Optimizing Perioperative Blood and Coagulation Management During Cardiac Surgery

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KEYWORDS

• Cardiac surgery • Cardiopulmonary bypass • Hemostasis • Bleeding • Coagulation
• Transfusion

KEY POINTS

- Bleeding and transfusion in cardiac surgery are common and associated with poorer outcomes.
- Hemostasis in cardiac surgery with cardiopulmonary bypass is complex and influenced by major surgical trauma, cardiopulmonary bypass–associated coagulopathy, anticoagulation management, and additional perioperative factors.
- Patient blood management aims to improve outcomes by the prediction, prevention, monitoring, and treatment of bleeding and transfusion.
- Patient blood management includes many options to improve outcome and should be combined in a multidisciplinary approach.

INTRODUCTION

Major blood loss remains common in cardiac surgery with an incidence of up to 15%.[1,2] Bleeding leads to anemia and blood product transfusion, and can lead to the need for rethoracotomy, which are all independently associated with an adverse outcome (**Fig. 1**).[3,4] Patient blood management is the bundle of measures to

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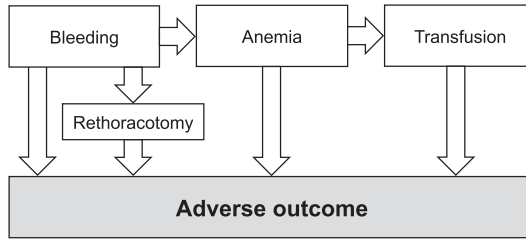

Fig. 1. The relationship between bleeding, rethoracotomy, anemia, transfusion, and outcome.

encounter bleeding and prevent unnecessary transfusion aiming to improve patient outcome.[5] This article focuses on these blood conservation strategies in cardiac surgery. For the understanding of patient blood management in this setting, the pathophysiology of coagulopathy during these procedures, including the effect of cardiopulmonary bypass (CPB), is first discussed. Thereafter, the most important patient blood management strategies are reviewed.

PATHOPHYSIOLOGY OF COAGULOPATHY IN CARDIAC SURGERY

During cardiac surgery with CPB, the coagulation system faces major alterations. First, patients undergo major surgical trauma including sternotomy, venesection, and arterial and venous cannulation, which all lead to hemostasis activation.[6] Second, blood flows over the large surface of the tubing of the heart lung machine, which despite heparinization is highly thrombogenic.[7]

During CPB several mechanisms lead to coagulopathy, as shown in **Fig. 2**. First, fibrinogen binds to the nonbiological surface of the extracorporeal circuit, which causes platelet activation.[8] Second, leukocytes that come in contact with the

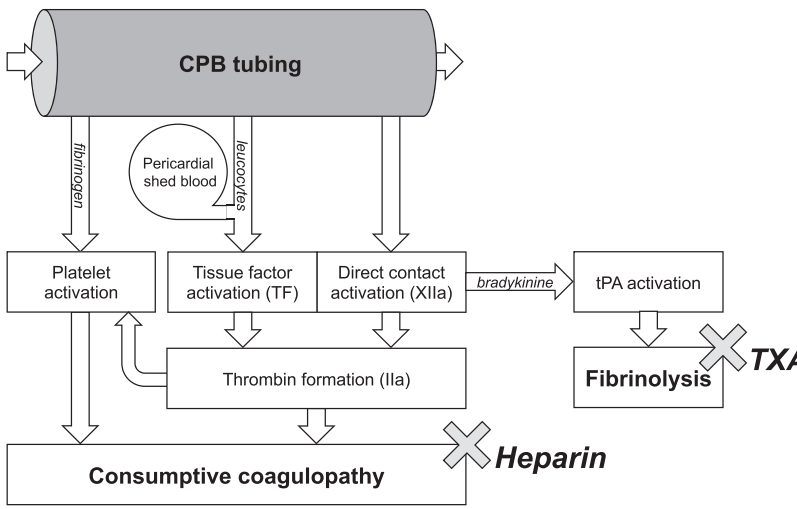

Fig. 2. Hemostasis activation during CPB leading to consumptive coagulopathy and fibrinolysis. IIa, coagulation factor IIa (eg, thrombin, XIIa is coagulation factor XIIa); TF, tissue factor; tPA, tissue plasminogen activator; TXA, tranexamic acid or other antifibrinolytic agent.

