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Chapter

Hemostasis in Cardiac Surgery: How We Do it with Limited Resources

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Abstract

Hemostasis in cardiac surgery is still a severe problem for surgeons. Blood and its products are the most valuable at the same time dangerous arms of surgeons. Industries produced many biological or non-biological products, which increase the cost of operations, are available for this issue. Decision making and producing solutions must be the most important properties of a cardiac surgeon. In any condition and resources, true strategy and patience will bring the success. Antiaggregants and anticoagulants are widely used agents, and in emergency or early cases, surgeons have to operate these patients. Both groups of drugs are growing, and in an emergency position, it is hard to know which drugs the patient using or given and what kind of medical status he/she has. For example non vitamin-K oral anticoagulants newer drugs and not known so much except cardiologists and cardiovascular surgeons. Simple solutions may have better results. Of course, in some conditions, urgent consultation can solve the problem. Cardiac surgeons have to figure out the problem by using their experience and surgical materials. Working as a team is a big advantage, more than one surgeon, experienced operation nurses and closer follow up in intensive care unit.

Keywords: cardiac surgery, bleeding, anastomosis, hemostasis

1. Introduction

Since 1956 Gibbon's first ASD closure using a heart-lung machine, cardiac surgery has made great strides. However, bleeding is still the fearful dream of surgeons. According to the World Bank, in upper-middle-income countries as in Turkey, certain restrictions are compulsorily brought to health-care costs. In this case, about 2000 US dollars is paid for open heart surgery in the social security system in Turkey. However, in today's conditions, the costs have exceeded the fee paid by the social security institution, and in this case, public hospitals continue to provide health-care services despite the loss. On the other hand, the society is aging, and compulsorily, the riskier patients are being operated, but the prolonged length of intensive care and the hospital stay of these patients increase the costs. In this case, the solution is to provide services with serious sacrifices on the basis of health care providers and institutions, especially surgeons. The main principle here should be to evaluate the patient well before the operation and to gain the patient during the operation and to pass through the intensive care period without any problem.

This can only be the result of achieving good cardiac functions and hemostasis with a successful operation.

Cardiac surgery is associated with an invasive procedure, serious anticoagulation requirement and perioperative blood loss due to cardiopulmonary bypass and accordingly high-probability allogenic blood transfusion. Risk factors:

i. Hemodilution (prime of cardiopulmonary bypass, cardioplegia, and perioperative fluids)

ii. Coagulation and fibrinolysis activation

iii. A consumptive coagulopathy

iv. Anticoagulation with unfractionated heparin

v. Other physiological disorders such as hypothermia, hypocalcemia, academia [1].

In cardiac surgery, patient blood management (PBM) contributes to the maintenance of perioperative hemostasis, which reduces the requirement for blood transfusion [2]. Both the use of high amounts of blood products and the requirement for reoperation are linked to undesirable clinical outcomes [3, 4]. The use of one or two units of packed red blood cells (PRBCs) in coronary artery bypass grafting (CABG) patients is associated with increased cost as well as dramatic mortality and morbidity [5]. However, it is unclear whether these complications are independent predictors of outcome or a sign of the complexity and complications of surgery [2]. In any case, re-exploration due to bleeding and tamponade is a strong predictor of early postoperative mortality and morbidity. It should be kept in mind that not performing re-exploration when it is required brings about more serious consequences. There is, however, no general consensus on when exploration for postoperative bleeding is indicated, and surgical practice varies considerably in this regard [6]. There may be limited resources to achieve hemostasis, as well as to detect cardiac tamponade or when the patient will be re-explored for bleeding. The cardiac surgeon should be skeptical about this and use all arguments in his or her hand. Hemodynamic deterioration, decrease in urine output, decreasing Hb levels while increasing base gap and lactate levels in blood gas analysis, deterioration in general condition of the patient and chest pain, and most importantly enlarged mediastinum on chest radiogram, hematoma accumulation in lung fields are the most important manifestations of cardiac tamponade and bleeding. The patient should be re-explored without hesitation. It should not be compromised on surgical site cleaning and antisepsis in postoperative cardiac tamponade patients, who are usually opened urgently with impaired hemodynamics. After the urgent removal of hematomas, anastomoses and cardiotomies should be checked first. After bleeding control, the patency of drainage tubes should be checked and they should be replaced, if necessary.

Numerous factors such as advanced age, preoperative dual antiplatelet therapy (DAPT), platelet dysfunction, preoperative anemia, small body surface area, female gender, non-elective surgery, non-isolated surgery, non-CABG surgery, and redo surgery are associated with increased bleeding [7–9].

A group of hemostatic agents including topical hemostats, sealants and adhesives are available to stop these bleedings. Despite these, hemostasis cannot be achieved due to the inappropriate use of hemostatic agents in 40% of surgical patients, as in the surgery of traumatic injuries [10].

2. Preoperative management

Failure to adequately optimize the patient prior to surgery increases the risk of bleeding and anemia during the operation [2]. The use of routine preoperative screenings has been highly discussed in terms of its ability to identify high-risk patients for postoperative bleeding and transfusion requirements. Preoperatively determined prothrombin time or the activated partial thromboplastin time (aPTT) could not be associated with perioperative blood loss or transfusion requirements [11–13]. The most commonly identified risk factor for postoperative bleeding is a low fibrinogen level [11, 12, 14–16]. However, despite its association with bleeding, the positive predictive value of a low-fibrinogen level remains poor (positive predictive value <20%) [15]. A low platelet count (<10,010–9/L) has been associated with increased risk of transfusion, and patients with the highest postoperative blood loss volumes show the lowest platelet counts [12]. It has been shown that patients with the highest postoperative blood loss volumes show the lowest thrombin generation rates, but this test is mainly used for research purposes and is not routinely used in everyday practice [12, 17].

In preoperative Hb evaluations of 1388 female and 3265 male patients undergoing elective cardiac surgery, it was found that borderline anemia (defined as the hemoglobin concentration of 120–129 g L^{-1}) was more common in the female group and about one-third of the patients were in this range. These women had increased morbidity, reflected by increased red cell transfusion and prolonged hospital stay compared with non-anemic women (Hb >130 g L^{-1}). It was also found that these women received more erythrocyte transfusion than male patients [18].

2.1 Preoperative drugs and their effects on postoperative bleeding

2.1.1 Acetylsalicylic acid

Acetylsalicylic acid (ASA) is one of the cornerstones for the treatment of acute and chronic cardiovascular disease. Primary and secondary prevention with ASA has been shown to reduce mortality, myocardial infarction (MI) and stroke but to increase the risk of bleeding complications [19]. All patients requiring emergency or elective CABG are treated with ASA. A meta-analysis showed that ASA reduced the risk of perioperative MI [odds ratio (OR) 0.56, 95% confidence interval (CI) 0.33–0.96] but not the risk of death (OR 1.16, 95% CI 0.42–3.22). Twelve-hour blood loss, PRBC transfusions and surgical re-exploration increased with ASA [20]. A large RCT compared the administration of ASA (100 mg) on the day of surgery versus placebo in patients having CABG [49]. The study showed no effect of treatment with ASA on 24-h bleeding (mean blood loss: 780 vs. 740 mL; P = 0.30) or on the incidence of death or thrombotic complications (19.3 vs. 20.4%; P = 0.55). Because patients were only eligible for inclusion if they were not using ASA or stopped ASA >4 days before surgery, these findings are difficult to generalize to other settings [21]. In another randomized clinical study, the use of preoperative 300 mg ASA was associated with post-surgical drainage of over 1000 mL [22].

