Peertechz


Medical Group

Global Journal of Anesthesiology

DOI: http://dx.doi.org/10.17352/gja

ISSN: 2455-3476 CC By

**Omer Baygin[1], Didem Gungor Arslan[2], Ayten Saracoglu[1]***

[1]Department of Anesthesiology and Intensive Care, Marmara University Medical School, Turkey
[2]Department of Thoracic Surgery, Marmara University Medical School, Turkey

**Received:** 02 November, 2018
**Accepted:** 08 November, 2018
**Published:** 09 November, 2018

***Corresponding author:** Doctor. Ayten Saracoglu, Associate professor. MD, Department of Anesthesiology and Intensive Care, Marmara University Medical School, Istanbul, Turkey, Tel: +90216 6254545; Fax: +90216 6254639; E-mail: anesthesiayten@gmail.com

**Keywords:** Thoracic anesthesia; Bleeding; Thrombosis

https://www.peertechz.com

Check for updates

Review Article

# The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery

## Abstract

Management of perioperative anti-coagulation is a general clinical dilemma, and generally accompanied by the significant adverse effects. A personalized approach is necessary to minimize the risks of anesthesia and surgery in patients with comorbidities. Patients with coronary artery disease may not tolerate decreased oxygen delivery and increased oxygen demand in myocardium due to bleeding. On the other side there is an increased use of new anticoagulants in thoracic surgery. The essentials of perioperative management should be determined by creating a balance between the use of oral anticoagulants in low bleeding risk, and bridging treatment for patients having high thromboembolic risk. In this opinion article, we aimed to review the factors affecting bleeding and thrombosis during thoracic surgery. Classification of bleeding and thrombosis risk in cardiac patients was reviewed with the recommendations for preventing the thrombotic complications.

## Introduction

The thirty-day mortality rate among patients having high level of cardiac risk, who had non-cardiac surgery history, is approximately 5% [1]. A personalized approach is necessary to minimize the risks of anesthesia and surgery in patients with comorbidities. A decision making team should be utilized by the anesthetist, surgeon, primary healthcare provider, and specialist physicians including hematologist and/or cardiologist [2]. Hereby assessment is important for the high risk surgical patients to minimize the risk. Establishing the balance between bleeding and thrombosis among cardiac patients, who use anticoagulant and will have thoracic surgery, is one of the questions that is frequently asked in nowadays and waiting for being answered. In this opinion article, we aimed to present the information about the management of this patient group.

The assessment of patients having cardiovascular disease requires a process of multiple steps. The risk factors should be determined in preoperative period, and patients should be optimized. Moreover, the situations affecting the cardiac risk such as surgery type and duration should also be discussed [3]. The risk factors for perioperative coronary thrombosis are listed in table 1, and the recommendations of ACC/AHA guideline about the management of patients undergoing non-cardiac surgery are summarized in table 2.

Following acute coronary syndrome or coronary stent implantation, almost 1/3 of the patients experience non-cardiac surgery [4]. The challenge in management of anti-thrombotic treatment is to establish the balance between bleeding and thrombotic risk. Especially for the patients receiving dual antiplatelet treatment, the preferences should be individualized and answered via a multidisciplinary discussion. American College of Chest Physicians divides the thrombotic risk into 3 main risk categories: 1) high risk (>10%), 2) medium risk (5-10%) and 3) low risk (<5%) [5]. At this point, in high risk and medium risk groups of patients in case that there is no high risk of bleeding, the bridging therapy is recommended.

Various clinically used cardiac risk determinants were developed. The most important one among them, used for the patients undergoing non-cardiac surgery, is Lee's Revised Cardiac Risk Index (RCRI) index [6]. Besides that, a classification was developed by using the database of American

**Table 1:** risk factors for perioperative coronary thrombosis.

| Clinic predictors | Angiographic predictors |
|---|---|
| Advanced age | Long stent |
| Acute coronary syndrome | Multiple lesions |
| Diabetes Mellitus | Stent in Bifurkation |
| Low EF | Smaller venous radius |
| Brachytherapy history | Suboptimal stenting |
| Renal Failure | Overlapping |



**Citation:** Baygin O, Arslan DG, Saracoglu A (2018) The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery. Glob J Anesth 5(2): 019-026. DOI: http://doi.org/10.17352/2455-3476.000043