pericardial cavity and CPB are activated and express tissue factor, activating the extrinsic coagulation cascade.[9] Furthermore, the tubing of the heart lung machine causes activation of factor XII, which initiates the intrinsic coagulation cascade.[10] Both coagulation pathways lead to thrombin formation and the consumption of coagulation factors (consumptive coagulopathy). Thrombin is a potent platelet activator that causes further thrombocyte degranulation, enhancing hemostasis activation.[11]

Heparin is administrated during bypass to prevent consumptive coagulopathy and the formation of (micro)-thrombi, with subsequent organ infarction. Also, the extracorporeal circulation is nowadays usually covered with a biocompatible heparin coating to damp the hemostatic and immunologic response during bypass.[12]

Activation of the intrinsic coagulation cascade further leads to the formation of active kallikrein that, in turn, enhances the formation of bradykinin.[13] Bradykinin activates tissue plasminogen activator, cleaving plasminogen to plasmin, which breaks down freshly formed clots, for example, fibrinolysis.[14] Usually bradykinin is inactivated in the pulmonary circulation; however, during extracorporeal circulation the lung circulation is bypassed leading to accumulation of bradykinin. This is the cause for massive fibrinolysis in cardiac surgery, which is usually counteracted by the administration of an antifibrinolytic drug (ie, tranexamic acid or Ɛ-aminocaproic acid).

After CPB, the anticoagulant effect of heparin needs to be reversed to restore hemostasis and prevent postoperative bleeding. Protamine is used for this purpose, which binds and inactivates heparin in a 1:1 ratio. However, over the last decades it has become more apparent that protamine itself has several anticoagulant properties.[15] When in excess, protamine inhibits platelet function, causes coagulation factor dysfunction, and enhances fibrinolysis. Therefore, adequate protamine management is important for optimal clot formation after bypass.[16]

Finally, other perioperative disturbances in cardiac surgery can lead to coagulopathy and need to be optimized to prevent a nonsurgical cause of bleeding. Inadequate tissue perfusion leads to anaerobic metabolism and lactate acid formation, which causes acidosis. Acidosis impairs clot formation and adequate hemodynamic management, especially in the cardiac patient with left ventricular dysfunction, is therefore important to optimize hemostasis.[17] However, when excessive fluid administration is used to improve tissue perfusion the prohemostatic components are diluted, impairing hemostasis.[18] Therefore (excessive) hemodilution should be prevented. Furthermore, red blood cell transfusion can lead to better tissue oxygenation, but also to the dilution of coagulation factors. Additionally, packed red blood cell transfusion can cause hypocalcemia by the concurrent administration of citrate.[17] Because calcium (coagulation factor IV) is an important factor in the activation of clotting factors in the coagulation cascade, a calcium debit should be supplemented to prevent coagulopathy. Finally, hypothermia inhibits enzyme activity (reversibly) and, therefore, temperature management is important to optimize clotting after surgery.[17] The most important factors affecting hemostasis in cardiac surgery are summarized in **Box 1**.

PATIENT BLOOD MANAGEMENT

The goal of patient blood management is to reduce bleeding and unnecessary blood transfusion, with the subsequent aim to prevent unfavorable outcomes. This is a multimodal approach comprising the identification of the patients at risk (prediction) as well as the prevention, monitoring, and treatment of microvascular bleeding caused by coagulopathy. **Fig. 3** provides an overview of the individual major patient blood management modalities in cardiac surgery. Each intervention attributes to a small

Box 1
Perioperative factors influencing hemostasis in cardiac surgery with CPB

- Major surgical trauma
  - Sternotomy
  - Venesection
  - Arterial and venous cannulation
- CPB-associated coagulopathy
  - Consumptive coagulopathy
  - (Hyper)fibrinolysis
- Anticoagulation management
  - Heparin
  - Protamine
- Additional perioperative factors
  - Acidosis
  - Hemodilution
  - Hypocalcemia
  - Hypothermia

improvement in outcome, and when combined these interventions lead to a major decrease in blood loss and transfusion requirements.[19,20] Importantly, all components must be combined in a multidisciplinary approach involving the anesthesiologist, cardiac surgeon, perfusionist, intensivist, and hematologist.

The first step in patient blood management should be the identification of patients at risk for bleeding and transfusion, for example, prediction. Based on this assessment an individual patient blood management strategy can be planned. In patients at high risk for major blood loss and/or transfusion, additional techniques might be appropriate to decrease this risk. These techniques comprise the prevention of unnecessary transfusion and the prevention of coagulopathy. After surgery the amount of blood loss needs to be closely observed and when bleeding is excessive patient's hemostatic potential needs to be monitored. Based on these test results, several treatment modalities aim to improve hemostasis, preventing further hemorrhage and transfusion.