Given all these results, the continuation of ASA treatment in patients undergoing CABG may be reason of increasing postoperative blood loss while reducing ischemic event [2]. In patients with high probability of re-exploration such as those who refuse the blood transfusion, who will undergo non-CABG surgery, complex cases, redo operations, and those who have severe renal failure, hematologic and inherited platelet function disorders, ASA should be discontinued 5 days before surgery. Prevention of thrombotic events outweighs the risk of bleeding in other patients. Current information suggests that ASA-inhibited platelet aggregation can be reversed by platelet transfusion, which supports the continuation of ASA treatment until operation [23, 24]. Mortality rates significantly decrease in patients who are initiated on ASA in the first 48 h after CABG compared to patients who are not initiated on ASA (1.3 vs. 4% $P < 0.001$) [25].

2.1.2 Dual antiplatelet therapy (DAPT)

The administration of DAPT, a P2Y12—receptor antagonist (clopidogrel, ticagrelor and prasugrel), in combination with ASA significantly reduces the risk of thrombotic complications in acute coronary syndromes compared to ASA alone [26]. Compared to clopidogrel, the risk of thrombotic complications is significantly reduced by ticagrelor and prasugrel, the second generation P2Y12 antagonists, while the risk of both spontaneous and surgical bleeding increases significantly [27]. Recently, cangrelor, a new reversible intravenous P2Y12 inhibitor with an ultrashort half-life to offset the effect after discontinuation, was introduced [28].

2.1.3 Glycoprotein IIb/IIIa inhibitors

Today, glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors (eptifibatide, tirofiban and abciximab) are almost exclusively used in conjunction with percutaneous coronary interventions, but may also be used for bridging high-risk patients on oral P2Y12 inhibitors to surgery [29, 30]. The discontinuation times of these drugs before surgery are based on pharmacokinetic assumptions. The recovery of platelet functions is obtained within 24–48 h for abciximab and 4–8 h for eptifibatide and tirofiban [31]. In a small retrospective study, tirofiban-treated patients having CABG showed more bleeding than patients who were not treated with tirofiban, but there was no difference between different discontinuation times [32]. Discontinuation of GPIIb/IIIa inhibitor at least 4 h before surgery should be considered to minimize the risk of postoperative bleeding.

2.1.4 Low-molecular-weight heparin

As enoxaparin and fondaparinux, LMWH mainly functions by inhibiting factor Xa and reaches plasma peak levels 3–4 h after the administration. In patients with normal renal function, their half-life is 5 h. Their anticoagulant effects can be monitored by measuring plasma anti-FXa activities. LMWH-induced bleeding may be treated with protamine, but this therapy does not completely reverse the anticoagulant effect of LMWH [2].

2.1.5 Vitamin K antagonists

Vitamin K antagonists (VKAs) are commonly used to prevent and treat thromboembolism in cases of atrial fibrillation, venous thromboembolic disease and mechanical heart valve. They are monitored by the international normalized ratio (INR) and prothrombin time. They should be stopped 3–5 days before surgery to obtain an INR <1.5. For emergency surgeries, their effects are completely reversed by prothrombin complex concentrate. Bridging non-cardiac surgery patients who are taking VKA with a full therapeutic dose of LMWH after surgery are associated with increased risk of bleeding but not with a significant reduction in thrombotic events [33]. Elective cardiac surgery is not recommended unless the INR value falls below 1.5. In cases where surgery cannot be postponed, coagulation factors should be used to antagonize the effects [2].

2.1.6 Direct oral anticoagulant

Direct oral anticoagulants (DOACs) is a group of drugs consisting of dabigatran, a direct thrombin inhibitor, and rivaroxaban, apixaban and edoxaban, oral FXa inhibitors, and novel formulations under development. They are increasingly used as an alternative anticoagulation strategy for VKAs [2]. Since emergency surgery in patients under dabigatran treatment has been associated with severe or even fatal bleeding, it is recommended that these drugs be discontinued 48 h before cardiac surgery [34–36]. The half-life of DOACs may be prolonged in the case of impaired renal function. For emergency reversal of dabigatran, the newly released antidote (idarucizumab) can be used in the pre- and postoperative settings. Treatment of postoperative FXa-related bleeding includes PCC, activated PCC (FEIBAV R, Shire US Inc., Lexington, MA, USA) and recombinant activated factor VII (rFVIIa), since no specific antidote is approved at the moment [2].

According to the EACTS/EACTA recommendations, ASA should be continued in the preoperative period in patients scheduled for CABG (Class IIa, Level C). ASA should be discontinued 5 days in advance (Class IIa, Level C) in patients with a high risk of bleeding, refusing the blood transfusion, or undergoing cardiac surgery other than CABG. If there is no severe bleeding in the first 24 h postoperatively, ASA should be initiated in isolated CABG patients (Class I, level B). If CABG is not urgent, ticagrelor should be discontinued 3 days, clopidogrel 7 days and prasugrel should be discontinued 5 days before surgery in patients taking DAPT (Class IIa, Level B). GPIIb/IIIa inhibitors should be discontinued 4 h before surgery (Class IIa, Level B). GP IIb/IIIa inhibitors should be discontinued 4 h before surgery (Class I, Level C). In order to reduce the risk of bleeding, oral anticoagulants should be discontinued only in patients with a high risk of thrombosis and it should be continued with UFH/LMWH (Class I, Level B). LMWHs should be discontinued 12 h before and fondaparinux before should be discontinued 24 h before (Class I, Level B). In the use of VKAs, surgery should be performed after the INR value reduces below 1.5 (Class IIa, Level C). DOACs should be discontinued 48 h before cardiac surgery (Class IIa, Level C).

3. Clinical effects of surgical bleeding

Bleeding is the most important complication of surgery, which increases mortality and morbidity rates [37–39]. Uncontrolled bleeding results in adverse clinical outcomes including anemia, hemodynamic instability, hypothermia, hypovolemia, reduced oxygen delivery to tissues, impaired visualization of the surgical site, and prolonged operative time. Surgical bleeding requires expensive blood transfusion and re-operation, in which a large amount of clinical and personnel resources is used [39]. Major bleeding is also associated with an increased risk of postoperative mortality reaching 20% in vascular surgery and 30–40% in trauma surgery [39].

Blood transfusion itself involves many risks. Transfusion-related acute lung injury, which occurs one in every 1000–5000 plasma and erythrocyte transfusions, is the leading cause of mortality and morbidity [40]. Bacterial contamination, which occurs one in every 2000–3000 platelet transfusions, is another complication of transfusion [40]. The authors have reported that the length of hospital stay is longer in patients with bleeding-related complications or more blood transfusion requirements than those without bleeding complications (10.4 vs. 4.4 days, respectively) [41].

3.1 Economic effects of surgical bleeding

Uncontrolled bleeding and transfusion requirement are associated with bleeding complications, resulting in a considerable amount of cost [42]. Stokes et al. also compared the total hospitalization costs for patients with bleeding-related complications or blood transfusions with those for patients without any complication and, again, noted a significant increase in costs among those with complications [41]. There are, of course, the costs of bleeding and blood and blood transfusion for all countries. In the country where I work, these costs are not as high as in the US.

It should be kept in mind that although blood transfusion is an indispensable treatment, whether clinical or economic, it is the most dangerous drug we have ever used [43].