Table 2: Recommendations of ACC/AHA Guideline for the perioperative management of cardiac patients having non-cardiac surgery.

| |
|---|
| **Class I:** |
| If non-cardiac surgery is planned for 4-6 weeks after the BMS yada DES implantation, and if the bleeding risk dominates the thrombotic risk, dual antiplatelet treatment should be maintained (Level of Evidence: C). |
| If the patient has coronary stent and if it is necessary to interrupt the P2Y12 platelet receptor–inhibitor treatment due to bleeding, it is recommended to maintain aspirin treatment (if possible) or to immediately start it after the surgery (Level of Evidence: C). |
| **Class II:** |
| For the patients to have elective non-cardiac surgery, who have no coronary stent, it is recommended to maintain aspirin treatment if the increased potential cardiac risk is higher than the bleeding risk (Level of Evidence: B). |
| **Class III:** |
| If the ischemic event doesn't dominate the surgical bleeding risk, and if the patient has no coronary stent history, then it wouldn't be useful to start and maintain aspirin treatment (Level of Evidence: C). |

College of Surgeons National Surgical Quality Improvement Program (NSQIP) [3].

Approximetely 4-7% of the patients having coronary stent, need a surgical intervention per year [7]. The most frequent reason for the perioperative stent thrombosis among the patient, who underwent non-cardiac surgery, is the termination of antiplatelet therapy together with the induced pro-thrombotic situation [8,9]. Sympathetic stimulation occurs as a result of the operation, so the myocardial oxygen demand increases [10]. The surgery also increases the fibrinogen level and causes an increase in platelet activation and aggregation. Besides that, the activation of tissue factor with the decrease in fibrinolysis and endothelial damage causes a pre-coagulant structure [1]. Approximately 18% of the surgical operations permormed by high cardiac risk, while approx. 25% of them also have high bleeding risk [11]. Urgent operations constitute the most risky group in terms of bleeding and thrombosis.

In treatment of patients having coronary stent, the platelet inhibition plays an important role [12]. The platelet amounts in preoperative period and the coagulation tests are the important markers in terms of the perioperative bleeding risk, while the importance of them is not yet known enough. But, however, it was reported that in non-cardiac surgeries the blood transfusion increased due to the thrombocytopenia in the preoperative period [13]. Even though the warfarin had been used clinically more than 6 decades, there is no consensus on how the recommendations will be for the management of preoperative patients [14].

The bridging treatment is to interrupt the oral coagulants temporarily and to use LMWH or unfractionated heparin. However, many systematic review and meta-analysis reported that the thrombotic effect didn't change but the bleeding risk increased [5]. The CARP trial indicated that, among the patients that have stable coronary artery disease and will undergo non-cardiac surgery, the coronary artery revascularization didn't create a significant decrease in postoperative myocardial infarct, mortality, and duration of hospital stay [15]. Temporarily interrupting the antiplatelet treatment for selected patients, can ensure the operations can be done without deteriorating the balance between thrombosis and bleeding [16,17]. Four important situations were determined as the timing of surgery, to interrupt or continue the antiplatelet treatment, returning to antiplatelet treatment, and the efficiency of bridging treatment [18,19].

## Are the antithrombotic agents helpful or harmful in thoracic surgery?

Management of perioperative anti-coagulation is a general clinical dilemma, and generally accompanied by the significant adverse effects [20]. It was shown that the bleeding risk increased in patients receiving dual antiplatelet treatment during the perioperative period [12].

In a study, where platelet mapping assay was used, the incidence of myocardial adverse cardiac events (MACEs) following the non-cardiac surgery was found to be high among patients having coronary stent even despite the use of aspirin, and the non-ST myocardial infarcts came to the forefront independently from the platelet function [8]. The analysis of selected publications on aspirin and bleeding is presented in table 3.

The incidence of cardiovascular events following the thoracic surgery operations is approximately 7%, whereas the mortality and morbidity rates are higher especially after non-cancer operations [21]. The most frequent reasons of the non-cancer operations are infections. In cardiovascular complications, the intraoperative hypertension and positive liquid balance are the independent risk factors.