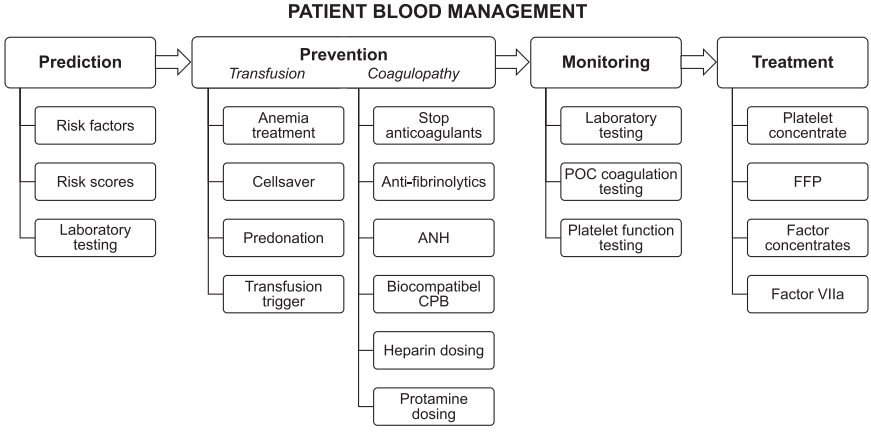

Fig. 3. Multimodal patient blood management in cardiac surgery. ANH, acute normovolemic hemodilution; FFP, fresh frozen plasma; POC, point of care.

Prediction

Risk scores

Many studies identified risk factors for bleeding and transfusion, which include patient-related factors (advancing age, female sex, low body surface area, poor left ventricular function, renal or hepatic impairment) and surgery-related factors (more complex or emergency surgery and a longer duration of CPB).[21,22] Although these risk factors give the clinician an idea about high-risk patients, they have a poor individual predictive value. Therefore, several studies developed scores to better discriminate which patients are at risk. Well evaluated scores include the TRACKS, TRUST, WILL-BLEED, and Papworth Bleeding Risk Score.[23–26] The predictive value of these scores is fair to good (area under the curve of receiver operator characteristic analysis of 0.70–0.80) and can easily be incorporated into daily practice to identify patients at risk for major bleeding and transfusion.

Hemostasis testing for prediction

Although it is common practice to perform routine hemostasis testing before cardiac surgery (prothrombin time, activated partial thromboplastin time, and platelet count) the predictive value of these tests is poor.[27] Only for fibrinogen there is a significant although weak to moderate association with bleeding.[28] As viscoelastometry emerged as an alternative to classical laboratory measurements, it is believed that the predictive value of this method is better. However, a recent systematic review shows that thromboelastometry has a poor positive predictive value for identifying patients at risk for bleeding and/or transfusion in cardiac surgery, although the negative predictive value is good.[29] Platelet function testing in contrast has a much higher positive predictive value, although its clinical applicability to guide interventions remains uncertain.[30,31]

Prevention of Transfusion

Treatment of preoperative anemia

Several studies have identified preoperative anemia as a major risk factor for perioperative transfusion, morbidity and short-term as well as long-term mortality.[32] Moreover, anemia before cardiac surgery is common, with an incidence of 1 in 3 patients.[33] In the cardiac surgical population, anemia is most frequently due to iron deficiency caused by chronic diseases (50%) followed by anemia owing to chronic renal impairment (16%).[34] The increase of the red blood cell mass in these iron-deficient patients can be achieved by the preoperative supplementation of iron with or without the addition of erythropoietin.[35]

Recently, several studies have investigated whether the treatment of preoperative anemia in cardiac surgery results in fewer blood transfusions and improves outcome.[36] So far, there are insufficient robust data to give a high-level recommendation on this matter. Yet, several studies showed positive results of even short-term anemia treatment before cardiac surgery.[37,38] The recent European guideline therefore recommends preoperative hemoglobin optimization by iron infusion with or without erythropoietin in selected patients.[5] Still, the definitive role of preoperative anemia treatment using iron with or without erythropoietin in cardiac surgery remains to be elucidated.

