatic mechanisms—provided that patient safety can be maintained in the interim.

Other preoperative strategies may not reduce the risk of bleeding but can reduce the need for blood transfusions [10]. These strategies include minimization of blood sampling and use of erythropoiesis-stimulating agents for those with defective erythropoiesis due to renal failure or marrow suppression. Proper selection of candidates for surgical procedures is paramount; consideration of the risk-benefit ratio is required for any surgical procedure, particularly in patients with acquired or inherited bleeding diatheses [15]. For example, some patient populations may require ongoing

and uninterrupted intensive antiplatelet therapy (e.g., patients with recent placement of drug eluting coronary artery stents) [16]. Unless the surgical indication is urgent, medical management should be elected until the procedure can be performed safely.

Technical Considerations

Traditional methods, such as suture ligation and electrocautery, are critical to achieve hemostasis, but may not be appropriate for all types of surgical terrains or in the presence of diffuse bleeding from soft or friable tissues [3].

Minimally invasive procedures, including endoscopic, laparoscopic, and percutaneous vascular procedures, are related to much lower rates of bleeding in comparison with open surgical procedures [11, 12]. Further, some evidence suggests that robotic-assisted surgical techniques can result in lower rates of intra- operative and perioperative bleeding [11, 12].

Patient conditions should be monitored closely during the surgical procedure and in the immediate postoperative period, as both hypothermia and acidosis can slow the enzymatic reactions of the coagulation cascade and thereby increase the risk of bleeding [1].

Blood Products

Therapies to correct intrinsic or induced coagulopathies can help prevent or stop perioperative bleeding. Transfusion of fresh frozen plasma or platelets is that the mainstay of therapy for relative deficiencies or depletion of coagulation factors or platelets, respectively; factor concentrates or cryoprecipitate are often administered to patients with specific clotting factor deficiencies [1]. Transfusion of packed red blood cells can help maintain lost oxygen-carrying capacity due to hemorrhage but does not correct the underlying deficiency in coagulation capacity.

CONCLUSION

Hemostatic capacity is dependent on multiple variables, including those related to the patient and the surgical procedure, as well as iatrogenic phenomena. Although transfusion of blood products and use of systemic hemostatic agents have been employed with some success, these measures are limited, costly, and carry the risk of various complications. By contrast, topical agents provide a strategy for directed hemostasis through mechanical means and/or manipulation of the coagulation cascade. The choice of topical hemostatic agent must take into account the risks and benefits to the individual patient. Although the utility of topical thrombin products is undeniable, questions remain regarding the risks associated with each formulation.

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Appendix-1: Topical Hemostatic Agents [11, 13, 21, 22]

| Class | Agents |
|-----------------|---|
| Adhesives | Two-component polyethylene glycol (PEG) polymers Bovine albumin plus glutaraldehyde Cyanoacrylates |
| Fibrin sealants | Bovine collagen, thrombin (Vitagel; Orthovita, Malvern, PA). Fibrinogen, aprotinin, human thrombin, bovine fibrinolysis inhibitor (Tisseel VH; Baxter Healthcare Corp., Westlake Village, CA) Fibrinogen, human thrombin (Evicel; Johnson & Johnson Wound Management, Somerville, NJ) Patient fibrinogen, thrombin (Cryoseal; Thermo Genesis Corp., Rancho Cordova, CA) [Not available in the United States] Thrombin and fibrinogen spray (CoSeal; Baxter Healthcare Corp., Hayward, CA) |
| Flowables | Gelatin granules/thrombin (Surgiflo; Johnson & Johnson Wound Management, and FloSeal; BaxterHealthcare Corp., Fremont, CA) |
| Mechanicals | Bovine collagen (multiple products) Oxidized regenerated cellulose (Surgicel; Johnson & Johnson Wound Management) Polysaccharide spheres (Arista AH; Medafor, Inc., Minneapolis, MN) Porcine gelatin (Gelfoam; Pharmacia & Upjohn Company Division of Pfizer Inc., New York, NY, and Surgifoam; Johnson & Johnson Wound Management) |
| Sealants | Microfibrillar bovine collagen-fibrin (CoStasis; Cohesion Technologies, Inc., Palo Alto, CA) PEG hydrogel (CoSeal; Baxter Healthcare Corp., Hayward, CA, and DuraSeal; Confluent Surgical, Inc., Waltham, MA) |
| Thrombin | Bovine (Thrombin-JMI; King Pharmaceuticals, Inc., Bristol, TN) Human pooled plasma (Evithrom; Johnson & Johnson Wound Management) Recombinant (Recothrom; ZymoGenetics, Inc., Seattle, WA) |

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