Several patients maybe presented with taking medications even though it is not necessary to take them anymore. This is frequent especially in deep vein thrombosis [20]. Interrupting the anticoagulant agents should be carefully considered. Bridging treatment generally represent; the interruption of taking the agent among the patients using warfarin and then using LMWH, and after surgery at first using both of them together then continue with only warfarin.

**Vitamin K antagonists (VKA):** For the patients having low thromboembolism risk, the oral treatment can be interrupted for 5 days preoperatively, and then restarted on the evening of operation day or the next morning unless there is a bleeding

Table 3: Selected publications on aspirin and bleeding.

| Study Group | Conclusion | Year and Journal of Publication |
|---|---|---|
| Burger W et al. (44) | Interruption of aspirin increases the thrombotic risk. | J Intern Med. 2005 |
| PEP (Pulmonary Embolism Prevention) trial. (45) | Aspirin has no benefit. | Lancet 2000. |
| POISE-2 Investigators. (46) | Major bleeding detected, no decrease in MI risk | N Engl J Med. 2014 |
| Livhits M et al. (47) | Increase in bleeding | Ann Surg. 2011 |
| Stratagem trial. (48) | No change in bleeding | Br J Anaesth. 2011 |
| Oscarsson A et al. (49) | No significant increase in bleeding | Br J Anaesth. 2010 |
| Eberli D et al. (50) | 10% thrombotic event upon the interruption of antiplatelet treatment | J Urol. 2010. |



Citation: Baygin O, Arslan DG, Saracoglu A (2018) The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery. Glob J Anesth 5(2): 019-026. DOI: http://doi.org/10.17352/2455-3476.000043

risk. In general, because there is 20% increase in bleeding risk, it is not recommended to use therapeutic doses of heparin in first 12-24 hours after the surgery [5]. It is recommended to measure INR in the day of operation, and its recommended level is <1.5 for major surgeries [1]. The surgery should be postponed in cases of higher levels [3]. For the patients having high bleeding risk and high thromboembolism risk, the bridging treatment is suggested after interrupting the oral anticoagulants [5]. This group is atrial fibrillation (AF) with a CHA2DS2-VASc [Cardiac failure, Hypertension, Age ≥75 (Doubled), Diabetes, Stroke (Doubled) – Vascular disease, Age 65–74 and Sex category (Female) [score of ≥4] or mechanical or biological prosthetic heart valves, or those having mitral valve restoration in last 3 months or those having venous thromboembolism in last 3 months or the patients with thrombophilia [3]. In bridging treatment, LMWH should be given 12 hours before the final procedure, and it should be repeated 12 hours after the procedure [3]. VKA should be restarted within 1-2 days in accordance with the hemostatic status. In cases requiring urgent surgery, low doses of Vitamin K is suggested. Normalization of INR may take up to 6-12 hours.

For the patients being treated with new generation oral anticoagulants, the bridging treatment is unnecessary because of more predictable pharmacokinetics and shorter half-lives (dabigatran, direct FXa inhibitors) [5] (Tables 4-6). So that, because of rapid on-off duration of direct acting oral anticoagulants, parenteral anticoagulation might not be required [22]. Moreover, these medications can be given in operations, for which warfarin can be used. Especially the well-defined on-off durations render bridging treatment unnecessary, except for the patients having high thrombosis risk. For the patients having normal level risk of bleeding, it is recommended to wait for 2-3 half-lives, while it is recommended to wait for 4-5 half-lives for the patients having high level of bleeding risk [3]. RE-LY trial revealed that almost 50% of the patients using dabigatran become suitable for the operation within 48 hours after ending the medication [20].

**Antiplatelet medications**: They are in the class of antithrombotic drugs (Table 7). The effects of medications causing irreversible platelet inhibition, do not end unless new platelets are formed. The drugs in this group include aspirin, clopidogrel, prasugrel, ticlopidine, and they are frequently used by cardiac patients. The antiplatelet agent management is important for patients undergoing coronary artery surgery. There may be a dilemma between interrupting the drug and possible thromboembolic events and between continuing the drug and relevant complications. While there is no need in procedures containing low level of bleeding risk, it is recommended to continue aspirin and to postpone the procedure until the effect of antiplatelet agent disappears in cases of high risk of bleeding [23].