Cell salvage

A well-proven method to decrease red blood cell transfusion in cardiac surgery is the (structural) use of cell salvage.[39] The technique washes blood sucked from the surgical field and/or remaining in the heart lung machine after weaning from CPB. After the processing, solely erythrocytes are retransfused with 2 subsequent benefits. First, patients receive their own red blood cells, increasing the hemoglobin level, preventing anemia

and allogenic blood transfusion. Second, after processing, the activated coagulation factors and blood cells are not retransfused, preventing consumptive coagulopathy and inflammation. However, large volumes of salvaged blood transfusion may dilute coagulation factors and platelets, which may increase the risk for dilutional coagulopathy.[40] Therefore, it is suggested to limit the transfusion of large amounts of cell salvaged blood. Still, routine use of cell salvage and the prevention of direct retransfusion of cardiotomy suction blood reduces patient's allogenic transfusion requirements.[39]

Autologous (pre)donation

A less frequently used method to prevent allogenic blood product transfusion is autologous (pre)donation of whole blood before cardiac surgery. In the weeks before surgery, a patient's blood is (repeatedly) withdrawn and stored. This induced anemia leads to increased erythropoiesis, restoring patient's hemoglobin level. Blood loss during surgery can then be substituted by the patient's own predonated blood, preventing the need for allogenic blood transfusion. However, this method is infrequently used because there are several downsides to the technique. First, surgery frequently needs to be postponed to recover from phlebotomy. Second, the stored blood is only temporarily preservable, risking the shed of the donated blood. Finally, patients with aortic stenosis and/or coronary insufficiency, together the most frequent indications for cardiac surgery, are frequently precluded because predonation and the induction of anemia may worsen their condition before surgery. In addition, the safety, criteria and indication for predonation have not yet been clarified. These downsides therefore largely limit its application and resulted in its sporadic use.

Transfusion trigger

In the last decades several large randomized controlled trials were published in search for the optimal red blood cell transfusion trigger in cardiac surgery, aiming to decrease blood product transfusion. First, the TRACS trial compared a hematocrit trigger of 30% with a hematocrit of 24% and found no difference in outcome.[41] The Titer2 trial compared a hemoglobin transfusion trigger of 90 g/L with 75 g/L and likewise found no major differences between the groups.[42] However, at 90 days a borderline statistically higher mortality was found in the restrictive group. In contrast, the more recent TRICS III trial did not find any differences between transfusion thresholds of 90 g/L and 75 g/L in the short- and long-term analysis.[43,44] These results suggest that a restrictive transfusion trigger is safe in patients undergoing cardiac surgery.

Despite these large, high-quality trails, the optimal transfusion threshold for packed red blood cell transfusion remains a matter of debate. This debate is understandable when we look at the rationale for packed red blood cell transfusion, for which we have to go back to the basic physiologic principle of the delivery of oxygen (DO_2). When the DO_2 meets its oxygen demands (V_{O_2}) mitochondria conduct aerobe metabolization as a source of energy. However, when the tissue oxygenation drops below the V_{O_2}, anaerobic metabolization starts, inducing an oxygen debt and lactate acidosis.

$$DO_2 = CO \times CaO_2$$

$$DO_2 = CO \times [(\underline{Hb} \times 1.39 \times SaO_2) + (P_{O_2} \times 0.003)]$$

The formula for oxygen delivery is:

DO_2 = oxygen delivery, CO = cardiac output, CaO_2 = arterial oxygen capacity, Hb = hemoglobin level, SaO_2 = arterial oxygen saturation, P_{O_2} = arterial oxygen tension.

Red blood cells are transfused to prevent tissue hypoxemia. However, tissue oxygenation depends on the patient's cardiac output, hemoglobin level, and arterial oxygen saturation, as shown by the DO_2 formula. Herein lies the difficulty for the optimal transfusion trigger. A patient with a normal cardiac reserve might have sufficient oxygen delivery with a hemoglobin level of 3.0 mmol/L when the circulating volume is appropriate. However, a patient with a decreased left ventricular function and a low arterial saturation might need a hemoglobin concentration of 5.0 mmol/L for adequate tissue oxygenation. Furthermore, the optimal transfusion trigger will be different when cooled and under anesthesia (with lower oxygen demands) compared with the increased oxygen demands when rehabilitating in the ward. These factors are difficult to incorporate into clinical trials. Most randomized controlled trials therefore randomized patients to 2 hemoglobin levels. However, it is advocated to incorporate signs of tissue oxygenation ($ScvO_2$, lactate, heart rate, etc) into the rationale for the transfusion of red blood cells and thereby individualize the transfusion trigger.[5]