3.2 Clinical responses to surgical bleeding

The surgical nurse plays an important role in optimizing hemostatic applications throughout the operation. To meet the requirements for hemostasis by questioning the surgeon before and during surgery. To know the material available to meet the requirements for surgical intervention. To adjust the time required for the preparation of the necessary material during the operation and be in constant communication with the surgeon [42]. Working with a nurse experienced in cardiovascular surgery is always a significant advantage for the surgeon. In general, I trained my surgical nurses myself in private hospitals where I worked in my surgical life. Private hospitals try to minimize the number of staff in order to limit input cost due to their commercial concerns. They also prefer less educated staff. At this point, the responsibility of the surgeon increases, s/he has to perform a successful operation while continuing the training activities of the nurse. In this respect, cardiovascular surgery centers in many private, public and universities in my country train their own surgical nurses. Personally, I have also trained many nurses and even made them gain the qualifications to perform proximal anastomosis and connect prolene sutures. After a while, the surgical nurse could follow the operation, know what to be asked in advance and quickly prepare the required instrument and material. In my opinion, the most serious disadvantage of this is that you are on your own in decision making since there is no experienced assistant surgeon assisting you (**Figures 1** and **2**).

Selection of the most appropriate method for achieving hemostasis is based on correctly defining the nature and severity of the patient's bleeding. If the patient presents with or develops uncontrolled bleeding in the operating room, first and

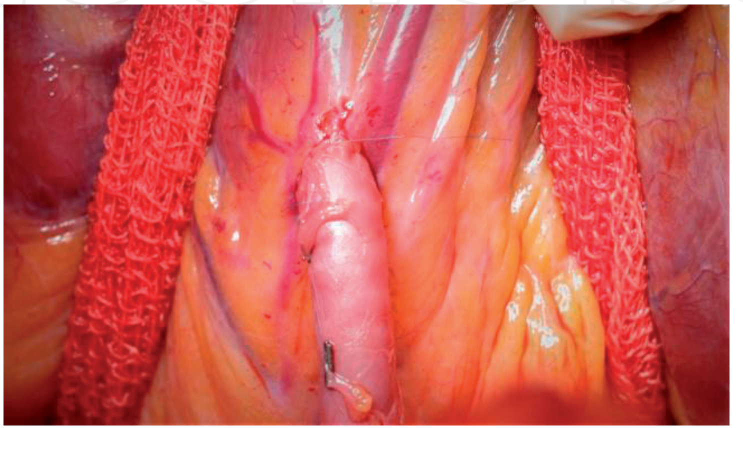

Figure 1.
Saphenous vein graft anastomosis to coronary artery. Small bites from epicardial tissue with appropriate size prolene suture.

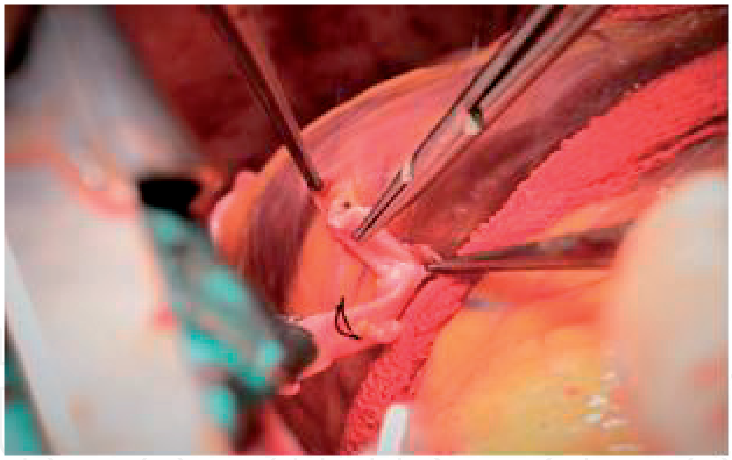

Figure 2.
Saphenous vein graft anastomosis to coronary artery. Small clips for the small branches of the saphenous graft.

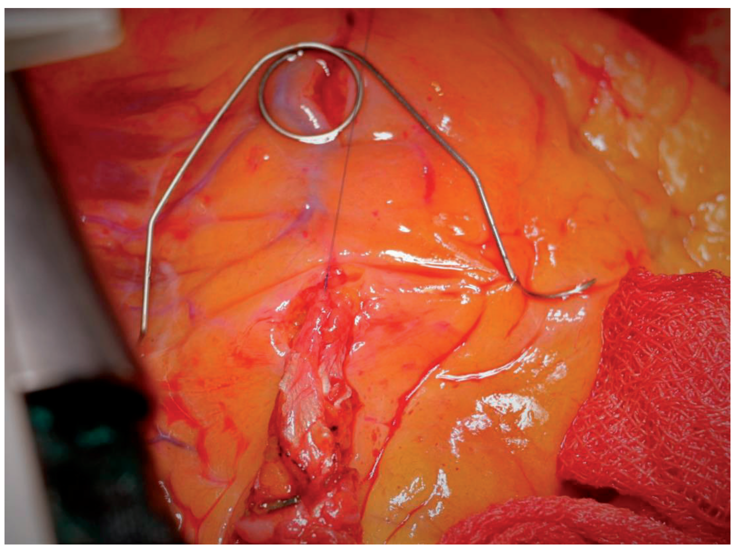

Figure 3.
Here is a left mammarian artery graft anastomosis to left anterior descending artery. A small retractor used for easy visualization of the arteriotomy. Again usage of small clips. When you are performing the repair sutures to bleeding side of the anastomoses, you have to be careful and you do not need to pass the whole layers of coronary artery.

to the extent permitted by time, a group of coagulation laboratory values (prothrombin time/international normalized ratio, activated partial thromboplastin time, complete blood count with differential and platelets, activated clotting time, fibrinogen, d-dimer and thromboelastography) should be examined [42]. In cases of unexpected or complex coagulopathy, it is necessary to get professional help from a subspecialist such as a hematologist and blood bank specialist. (While such aids actually work in intensive care follow-ups, it seems difficult for the specialist to comprehend the situation in the operation room and offer solutions in the complexity of the surgery. Therefore, the responsible surgeon must be able to master these issues and produce urgent solutions.) (**Figure 3**).

4. Mechanical solutions

Mechanical approaches usually provide hemostasis without the need for any hemostatic product. The most basic practice is to apply compression with finger or fingers to the bleeding site. Especially in bleedings of the tissues with high pressure such as the ascending aorta, compression should absolutely be applied with finger to save time for strategies to create solutions. In fact, it is the most basic approach to be performed in the case of unexpected bleedings during a routine operation. While the surgeon is using the fingers of his/her non-dominant hand to restrict bleeding, s/he should give the surgical nurse order for repair. Here, a few simple maneuvers can be life-saving. The venous return should be reduced for lowering the pressure in the ascending aorta. Tilting the patient's head up by operating table is simple and effective. If you fail for lowering the arterial pressure, transient inferior caval clamping before neutralization of heparin may be very helpful, especially when pulling out the aortic cannula. Another technique in old textbooks is total inflow occlusion. In this technique, it has been described that repairs are carried out in a few minutes with cross-clamps placed on both cavas. However, when removing the caval cross clamp, it should be absolutely ensured that the clamp is fully opened. Moreover, a simple approach in aortic cannulation is using teflon pledgets for outer purse-string suture.