**Table 4:** Classification of new generation oral anticoagulants.

| Direct thrombin inhibitors | Active Factor 10 inhibitors |
|---|---|
| Dabigatran | Apixaban<br>Rivaroxaban<br>Edoxaban |

**Table 5:** Analysis of NOACs and their effects.

| NOAC | Study | Conclusion |
|---|---|---|
| Dabigatran | 1. RE-MOBILIZE, RE-MODEL, RE-NOVATE and RE-NOVATE II | Dabigatran is as affective as enoxaparin for thrombophylaxis following the orthopedic surgeries, and has same incidence of bleeding. |
| | 2. RE-COVER, RE-MEDY and RE-COVER II | Dabigatran is as effective in acute management of VTE as warfarin is, and the incidence major bleeding in prolonged treatments is low |
| | 3. RE-LY | Used for preventing the stroke in patients having atrial fibrillation, dabigatran was not different from warfarin, but risk of major bleeding increased since 2nd year of treatment among the patients that have used high doses of dabigatran |
| Apixaban | 1. ADVANCE-1, ADVANCE-2 and ADVANCE-3 | decrease in VTE and bleeding risk, when compared to enoxaparin after orthopedic surgery |
| | 2. AMPLIFY | decrease in major bleeding without any increase in incidence of thromboembolism, when compared to enoxaparin/warfarin in treatment of acute VTE |
| | 3. ARISTOTLE | it is superior in preventing the stroke and systemic embolism, and decreases the bleeding mortality, when compared to warfarin in patients with atrial fibrillation |
| | 4. AVERROES | decrease in incidence of stroke and same level of major bleeding, when compared to aspirin among the patients, for whom the anticoagulation with VKA was not optimized, |
| Edoxaban | 1. STARS-E3, STARS-J4, and STARS-J5 | Similar level of safety, when compared to enoxaparin in major orthopedic surgery patients |
| | 2. Hokusai-VTE | Less major bleeding when compared to warfarin in acute symptomatic VTE treatment |
| | 3. ENGAGE-AFA-TIMI48 | Decrease in bleeding and in cardiovascular mortality when compared to warfarin used in order to prevent the stroke or systemic embolism among the patients with atrial fibrillation |
| Rivaroxaban | 1. RECORD-1, RECORD-2, RECORD-3, RECORD-4 | Significant protection without increase in bleeding when compared to enoxaparin in preventing VTE following major orthopedic surgery |
| | 2. EINSTEIN-DVT56 and EINSTEIN-PE57 | 41% decrease in major bleeding when compared to Enoxaparin/Warfarin in terms of acute VTE treatment |
| | 3. ROCKET-AF | Difference in neither bleeding nor stroke when compared to warfarin among the patients having atrial fibrillation and increased stoke risk |



**Citation:** Baygin O, Arslan DG, Saracoglu A (2018) The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery. Glob J Anesth 5(2): 019-026. DOI: http://doi.org/10.17352/2455-3476.000043

Table 6: Comparison of the characteristics of new generation oral anticoagulants.

| | Dabigatran | Rivaroxaban | Apixaban | Edoxaban |
|---|---|---|---|---|
| Action mechanism | Anti-IIa | Anti-Xa | Anti-Xa | Anti-Xa |
| Half-life (h) | 14-17 | 5-9 | 8-15 | 6-11 |
| Bioavailability | ~6 | 80-100 | 34-88 | ~40 |
| Renal excretion (%) | ~80 | 33 | ~22 | ~40 |

Table 7: Classification of antithrombotic agents.

| Anticoagulant Agents | Antithrombotic agents | Thrombolytic and Fibrinolytic agents |
|---|---|---|
| • Unfractionated and LMWH<br>• Vitamin K Antagonists<br>• Direkt Tromben Inh. (Dabigatran, Bivalirudin)<br>• Factor Xa Inh (Fondaparinuks, Rivaroxaban, Apixaban, Edoxaban) | • Aspirin<br>• Tienopiridin Derivatives (Clopidogrel, Tiklopidin, Tikagrelor)<br>• Glikoprotein IIb/IIIa Inhibitors (Absiksimab, Tirofiban, Eptifibatid) | • tPA Streptokinase<br>• Urokinase<br>• Alteplase |

Interrupting the clopidogrel treatment creates a rebound effect, and a predisposition towards hyper-coagulation occurs with pro-thrombotic status.