Prevention of Coagulopathy

Stop anticoagulation

An important part of patient blood management is the preoperative cessation of anticoagulants. Guidelines exist for the optimal timing for interruption of antithrombotic drugs.[5,45] However, when anticoagulants are stopped the bleeding risk decreases and the thrombotic risk increases. Some drugs are given to prevent low risk incidence thrombotic events whereas others have a high risk of thrombosis when stopped. Therefore, it is important to keep the overall outcome (eg, morbidity and mortality) in mind when stopping anticoagulants before surgery and individually weigh the risk of reduction of transfusion and thrombotic complications.[46]

Antifibrinolytics

It is common practice to use antifibrinolytics to prevent clot breakdown. Formerly, aprotinin was used for this purpose with pleiotropic positive effects on hemostasis, including the prevention of fibrinolysis. However, owing to safety concerns aprotinin has been withdrawn from the market in 2007 as it was associated with kidney failure and increased mortality, although it was superior in hemostasis optimization. After critical reappraisal of the risks, aprotinin has recently been readmitted to the European market.[47] However, its use has largely been replaced by tranexamic acid (and ε-aminocapron acid).[48,49] However, when tranexamic acid is administrated in high dosage, there is an increased incidence of postoperative seizures, associated with poorer outcomes.[49,50] A dosage more than 50 mg/kg^{-1} is, therefore, not recommended.

Acute normovolemic hemodilution

An easier alternative to preoperative autologous predonation is acute normovolemic hemodilution. The patient's whole blood is withdrawn directly before CPB and replaced with crystalloids to intercept the hemodynamic consequences. After weaning from bypass, the patient's own blood is retransfused. The advantage of this method is that the stored autologous whole blood is not exposed to the coagulopathic effects of the extracorporeal circulation, preserving its hemostatic potential. The technique is mainly used in patients with high preoperative hemoglobin levels and is associated with a decrease in bleeding and transfusion.[51] However, some patients cannot withstand an acute decrease in hemoglobin level or circulating volume. This limits its use in patients with cardiovascular compromise.

A similar method is available for the harvesting patient's thrombocytes before bypass by acute preoperative platelet pheresis. By returning the preserved platelets to the patient after bypass, thrombocytopathy can be prevented. Although this

method might lead to a decrease in blood product transfusion, the evidence for this technique is scarce, outdated, and of poor quality.[52]

Anticoagulation during cardiopulmonary bypass

Heparin is administrated in cardiac surgery to prevent the formation of (micro)thrombi caused by the CPB. However, there is poor evidence for the optimal anticoagulation regimen and even at target anticoagulation levels thrombin formation can still be observed.[53] The typical activated clotting time target is 400 to 480 seconds, for which the rationale dates back to the 1970s.[54,55] Although some more recent studies show advantages of lower anticoagulation regimes (activated clotting time target 180–250 seconds), this practice has not found way into daily practice.[56,57] So, despite advances in the development of biocompatible and heparin-coated circuits, the problem of how to monitor the efficacy of heparinization during CPB persists.[12,58,59]

Protamine dosing

In the last decade, interest in protamine emerged as it became clear that protamine overdosing impairs hemostasis, as mentioned.[15] In 1994, Despotis and colleagues[60] showed that, although the activated clotting time remains above the desired target, the heparin concentration decreases during bypass. This leads to overdosing when the protamine dose is based on the full initial heparin dose administrated. However, for many years this has been common practice because high protamine dosing was thought to be harmless. More recently, many studies have investigated the effect of protamine dosing based on a pharmacokinetic model of heparin. This practice has led to a major decrease in the amount of protamine administrated and decreased bleeding and transfusion.[16,61] It is therefore recommended to decrease protamine dosing to a dosing ratio less than 1:1 based on the initial heparin dose to prevent postoperative coagulopathy.

Monitoring

Bleeding in cardiac surgery has many causes and various diagnostic algorithms exist to identify its source and guide its treatment. First, it is important to distinguish a surgical bleed (the origin of bleeding in up to 70% of the cases) from a nonsurgical origin because they require different therapy.[2] For the latter, also known as coagulopathic bleeding or oozing, still many causes remain in cardiac surgery, including decreased thrombin formation (coagulation factor deficiency, residual heparin or protamine overdosing), hypofibrinogenemia, thrombocytopenia, platelet dysfunction, or excessive fibrinolysis (**Fig. 4**).[62] Obviously, multiple causes can occur simultaneously.

