Bleeding and management of coagulopathy

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Bleeding after cardiac surgery remains a significant problem, increasing both length of stay and mortality, and is caused by multiple factors including dilutional changes, ongoing fibrinolysis, and platelet dysfunction. The evaluation of coagulopathy is problematic because of the long turnaround time of standard coagulation tests. Algorithms involving point of care testing, including thromboelastography and thromboelastometry, have been published; all have the potential to reduce transfusion requirements. Massive transfusion coagulopathy that occurs in trauma can also be seen in complex aortic surgery and other massive bleeding patients and should prompt consideration of a transfusion protocol involving fixed ratios of fresh frozen plasma, platelets, and red blood cells. Pharmacologic agents such as antifibrinolytics are commonly administered, but a multimodal approach to management is important. Recombinant and purified coagulation products are being studied and provide clinicians specific agents to treat targeted deficiencies. A general multi-modal approach is required and recommendations are made for the management of bleeding and coagulopathy in cardiac surgical patients. (J Thorac Cardiovasc Surg 2011;142:662-7)

Approximately 5% to 7% of patients undergoing cardiac surgery lose more than 2 L of chest tube drainage during the first 24 hours postoperatively, and up to 5% require reexploration for bleeding, resulting in an increased length of stay and higher mortality.[1-3] Multiple causes, including activation of the coagulation, fibrinolytic, and inflammatory pathways, dilutional changes, hypothermia, and other surgical factors, contribute to this problem. Bleeding may also be further exacerbated by perioperative use of various anticoagulants, including heparin, thrombin inhibitors, and platelet inhibitors. There is a complex equilibrium among red blood cells (RBCs), platelets, coagulation factors, natural inhibitors of coagulation, and the fibrinolytic system that is significantly altered in cardiac surgery. Therefore, simple replacement of blood volumes may not always be effective. This review will focus on current therapies to treat bleeding after cardiac surgery. An overview of the coagulation process, with potential sites of intervention, is presented in Figure 1.

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LABORATORY TESTING AND USE OF ALGORITHMS

Most studies demonstrate that transfusion algorithms reduce the need for platelets, fresh-frozen plasma (FFP), or cryoprecipitate. However, any test that prevents empirical administration likely will reduce this need.[4] Most algorithms suggest transfusion when bleeding is accompanied by a prothrombin time/activated partial thromboplastin time more than 1.5 times normal, a platelet count less than 50 to 100,000, or fibrinogen concentration less than 100 mg/dL (1 g/L).[5] Measurement of D-dimers or fibrin degradation products is also frequently done to see whether fibrinolysis is occurring. Because most laboratory testing is slow, point of care testing has been the focus of research as recently reviewed.[5] Thromboelastography and rotational thromboelastometry are useful to determine fibrinolysis, and thromboelastography or rotational thromboelastometry-based algorithms have been shown to decrease blood product use. However, the machines require quality-control follow-up and are not available everywhere. Platelet function testing has also been reported but is problematic because most tests need a relatively high platelet count to work and may not be applicable to post-cardiopulmonary bypass (CPB) platelet dysfunction.

TRANSFUSION THERAPY FOR BLEEDING

Volume replacement after cardiac surgery with critical bleeding may require large fluid volumes. RBC transfusions provide oxygen-carrying capacity, but crystalloids, colloids, and RBCs provide neither coagulation factors nor platelets and can exacerbate coagulopathy by dilution. Thrombocytopenia often follows volume replacement, and the inability to evaluate platelet function complicates matters. Severe bleeding requires FFP, platelets, cryoprecipitate, and potentially factor concentrates (eg, fibrinogen and prothrombin complex concentrates [PCCs]) to restore circulating levels of hemostasis factors. After massive transfusion therapy, hypothermia and acidosis frequently occur, further complicating bleeding. Blood temperature and pH must be monitored and corrected during any ongoing transfusion effort. Perioperative blood conservation guidelines in cardiac surgery have been published, recommending institution-specific

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Abbreviations and Acronyms

CPB = cardiopulmonary bypass
FFP = fresh-frozen plasma
FXIII = Factor XIII
PCC = prothrombin complex concentrate
RBC = red blood cell
rFVIIa = recombinant activated factor VIIa
TXA = tranexamic acid

transfusion algorithms, point-of-care testing, and a multimodal approach to coagulopathy treatment.[6]

Massive transfusion coagulopathy, generally defined as 10 RBC units or more transfused in a 24-hour period, is best studied from trauma literature. Because several blood volumes may be replaced in these patients by the time results are available, laboratory testing is problematic. As a result, transfusion protocols have been developed where fixed doses of FFP and platelets are administered after a specific number of RBC units have been given, often in a 1:1:1 ratio.[4] Whether these fixed ratios prevent coagulopathy is not established in cardiac surgery, but in trauma and in noncardiac surgical battlefield conditions, fixed transfusion ratios improve survival.[7,8] Thus, with life-threatening hemorrhage, transfusion of fixed ratios of RBCs, FFP, and platelets should be administered when situations analogous to trauma situations are encountered, such as coagulopathy after complex aortic surgery.