**Dual antiplatelet treatment:** It is reported that, when compared to stent thrombosis of patients with coronary stent, de novo development of coronary occlusion has a worse prognosis [3]. Besides that, early cut of DAPT is the most important predictor of coronary stent occlusion. MACE risk is observed during the first year following the implantation of stent, and its mortality rate is approx. 45% [5]. In general, it is recommended to wait for the endothelization. In elective surgeries, the most ideal way is waiting 3 months after the implantation metal stent or 4 months for an urgent surgery, while this duration is 12 months for the stents with drug delivery, and the dual antiplatelet treatment should be maintained in this duration [24]. But, no ideal timing was reported for non-cardiac surgery following the CABG. If it is not an urgent surgery following the balloon angioplasty, it is necessary to wait for 2 weeks. In many studies representing the expert opinion, it is recommended to postpone the non-urgent surgeries or to maintain the aspirin as long as possible [25]. In surgeries, where the drug coated stent is implanted time-independently, at least one antiplatelet treatment should be prefered [3].

## Aspirin

Ending the aspirin treatment increases the MACE risk due to both of platelet rebound effect and development of pro-thrombotic event [26]. The normalization of platelet function via platelet inhibition is not a basic on-off phenomenon.

Studies on aspirin may present conflicting expressions. In POISE-2 trial, besides that it wasn't shown to decrease the mortality and non-fatal cardiac events, it was also reported that it increased the incidence of bleeding in aspirin group [3]. Even though the studies do not recommend the routine use of aspirin, it was also reported that low-dose aspirin might be useful in cases of low level of bleeding risk [27]. If the risk of bleeding leads to potential cardiovascular events, stopping the use of aspirin is recommended.

In studies on aspirin, there is contradictory information regarding that the continuance of aspirin is effective from the aspect of thromboembolic events. But, the general opinion is that it decreases the MACE, while it can increase the bleeding risk in patients, undergoing high risk non-cardiac surgery [4,5,11]. In general, the termination of the aspirin therapy is recommended for the patients, who have low thromboembolic risk and will undergo major surgery, and the patients having high level of bleeding risk [5]. On the other hand, heparin is not recommended for the patients for whom the antiplatelet treatment is ended. If the risk of bleeding leads to potential cardiovascular events, termination of the aspirin therapy is recommended [28]. In summary, when the myocardial ischemia risk exceeds the bleeding risk, it is recommended to continue the aspirin treatment [29]. Parenteral anticoagulation might be useful for the patients with high thromboembolic risk.

**Reverse of anticoagulant treatment:** In patients receiving vitamin K antagonists, the effect may be reversed within 6-12 hours following the administration of vitamin K for urgent surgery. For a faster effect, it would be useful to transfuse fresh frozen plasma or prothrombin complex concentrate. In urgent operations involving high bleeding risk, one should consider postponing the anticoagulant agent for 1 or 2 half-lives.

**Bridging treatment:** The chronic oral anticoagulation treatment can be terminated for many reasons. For these patients, bridging treatment is a dilemma, and its benefits have not been clearly shown [20,22]. There are many variations of bridging treatment. In some of the studies, it is performed by low molecular weight heparin (LMWH), but in other studies adenosine diphosphate P2Y12 receptor antagonists (cangrelor), and glycoprotein IIb/IIIa inhibitors (eptifibatide, tirofiban) are used [11]. In BRIDGE trial, it was reported that, for the patients having medium level of thromboembolic risk and atrial fibrillation receiving Vitamin-K antagonists, mixing the deltaparin with placebo leads no statistically significant decrease but the major bleeding was statistically higher [22].

Bridging treatment is mainly preferred for mechanic heart valve, atrial fibrillation, and venous thromboembolism, which involve high risk. For the patients receiving bridging treatment, the ratio of bleeding/thrombosis was reported to be 13/1 [20]. Besides that, bridging treatment is applied to many patients only in order to remain in "confidence level".