The most basic hemostasis approach is to create a mechanical barrier. The use of a needle and suture in an appropriate size and supporting it with teflon pledgets is the most effective, simple and accurate approach. The suture material to be selected is usually prolene. In order to reduce tissue injury, the needle should be as small as possible along with fine needles, but of sufficient thickness to withstand the tension in the tissue and appropriate thickness to be securely attached. (The most important issue to be considered here is that the other hand knot should be tied tightly enough to stop bleeding and ensure tissue integrity not to allow non-dominant hand suture to loosen when making a suture. Excessively tight and hard knots may cause more severe tissue injuries and bleedings.) For sutures that will both stop bleeding and provide anastomosis, it is necessary to use stronger fibrous tissues of the patient such as the adventitia and epicardial layer (**Figure 4**).

Sponges are the most commonly used inexpensive materials to stop bleeding in the operation field. They are very effective with mechanical compression, especially in oozing-type bleedings. Sponges should be intensely applied to the mediastinum after the clamps are removed and it should be waited until the end of protamine neutralization. As a result of reapplication of a clean sponge, especially after ending the heparin effect, locally contaminated sponges may give information about the site of bleeding other than providing hemostasis (**Figure 5**).

Hemoclips are an effective and fast method especially for harvesting arterial grafts and ligating small vessels. However, it is necessary to pay particular attention to the

Figure 4.
Two anastomoses to LAD. There is no bleeding from anastomotic sides.

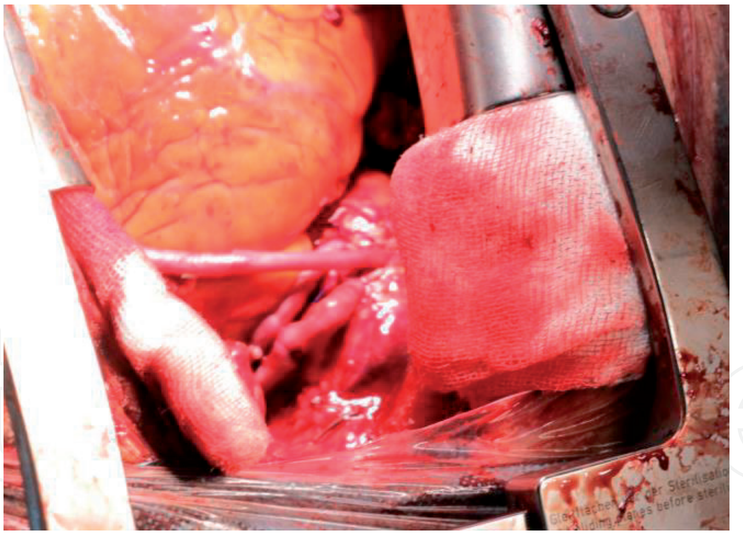

Figure 5.
No bleeding from proximal anastomotic sides of sapheneous vein grafts. Also adventitial tissue bites performed. Sponges under the retractor compress the cavernous tissue of sternum.

selection of hemoclips. Especially, large hemoclips may damage a small vessel and increase bleeding as a result of tissue injury. It is important to remember that these hemoclips may drop when applying sponge to the operation site or performing bleeding control. Therefore, ligation or suturing may be more effective in appropriate cases.

Other mechanical solutions include electrosurgery, laser, radio-frequency energy, argon beam coagulation, ultrasonic scalpel or ultrasonic surgical aspirator use. When using electrocautery, it is beneficial to use it at the lowest energy and appropriate program that can do our work. It should be kept in mind that especially high energy will increase tissue injury.

5. Pharmacological drugs

Pharmacological strategies for blood preservation are also an important tool in the arsenal of the surgical team since these agents alleviate the activation of the hemostatic system without the clinical and economic consequences associated with transfusion [44]. Pharmacological agents may be of some benefit in diffuse surgical bleedings or in those with a hemostatic defect. These agents may be used in combination with surgical hemostatic agents. These agents are recombinant factor VIIa, desamino-d-arginine vasopressin, and antifibrinolytics (e.g., epsilon aminocaproic acid (EACA), tranexamic acid (TXA)) [44, 45]. The recombinant factor VIIa activates platelets to increase thrombin production. It is used in trauma and surgical refractory bleeding. It acts quickly and is quite expensive. Although it is not a preferred product in our country, we prefer fresh frozen plasma (FFP) in such cases. Desmopressin acetate (vasopressin) factor VIII is a selective V2 agonist that causes the release of von Willebrand factor and tissue plasminogen activator. It is used in platelet dysfunction. It acts in a short time, tachyphylaxis and repeated doses increase the risk of bleeding. The parenteral form is not available in Turkey, the nasal spray form is not very effective.

Antifibrinolytic therapy reduces bleeding, the use of blood and blood products and reoperations due to bleeding [2]. This group includes tranexamic acid (TXA), aprotinin and EACA. The sale of aprotinin has stopped in some countries, especially because it increases mortality rates.

The Aspirin and Tranexamic Acid for Coronary Artery Surgery (ATACAS) randomized controlled trial compared TXA with placebo in patients undergoing

CABG surgery and demonstrated a reduction in the risk for reoperation due to major hemorrhage (RR 0.36, 95% CI 0.21–0.62; $P < 0.001$) and in the need for the transfusion of any blood products (37.9 vs. 54.7%; $P < 0.001$.(13 C)). In a systemic review and cumulative meta-analysis comparing those having cardiac surgery with the control group, TXA was shown to reduce the requirement for blood transfusion [47]. The most significant reported side effect of TXA was a convulsive seizure [48]. The findings from the ATACAS trial showed that low-dose (50 mg/kg) versus high-dose (100 mg/kg) TXA was not safer in terms of seizures (0.7 vs. 0.6%, respectively), but the higher dose significantly reduced blood loss ($P = 0.026$) and PRBC transfusion (P = 0.017) [46].

Tranexamic acid is also an antifibrinolytic agent that we use frequently. It inhibits plasmin and plasminogen proteases and reduces surgical bleeding. It may cause thrombosis and hypotension.

6. Transfusion

These blood products include FFP, platelets, prothrombin complex concentrate, cryoprecipitate, and whole blood. Thrombocytes in plasma are indicated when platelet levels are less than 50×10^9/L. It contains cryoprecipitate factor VIII, von Willebrand factor, fibrinogen and fibronectin, and is indicated when the patient's fibrinogen is less than 100 mg/mL or when the patient has von Willebrand factor deficiency [49]. FFP contains coagulation factors and fibrinogen in variable amounts, while prothrombin complex concentrate contains factors II, VII, IX, and X and prothrombin, as well as proteins in variable amounts. Both FFP and prothrombin complex concentrate are indicated when a surgical patient who is bleeding has an international normalized ratio greater than 1.5 [49].

6.1 Fresh frozen plasma

FFP is obtained from the plasma of volunteer blood donors containing coagulation factors and other proteins. An increasing number of countries use pooled plasma. Pooled plasma contains plasma from multiple donors and is inactivated for viruses with a lower risk of transfusion-induced lung injury [2]. The largest body of evidence is gathered on the prophylactic administration of FFP to patients without a diagnosed coagulopathy and is summarized in a Cochrane review and three other systematic reviews [50–53]. In patients undergoing cardiac surgery, there was no difference in blood loss and allogeneic blood transfusion requirement when patients intraoperatively receiving FFP were compared with the control group. The RCTs included were limited by small sample sizes and divergent doses of FFP [51–53]. It has also been shown that FFP is not effective in 24-h blood loss in patients with diagnosed coagulopathy or in the reversal of oral anticoagulation when it is used at a therapeutic dose [51, 53]. In summary, FFP might be used to reverse the action of oral anticoagulation or in the case of persistent perioperative bleeding, but there is no evidence that prophylactic or therapeutic FFP transfusions reduce blood loss after cardiac surgery [2].