ANTIFIBRINOLYTIC AGENTS: LYSINE ANALOGS

The lysine analogs epsilon aminocaproic acid and tranexamic acid (TXA) competitively inhibit activation of plasminogen to plasmin, an enzyme that degrades fibrin clots. TXA also inhibits plasmin at higher doses, and most studies reported in cardiac surgery involve TXA. Epsilon aminocaproic acid does not consistently reduce transfusion requirements or surgical reexploration.[9] Multiple meta-analyses of randomized controlled trials consistently report a decrease in bleeding with these agents, but data regarding safety are limited. Postoperative convulsive seizures at one institution were reported to increase from 1.3% to 3.8% after cardiac surgery, temporally coincident with high-dose TXA.[10] In 24 patients with postoperative seizures, all received high doses of TXA intraoperatively from 61 to 259 mg/kg, mean ages were 70 years, and 21 of 24 had open-chamber procedures.[10] Although these agents are typically used during CPB, additional use of them should be considered postoperatively with evidence of ongoing fibrinolysis.

ANTIFIBRINOLYTIC AGENTS: APROTININ

Aprotinin, a polypeptide serine protease inhibitor, inhibits plasmin and other serine proteases. In cardiac surgery, multiple randomized, placebo-controlled trials reported that aprotinin reduced bleeding and allogeneic transfusions.[11] However, recent reports from observational databases and one randomized study questioned the safety of aprotinin.[12]

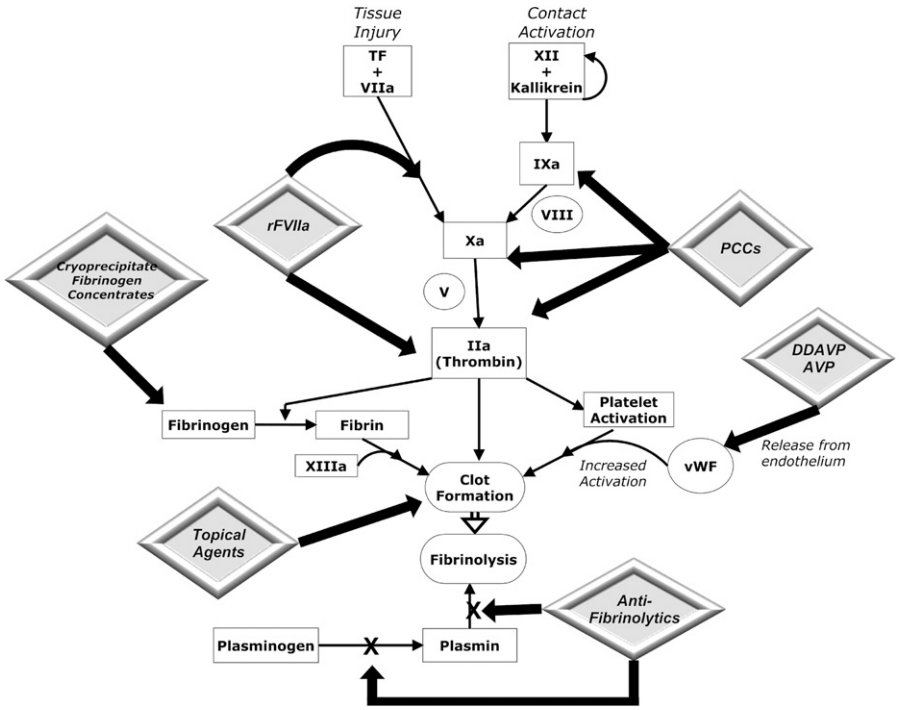

FIGURE 1. An overview of clot formation, demonstrating points of intervention. *TF,* Tissue factor; *rFVIIa,* recombinant factor VII; *PCC,* prothrombin complex concentrates; *AVP,* arginine vasopressin; *vWF,* von Willebrand factor.

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