Clinically, it can be difficult to distinguish a surgical from a nonsurgical cause of bleeding and both can occur concurrently. Furthermore, when blood loss persists coagulopathy can be induced or aggravated by the dilution, consumption and loss of prohemostatic components (ie, platelets and coagulation factors). Therefore, when a nonsurgical cause of bleeding is suspected, it is important to promptly reverse the coagulopathic state to prevent further hemorrhage and transfusion.

Laboratory coagulation tests can be used to investigate the cause of bleeding. However, owing to their long turnaround times, treatment will be delayed and the test results do not reflect the present coagulation status. This leads to the blind administration of prohemostatic components and risks the patient for inadequate or excessive treatment.[63] To overcome this limitation several point-of-care devices have emerged to rapidly investigate patient's hemostasis status.

Point-of-care coagulation testing is a popular method to identify coagulopathic causes of bleeding, described in detail elsewhere.[64] In the last decades, many studies

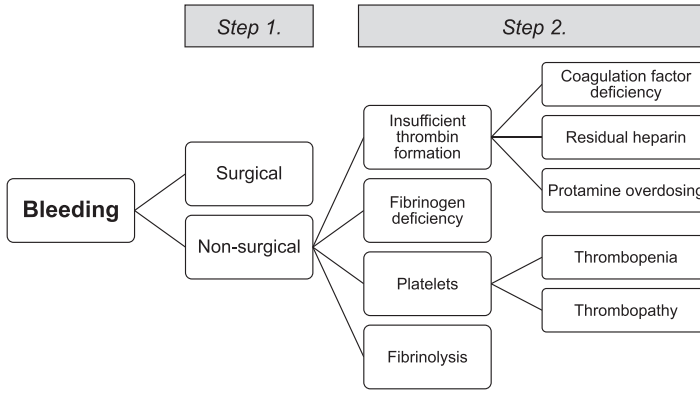

Fig. 4. Flowchart for bleeding causes after cardiac surgery, suggested by the authors. NB: basic prerequisite hemostasis conditions (temperature, calcium concentration, and pH) are not incorporated in the flowchart.

investigated its potential for the decrease of bleeding and transfusion. Although the first studies showed very positive results, more recent investigations toned down its advantages.[65] Still, it remains advised to use point-of-care testing to guide hemostasis treatment because it may facilitate a more targeted treatment of the underlying coagulation defect. Its practice may also prevent overtransfusion and decrease the risk on thrombosis postoperatively.[66] Moreover, because this method has a high negative predicting value, a surgical cause of bleeding can be suggested.[29] Still, a large limitation of viscoelastometry is the incapability to assess platelet function. To overcome this limitation, several point-of-care platelet function testing devices, for example, whole blood multiple electrode aggregometry (MEA, Multiplate, Roche, Mannheim, Germany), VerifyNow (Werfen, Germany), platelet function analyzer (PFA-200, Siemens, Munich, Germany) Platelet works (Helena Laboratories, Beaumont, TX) thromboelastography platelet mapping (Haemoscope, Niles, IL) ROTEM platelet (TEM International, GMBH, Munich, Germany), are available. However, clear recommendations for treatment guidance by platelet aggregometry remains to be elucidated.

Treatment

Once a coagulopathic cause of bleeding is detected, specific and causal treatment can be initiated. Although the treatment of some coagulation disorders seems to be straightforward, others can be managed by multiple options. In the subsequent sections, we discuss the most frequently used products after cardiac surgery.

Platelet concentrate

Platelet concentrate is, after packed red blood cells, the most transfused blood product in cardiac surgery.[2] However, evidence to support its use is largely lacking. A frequently mentioned indication for its administration is a platelet count of less than 50 to 100 $\times$ 10^9/L.[5,21] However, when critically investigating the foundation for this threshold strong evidence is absent. Another indication for thrombocyte concentrate transfusion is platelet dysfunction, which can be caused by antiplatelet drugs or by long CPB pump runs.[67] Although the degree of the inhibition of platelet aggregation can be tested by point-of-care platelet function testing, transfusion thresholds are largely lacking.[68] Interestingly, several preclinical studies found that a lack of platelets

can be intercepted by the administration of fibrinogen concentrate.[69] The hypothesis behind this notion is that in part fibrinogen can compensate the platelets contribution to clot firmness. Whether thrombocytopenia can safely be compensated by the administration of fibrinogen concentrate remains uncertain and need further investigation in the clinical setting.[70]