7. Topical hemostats

Topical hemostatic agents consisting of mechanical, active, flowable, and fibrin sealants provide hemostasis by forming blood clots [54–56]. Agents in this class vary greatly with respect to safety, efficacy, usability, and cost. An appropriate agent should be selected for each clinical situation.

7.1 Mechanical hemostats

It consists of combining hemostatic agent and sponge, foam or pad absorbable material. They create a surface against blood flow where blood clots can form [56]. Common mechanical hemostatic agents include porcine gelatin products (e.g., Gelfoam®, Gelfoam Plus®, Surgifoam®), cellulose products (e.g., Surgicel®, Surgicel Fibrillar™, Surgicel Nu-Knit®), bovine collagen products (e.g., Avitene™ sheets, Avitene Ultrafoam™ collagen sponges), and polysaccharide spheres (e.g., Arísta®, Hemostase MPH®, Vitasure™) [54–56]. They are effective in minimal bleedings and when the coagulation cascade is normal. They are easy to use since they are ready-to-use packaged products, do not require special preparation, are easy to store and act by direct application to the bleeding site [56]. It is important to slightly irrigate before removal not to take clotting beneath them. These products are relatively inexpensive and well-tolerated, while swelling and increased risk of infection are possible side effects [44]. They are usually used as the initial response to bleeding [56]. Cellulose-containing products such as Surgicel are commonly used since they are cheap and easily accessible. Because these products are absorbable, they are easily applied to the bleeding site. They should be used carefully and practically, as they easily disintegrate by swelling when they get wet or come into contact with blood. Although they can be used directly, we use it by mixing with a small amount of cyanoacrylate in a tablespoon for bleedings of difficult to reach points such as the posterior of the aortic root during the operation. In this application, the most important point to consider is to pay attention to the amount of cyanoacrylate used, as it may cause tissue injury. It quickly hardens in a short time when mixed with the polymerized cyanoacrylate cellulose. Therefore, it should be applied quickly and practically. However, it is not effective in severe bleeding since it does not adhere to the tissue. It can be applied hypotensively or by applying compressed medical air to the point of bleeding while the blood is removed. Cyanoacrylate products prepared for medical purpose can also be used, which should be preferred. In emergency situations, products prepared as adhesive can be used as well.

The tablespoon is a simple but effective tool when necessary that should be included in the open heart surgery set. It can be very helpful ascending aorta bleedings especially in proximal anastomosis after weaning from CPB, it gives repair chance to surgeon by keeping it like a shed 4–5 cm distance above. Also helpful for delivering hemostatic powders to bleeding site. It can be herbal powders sold for this purpose, as well as crystallized vancomycin powder, which we usually use. It can also be helpful in the excision of brittle tissues such as fluid or myxoma.

As a cardiac surgeon, I think the most important side effect of such products is that they offer the surgeon extra confidence. The surgeon must provide the patient with hemostasis during the operation, otherwise the drainage ongoing in the intensive care process brings about serious consequences. For this, the surgeon should repeatedly check anastomoses, cardiotomies, surround tissues, especially the sternotomy and stop bleeding with appropriate sutures and ligations.

7.2 Active hemostatics

By converting fibrinogen to fibrin, active hemostats—namely the three topical thrombin products: bovine thrombin (Thrombin-JMI®), pooled human plasma thrombin (Evithrom®), and recombinant thrombin(Recothrom®)—facilitate clot formation at the bleeding site [55–57]. Active hemostatic agents are the most commonly used adjunctive hemostatic therapies in the surgical setting and conservative estimates show that more than one million patients are treated with topical thrombin administration annually in the United States [58].

While all three preparations are applied to the locally bleeding area or larger areas in diffuse bleedings in the form of spray, they also require certain preparations before application. For example, bovine and recombinant thrombin are stored in powder form at room temperature and prepared with certain special liquids before use. Pooled human thrombin is available in a liquid form and can be stored in a refrigerator for as long as 1 month [56]. In such cases, it should be used together with active hemostatic agents such as absorbable gelatin sponge or powder, since thrombin administered in the presence of active bleeding can be rapidly irrigated. IV should not be used since it may cause a major anaphylactic reaction [59–61].

As the results showed similar efficacy in all three products, health care providers canalized their next assessment to select the most appropriate agent for the clinical situation. For example, although there are clinical studies showing similar safe use of all these products, bovine thrombin administration has been associated with antibody formation that can lead to immune-mediated coagulopathy and death, which is why this product carries a black box warning [59, 62]. These preparations are not available in Turkey. Even if they are, social security providers do not cover them since they are very expensive.

7.3 Flowable hemostatic

These products (e.g., Surgiflo®, Floseal®) contain thrombin along with a mechanical gelatin agent. They work together to obstruct blood flow and convert fibrinogen to fibrin [55, 56]. Although the mechanism of action is similar, Surgiflo is porcine gelatin available for use with bovine, human pooled plasma, or recombinant thrombin, whereas Floseal includes absorbable bovine gelatin particles combined with pooled human thrombin [55, 56]. All these agents are most effective in local bleedings and with the help of a syringe, they are applied downward into the wound, on the wound edges, providing an ultimate mechanical barrier and forming an active clot [55, 56]. The surgeon can spray these agents not only on the upper parts of the wound, but also on large irregular surfaces. The product forms a thick structure in the bleeding site approximately 3 min after administration. At the same time, the surgeon can apply pressure with a sponge soaked with saline [56].

7.4 Fibrin sealant

While many fibrin sealants are available as topical hemostat, sealant and adhesive, Tisseel has received FDA approval for use only [56, 63]. This product is also available in our country and is used especially in aortic surgery. Since they contain high concentrations of fibrinogen and thrombin, which are naturally found in the blood, they cause blood clot formation [56]. Fibrin sealants—namely Tisseel™, Evicel®, and Vitagel™—are effective for both local and diffuse bleeding and can be applied using either a syringe for local bleeding or spray with a gas-driven device for diffuse-bleeding areas [55, 56]. These agents act better when applied to a relatively dry surface and can be used with absorbable gelatin sponge as the surgeon can press with the finger [56]. In aortic root surgeries such as Bentall procedure, after the placement of valved conduit in the aortic root and left coronary button anastomosis, Tisseel can be applied to this region providing sealing since this area cannot be re-visualized again.

7.5 Albumin and glutaraldehyde

Bovine albumin and glutaraldehyde (BioGlue®) is a cross-linkage between bovine serum albumin and 10% glutaraldehyde [56]. It has been approved by the

FDA for adhering intimal and adventitial layers to each other in aortic dissection. This sealant agent is also available, and we especially use it in aortic surgery dissections. In particular, it is applied between the layers of the media at the distal of the primary intimal tear so the layers are adhered to each other.

7.6 Cyanoacrylates

Octyl cyanoacrylate (e.g., Dermabond™) and butyl cyanoacrylate (e.g., Indermil®, Histoacryl®, Histoacryl® Blue) are for topical use only. While these agents hold the edges of the skin together, they also form a barrier against bacteria [55, 56]. Cyanoacrylates are quick and easy to use, are stored at room temperature, and are relatively inexpensive. However, they have an exothermic reaction when applied to the skin and thus can cause some discomfort in patients. Safety concerns include potential eye injury, and its use on infected, wet, or poorly healing wounds should be avoided [55, 56]. N-butyl cyanoacrylate is currently used for endovenous ablation of varicose saphenous veins. It is a rapidly polymerizing agent in contact with blood. In special cases, it can be applied directly on the tissue and adhered to topical hemostatic agents with cellulose content. It is a simple but effective application.

8. Conclusion

What are the limited resources in health care delivery? In underdeveloped and developing countries, both the social insurance provider and the delivery of healthcare

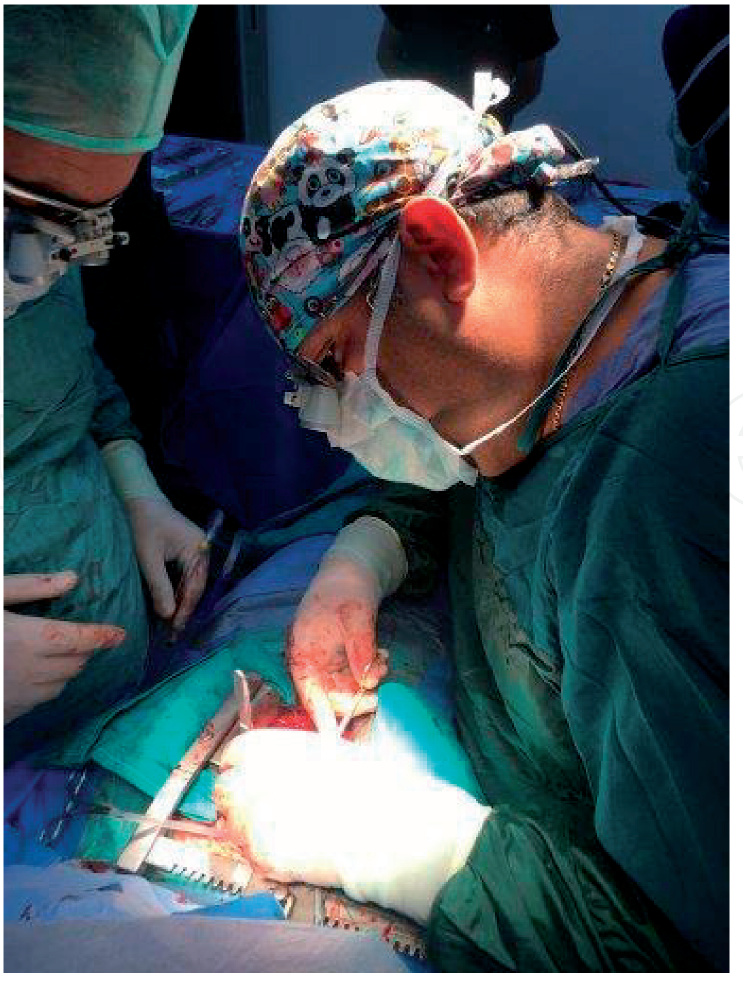

Figure 6.
Me and my colleague performing a mitral valve operation with classical sternotomy.

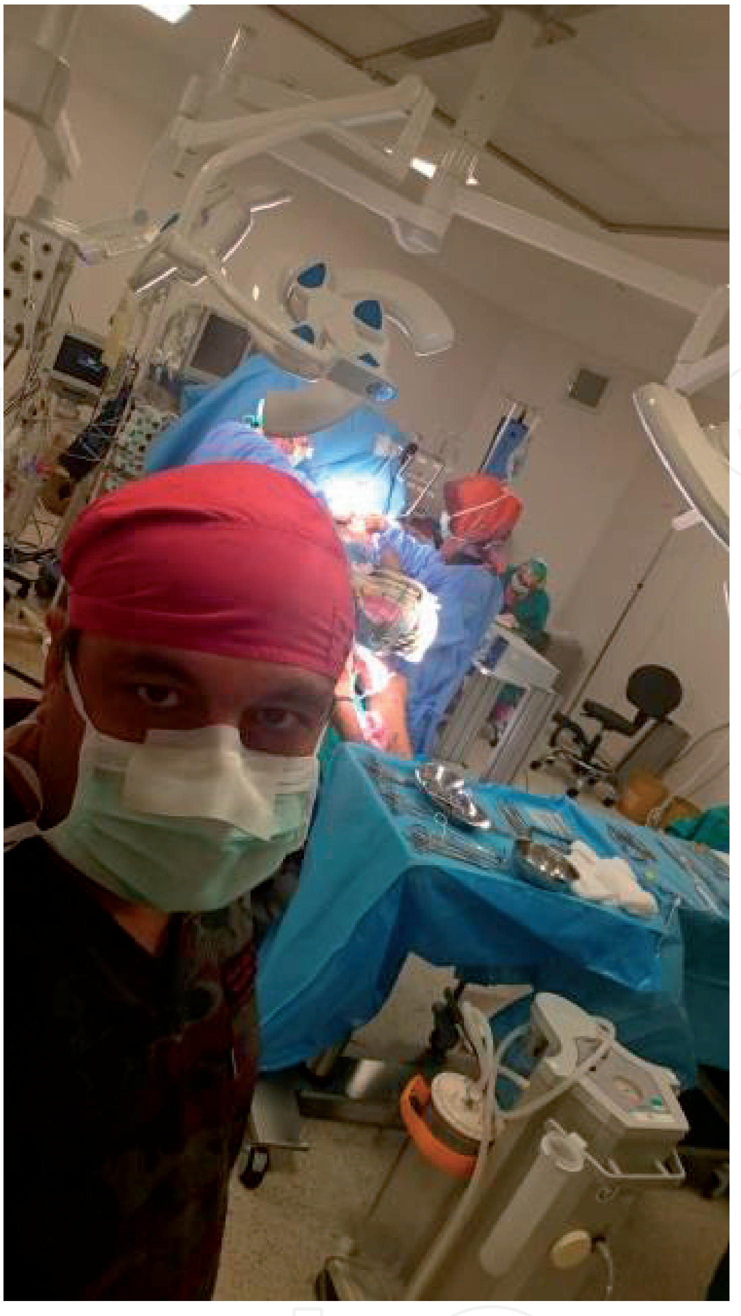

Figure 7.
To be a team can figure the problems out in cardiac surgery.

services substantially belong to the state. This has advantages as well as disadvantages. These limited resources inevitably create limitations in the delivery of healthcare services. If you cannot produce your technology and buy it from outside, these products cost too much, and even if they are used, serious limitations are required. In this case, the surgical team creates solutions to the current situation; the basic rule of being a surgeon is to make the right decision at the right time. At this point, from patient admission to surgical planning, the right assessment, the right strategy and the right indication should be established for the patient. The surgeon should be skeptical, question and investigate. Beginning a cardiac surgery is an irreversible process. Detection and solution of the problems in the preoperative approach will absolutely increase the surgical success in the preoperative and postoperative periods.

Right indication and correct surgical planning are absolutely necessary. Your nick names have to be patience during surgery. The surgeon's overconfidence, hastiness and misapplication may lead to serious problems. The surgeon and his/her team should determine all materials required for hemostasis in their hands in the preoperative planning and make their preparations accordingly. The blood bank is an essential concept in cardiac surgery. It is essential to use blood products by determining the patient's need. Hemostasis should be provided during the operation and this should not be left to the intensive care process. Creating a solution is the basic principle of the surgeon and surgery (**Figures 6** and 7).