Coagulation factor replenishment

Coagulation factor replenishment is more broadly investigated compared with platelet concentrate and different products for this purpose are available. For years, fresh frozen plasma (FFP) was the only source of coagulation factors and fibrinogen. However, FFP transfusion is associated with several downsides. First, the product needs to be thawed before transfusion, delaying treatment. Second, because an FFP unit contains low concentrations of coagulation factors large amounts of plasma (15 mL/kg) need to be transfused to reverse coagulopathy.[71] This can lead to hemodilution and consecutive increased packed red blood cell requirements, as well as fluid overload. Another concern with FFP transfusion was the risk of transfusion-related acute lung injury. However, because multiparous women are withheld from plasma donation the incidence of transfusion-related acute lung injury has diminished greatly.[72] A possible advantage of FFP, over other products, is the preservation of the glycocalyx found in the preclinical setting.[73,74] However, current evidence does not support prophylactic FFP transfusion to decrease bleeding after cardiac surgery.[75,76] An alternative to FFP is cryoprecipitate, which is the precipitate of centrifuged FFP. Great advantage of this product is the high concentration of coagulation factors (especially fibrinogen, factors VIII and XIII, and von Willebrand factor).[71] Apart from FFP or cryoprecipitate, fibrinogen concentrate is also available in several countries for the treatment of hypofibrinogenemia.[77] This is a concentrate of solely fibrinogen derived from plasma. Because fibrinogen is the first coagulation factor to critically cease after major blood loss, several studies recently investigated its potential.[78] Routine use in cardiac surgery did not show benefit, whereas its administration is advised in cases of measured low fibrinogen levels.[5,79] Although fibrinogen concentrate does not seem to be associated with increased thrombosis its safety profile has not yet been fully elucidated.[80]

Prothrombin complex concentrate (PCC) is another alternative for FFP to treat coagulation factor deficiencies. The factor concentrate was designed to revert the anticoagulant effect of vitamin K antagonists as it contains coagulation factors II, VII, IX, and X, as well as proteins C and S. However, its off-label use spread to cardiac surgery as an effective low-volume measure to treat coagulopathy.[81] Some clinicians argue that FFP is superior because plasma contains all clotting factors and is, therefore, superior to PCC in restoring hemostasis.[82] However, this argument is refuted by current evidence as PCC contains most critical coagulation factors.[83] The evidence for its use in cardiac surgery is limited, although its potential seems promising. Still, its risks should be kept in mind, because PCC is known to generate substantial amounts of thrombin, which may be associated with an increased risk of thromboembolic complications.[84]

Miscellaneous

Finally, there are other prohemostatic drugs that are less often used. Desmopressin became popular in the 1990s to improve platelet function after cardiac surgery. The drug stimulates the release of von Willebrand factor and coagulation factor VIII stored in the Weibel Palade bodies of the endothelium. However, a systematic evaluation of the literature shows no benefit for its use in cardiac surgery.[85]

A less known product is coagulation factor XIII concentrate, which stabilizes a freshly formed fibrin network. CPB diminishes the concentration of this factor and bleeding can be reduced when it is supplemented in the case of an FXIII plasma activity of less than 70%.[86,87] However, only few centers have the option to rapidly measure its activity and its use is therefore limited in common practice.

In the beginning of this century recombinant factor VIIa emerged a "magic bullet" for coagulopathy-induced bleeding. However, when the data of its trials were systematically investigated, it became apparent that activated factor VII increased the risk of severe thromboembolic events.[88] Therefore, its use should be reserved for patients in which all other treatment options fail.

SUMMARY

Bleeding and transfusion remain common in cardiac surgery and are associated with adverse outcomes. Bleeding is frequently due to, or aggravated by, coagulopathy, which is caused by the complex interaction between the CPB, major surgical trauma, anticoagulation management and additional perioperative factors. Patient blood management strategies emerged to improve outcome by the prediction, prevention, monitoring, and treatment of bleeding and transfusion. Each part of this chain has several individual modalities and when combined improves outcome. It is important to implement patient blood management in a multidisciplinary approach, involving the anesthesiologist, cardiac surgeon, perfusionist, intensivist, hematologist and cardiologist for it to lead to optimal results.

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