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References

[1] Faroni D, Meir J, New HV, Van der Linden PJ, Hunt BJ. Patient blood management for neonates and children undergoing cardiac surgery: 2019 NATA guidelines. Journal of Cardiothoracic and Vascular Anesthesia:S1053-0770(19)30296-4

[2] Task Force on Patient Blood Management for Adult Cardiac Surgery of the European Association for Cardio-Thoracic Surgery, the European Association of Cardiothoracic Anaesthesiology, Boer C, Meesters MI, Milojevic M, Benedetto U, Bolliger D, et al. 2017 EACTS/EACTA guidelines on patient blood management for adult cardiac surgery. Journal of Cardiothoracic and Vascular Anesthesia. 2018;**32**:88-120

[3] Karkouti K, Wijeysundera DN, Yau TM, Beattie WS, Abdelnaem E, McCluskey SA, et al. The independent association of massive blood loss with mortality in cardiac surgery. Transfusion. 2004;**44**:1453-1462

[4] Ranucci M, Bozzetti G, Ditta A, Cotza M, Carboni G, Ballotta A. Surgical reexploration after cardiac operations: Why a worse outcome? The Annals of Thoracic Surgery. 2008;**86**:1557-1562

[5] Paone G, Likosky DS, Brewer R, Theurer PF, Bell GF, Cogan CM, et al. Transfusion of 1 and 2 units of red blood cells is associated with increased morbidity and mortality. The Annals of Thoracic Surgery. 2014;**97**:87-93. discussion 93-4

[6] Frojd V, Jeppsson A. Reexploration for bleeding and its association with mortality after cardiac surgery. The Annals of Thoracic Surgery. 2016;**102**:109-117

[7] Alghamdi AA, Davis A, Brister S, Corey P, Logan A. Development and validation of transfusion risk understanding scoring tool (TRUST) to stratify cardiac surgery patients according to their blood transfusion needs. Transfusion. 2006;**46**:1120-1129

[8] Ranucci M, Aronson S, Dietrich W, Dyke CM, Hofmann A, Karkouti K, et al. Patient blood management during cardiac surgery: Do we have enough evidence for clinical practice? The Journal of Thoracic and Cardiovascular Surgery. 2011;**142**:249.e1-249.32

[9] Ferraris VA, Brown JR, Despotis GJ, Hammon JW, Reece TB, Saha SP, et al. 2011 update to the Society of Thoracic Surgeons and the Society of Cardiovascular Anesthesiologists blood conservation clinical practice guidelines. The Annals of Thoracic Surgery. 2011;**91**:944-982

[10] Stokes ME, Ye X, Shah M, et al. Impact of bleeding-related complications and/or blood product transfusions on hospital costs in inpatient surgical patients. BMC Health Services Research. 2011;**11**:135. DOI: 10.1186/1472-6963-11-135

[11] Blome M, Isgro F, Kiessling AH, Skuras J, Haubelt H, Hellstern P, et al. Relationship between factor XIII activity, fibrinogen, haemostasis screening tests and postoperative bleeding in cardiopulmonary bypass surgery. Thrombosis and Haemostasis. 2005;**93**:1101-1107

[12] Bosch Y, Al Dieri R, Ten Cate H, Nelemans P, Bloemen S, Hemker C, et al. Preoperative thrombin generation is predictive for the risk of blood loss after cardiac surgery: A research article. Journal of Cardiothoracic Surgery. 2013;**8**:154

[13] Karlsson M, Ternstrom L, Hyllner M, Baghaei F, Nilsson S, Jeppsson A. Plasma fibrinogen level, bleeding, and transfusion after

on-pump coronary artery bypass grafting surgery: A prospective observational study. Transfusion. 2008;**48**:2152-2158

[14] Ranucci M, Jeppsson A, Baryshnikova E. Pre-operative fibrinogen supplementation in cardiac surgery patients: An evaluation of different trigger values. Acta Anaesthesiologica Scandinavica. 2015;**59**:427-433

[15] Walden K, Jeppsson A, Nasic S, Backlund E, Karlsson M. Low preoperative fibrinogen plasma concentration is associated with excessive bleeding after cardiac operations. The Annals of Thoracic Surgery. 2014;**97**:1199-1206

[16] Gielen C, Dekkers O, Stijnen T, Schoones J, Brand A, Klautz R, et al. The effects of pre- and postoperative fibrinogen levels on blood loss after cardiac surgery: A systematic review and meta-analysis. Interactive Cardiovascular and Thoracic Surgery. 2014;**18**:292-298

[17] Coakley M, Hall JE, Evans C, Duff E, Billing V, Yang L, et al. Assessment of thrombin generation measured before and after cardiopulmonary bypass surgery and its association with postoperative bleeding. Journal of Thrombosis and Haemostasis. 2011;**9**:282-292

[18] Blaudszun G, Munting KE, Butchart A, Gerrard C, Klein AA. The association between borderline pre-operative anaemia in women and outcomes after cardiac surgery: A cohort study. Anaesthesia. 2018;**73**(5):572-578. DOI: 10.1111/anae.14185

[19] Antithrombotic Trialists Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. British Medical Journal. 2002;**324**:71-86

[20] Sun JC, Whitlock R, Cheng J, Eikelboom JW, Thabane L, Crowther MA, et al. The effect of pre-operative aspirin on bleeding, transfusion, myocardial infarction, and mortality in coronary artery bypass surgery: A systematic review of randomized and observational studies. European Heart Journal. 2008;**29**:1057-1071

[21] Myles PS, Smith JA, Forbes A, Silbert B, Jayarajah M, Painter T, et al. Stopping vs. continuing aspirin before coronary artery surgery. The New England Journal of Medicine. 2016;**374**:728-737

[22] Deja MA, Kargul T, Domaradzki W, Stącel T, Mazur W, Wojakowski W. Effects of preoperative aspirin in coronary artery bypass grafting: A double-blind, placebo-controlled, randomized trial. The Journal of Thoracic and Cardiovascular Surgery. 2012;**144**:204-209

[23] Hansson EC, Shams Hakimi C, Astrom-Olsson K, Hesse C, Wallen H, Dellborg M, et al. Effects of ex vivo platelet supplementation on platelet aggregability in blood samples from patients treated with acetylsalicylic acid, clopidogrel, or ticagrelor. British Journal of Anaesthesia. 2014;**112**:570-575

[24] Martin AC, Berndt C, Calmette L, Philip I, Decouture B, Gaussem P, et al. The effectiveness of platelet supplementation for the reversal of ticagrelor-induced inhibition of platelet aggregation: An in-vitro study. European Journal of Anaesthesiology. 2016;**33**:361-367

[25] Mangano DT, Multicenter Study of Perioperative Ischemia Research Group. Aspirin and mortality from coronary bypass surgery. The New England Journal of Medicine. 2002;**347**:1309-1317

[26] Yusuf S, Zhao F, Mehta SR, Chrolavicius S, Tognoni G, Fox KK.

Effects of clopidogrel in addition to aspirin in patients with acute coronary syndromes without ST-segment elevation. The New England Journal of Medicine. 2001;**345**:494-502

[27] Wiviott SD, Braunwald E, McCabe CH, Montalescot G, Ruzyllo W, Gottlieb S, et al. Prasugrel versus clopidogrel in patients with acute coronary syndromes. The New England Journal of Medicine. 2007;**357**:2001-2015

[28] Qamar A, Bhatt DL. Current status of data on cangrelor. Pharmacology & Therapeutics. 2016;**159**:102-109

[29] Kolh P, Windecker S, Alfonso F, Collet JP, Cremer J, Falk V, et al. 2014 ESC/EACTS guidelines on myocardial revascularization: The task force on myocardial revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). Developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). European Journal of Cardio-Thoracic Surgery. 2014;**46**:517-592

[30] Ferraris VA, Saha SP, Oestreich JH, Song HK, Rosengart T, Reece TB, et al. 2012 update to the Society of Thoracic Surgeons guideline on use of antiplatelet drugs in patients having cardiac and noncardiac operations. The Annals of Thoracic Surgery. 2012;**94**:1761-1781

[31] Patrono C, Coller B, FitzGerald GA, Hirsh J, Roth G. Platelet-active drugs: The relationships among dose, effectiveness, and side effects: The seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest. 2004;**126**:234S-264S

[32] Boeken U, Litmathe J, Kurt M, Feindt P, Gams E. CABG-procedures in patients with pretreatment with the GPIIb/IIIa-receptor antagonist tirofiban (Aggrastat): Modification of perioperative management? International Journal of Cardiology. 2008;**127**:257-259

[33] Douketis JD, Spyropoulos AC, Kaatz S, Becker RC, Caprini JA, Dunn AS, et al. Perioperative bridging anticoagulation in patients with atrial fibrillation. The New England Journal of Medicine. 2015;**373**:823-833

[34] Ashikhmina E, Tomasello N, Connors JM, Jahanyar J, Davidson M, Mizuguchi KA. Type A aortic dissection in a patient on dabigatran: Hemostasis post circulatory arrest. The Annals of Thoracic Surgery. 2014;**98**:2215-2216

[35] Stein P, Bosshart M, Brand B, Schlicker A, Spahn DR, Bettex D. Dabigatran anticoagulation and Stanford type A aortic dissection: Lethal coincidence: Case report with literature review. Acta Anaesthesiologica Scandinavica. 2014;**58**:630-637

[36] Crapelli GB, Bianchi P, Isgro G, Biondi A, de Vincentiis C, Ranucci M. A case of fatal bleeding following emergency surgery on an ascending aorta intramural hematoma in a patient taking dabigatran. Journal of Cardiothoracic and Vascular Anesthesia. 2016;**30**:1027-1031

[37] Hall MJ, DeFrances CJ, Williams SN, Golosinsky A, Schwartzman A. National Hospital Discharge Survey: 2007 summary. National Health Statistics Reports. 2010;**26**(29):1-20 2

[38] Zimmerman LH. Causes and consequences of critical bleeding and mechanisms of blood coagulation. Pharmacotherapy. 2007;**27**(9 Pt 2):45S-56S

[39] Shander A. Financial and clinical outcomes associated with surgical bleeding complications. Surgery. 2007;**142**(4 Suppl):S20-S25

[40] Boucher BA, Hannon TJ. Blood management: A primer for clinicians. Pharmacotherapy. 2007;**27**(10):1394-1411

[41] Stokes ME, Ye X, Shah M, et al. Impact of bleeding related complications and/or blood product transfusions on hospital costs in inpatient surgical patients. BMC Health Services Research. 2011;**31, 11**:135-147

[42] Neveleff DJ. Optimizing hemostatic practices: Matching the appropiate hemostat to the clinical situation. AORN Journal. 2012;**96**(5):S1-S17. DOI: 10.1016/j.aorn.2012.08.005

[43] Türker FS. Hemorrhagic shock. In: Clinical Management of Shock—The Science and Art of Physiological Restoration. 2019

[44] Levy JH. Overview of clinical efficacy and safety of pharmacologic strategies for blood conservation. American Journal of Health-System Pharmacy. 2005;**62**(18 Suppl 4):S15-S19

[45] Porte RJ, Leebeek FW. Pharmacological strategies to decrease transfusion requirements in patients undergoing surgery. Drugs. 2002;**62**(15):2193-2211

[46] Myles PS, Smith JA, Forbes A, Silbert B, Jayarajah M, Painter T, et al. Tranexamic acid in patients undergoing coronary-artery surgery. The New England Journal of Medicine. 2017;**376**:136-148

[47] Ker K, Edwards P, Perel P, Shakur H, Roberts I. Effect of tranexamic acid on surgical bleeding: Systematic review and cumulative meta-analysis. British Medical Journal. 2012;**344**:e3054

[48] Sharma V, Katznelson R, Jerath A, Garrido-Olivares L, Carroll J, Rao V, et al. The association between tranexamic acid and convulsive seizures after cardiac surgery: A multivariate analysis in 11529 patients. Anaesthesia. 2014;**69**:124-130

[49] Quarishy N, Bachowski G, Benjamin RJ, et al. A Compendium of Transfusion Practice Guidelines. American Red Cross. Available from: http://www.redcrossblood.org/sites/arc/files/pdf/Practice-Guidelines-Nov2010-Final.pdf [Accessed: July 25, 2012]

[50] Desborough M, Sandu R, Brunskill SJ, Doree C, Trivella M, Montedori A, et al. Fresh frozen plasma for cardiovascular surgery. Cochrane Database of Systematic Reviews. 2015;7:CD007614

[51] Stanworth SJ, Brunskill SJ, Hyde CJ, McClelland DB, Murphy MF. Is fresh frozen plasma clinically effective? A systematic review of randomized controlled trials. British Journal of Haematology. 2004;**126**:139-152

[52] Casbard AC, Williamson LM, Murphy MF, Rege K, Johnson T. The role of prophylactic fresh frozen plasma in decreasing blood loss and correcting coagulopathy in cardiac surgery. A systematic review. Anaesthesia. 2004;**59**:550-558

[53] Yang L, Stanworth S, Hopewell S, Doree C, Murphy M. Is fresh-frozen plasma clinically effective? An update of a systematic review of randomized controlled trials. Transfusion. 2012;**52**:1673-1686; quiz

[54] Kessler CM, Ortel TL. Recent developments in topical thrombins. Thrombosis and Haemostasis. 2009;**102**(1):15-24

[55] Spotnitz WD, Burks S. Hemostats, sealants, and adhesives: Components of the surgical toolbox. Transfusion. 2008;**48**(7):1502-1516

[56] Spotnitz WD, Burks S. State-of-the-art review: Hemostats, sealants, and adhesives II: Update as well as

how and when to use the components of the surgical toolbox. Clinical and Applied Thrombosis/Hemostasis. 2010;**16**(5):497-514

[57] Neveleff DJ, Kraisis LW, Schulman CS. Implementing methods to improve perioperative hemostasis in the surgical and trauma settings. AORN Journal. 2010;**92**(5):S1-S15

[58] Ham SW, Lew WK, Eaver FA. Thrombin use in surgery: An evidence-based review of its clinical use. Journal of Blood Medicine. 2010;**1**:135-142

[59] Thrombin-JMI® [Package Insert]. Bristol, TN: King Pharmaceuticals, Inc; 2007. Available from: http://labeling.pfizer.com/ShowLabeling.aspx?id=695 [Accessed: July 29, 2012]

[60] Evithrom® [Package Insert]. Somerville, NJ: Ethicon, Inc; 2007. Available from: http://www.ethicon360.com/products/evithrom-thrombin-topical-human [Accessed: July 29, 2012]

[61] Recothrom® [Package Insert]. Seattle, WA: ZymoGenetics, Inc; 2008. . Available from: http://www.recothrom.com/prescribing_info/default.aspx [Accessed: July 29, 2012]

[62] Voils SA. Thrombin products: Economic impact of immune-mediated coagulopathies and practical formulary considerations. Pharmacotherapy. 2009;**29**(7 Pt 2):18S-22S

[63] Tisseel™ [Package Insert]. Westlake Village, CA: Baxter Healthcare Corp; 2009. Available from: http://www.baxter.com/healthcare_professionals/products/tisseel.html