## Recommendations for preventing the thrombotic complications

The incidence of perioperative thromboembolic event is 0.53%, and this risk doubles in patients having mechanic heart valve [20]. In general, the guidelines on this issue agree on 3 main themes:

1) The use of oral anticoagulants should not be terminated among patients with low bleeding risk,

2) Bridging treatment should be considered for patients having high thromboembolic risk in cases of low bleeding risk,



Citation: Baygin O, Arslan DG, Saracoglu A (2018) The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery. Glob J Anesth 5(2): 019-026. DOI: http://doi.org/10.17352/2455-3476.000043

3) Individualized treatment option should be considered for the patients in medium risk group.

In short, it is necessary to avoid from terminating the anticoagulant treatment as long as possible. If it is necessary to end the treatment, the non-pharmacological approaches should also be considered.

One should avoid from periprocedural interruption of warfarin. Many clinical studies show that the oral anticoagulant treatments are terminated unnecessarily by up to 60% [20]. Moreover, even in operations involving low level of bleeding risk, the oral anticoagulant treatment might be ended without considering the thromboembolic risk.

## Classification of bleeding and thrombosis risk in cardiac patients undergoing thoracic surgery

Early interruption of dual antiplatelet treatment in patients having stent creates thrombotic risk, while the most frequent reason for this is the surgery. On the other hand, in case of maintaining the treatment, an increase might be seen in bleeding risk. Evaluation of thrombotic risk should be for preventing the arterial thrombus among patients actually receiving antithrombotic treatment. These patients can be divided into 3 groups: high risk, medium risk, and low risk groups.

Two important issues should be emphasized in determining the perioperative bleeding risk. Use of anticoagulant and antiplatelet drugs and the relationship of these drugs with the duration of operation play important role at this point. Many minor procedures might lead us to face with bleeding risk.

Warfarin treatment management in invasive procedures requires determining the thrombotic risk in case of termination of warfarin treatment and possible bleeding caused by continuation. Bridging treatment with LMWH was reported to cause an increase in bleeding regardless of any change in thromboembolic events [14]. BRIDGE trial revealed that the placebo didn't cause any change in arterial thromboembolic events when compared to bridging treatment with LMWH [14]. Similarly, in this study, it was also reported that there is no difference in bridging treatment in invasive procedures in terms of venous thromboembolism. For the surgical patients with high bleeding risk, the warfarin treatment should be terminated 4-5 days before the surgery and the INR should be normalized. For the patients having high venous thrombosis risk, it is recommended to consider the bridging treatment [14].

Among patients undergoing lung cancer surgery, the allogenic blood transfusion was reported to be related with recurrence and decreased survival [30,31]. MACE risk was found maximum in the 1st year following the stent implantation, and it has 45% of mortality rate [5]. No ideal timing was reported for non-cardiac surgery following CABG. If it is not an urgent surgery, one should wait for 2 weeks before the balloon angioplasty [1]. Major embolism risk can be high especially among patients undergoing mitral valve surgery.

In patients with atrial fibrillation, the CHADS2 and/or CHA2DS2-VASc score can be considered for thrombotic risk. In general, the score of CHA2DS2-VASc is used. The values between 0 and 2 are considered low, those between 2 and 4 to be medium risk, and scores >4 to be high risk. It can be seen that bridging treatment is not necessary for patients aged between 0 and 2, while bridging treatment is recommended for the scores higher than 4 [32].

In venous thromboembolic events, termination of anticoagulation in 3 months indicates high risk. However, for rapidly progressing/metastatic patients and patients with antiphospholipid syndrome, the risk further increases. The surgical patients within 3 months or accompanied by both of two conditions are recommended to receive bridging treatment, while LMWH thromboprophylaxis is recommended for the others [32].

In general, considering the thrombotic risk following the termination of anticoagulant, it is recommended to perform the surgery without interrupting the medications. Although an increase in bleeding is reported for some of the procedures, these events are generally minor or restricting themselves [5].

If termination of the antiplatelet treatment is planned, it should be performed 3-5 days before for aspirin, 5-7 days for clopidogrel and ticagrelor, and 10 days for prasugrel. Platelet function tests might provide better insight about this matter [18]. Besides that, it is necessary to return to the antiplatelet treatment at the right time.

## Neuro-axial blockage in thoracic surgery

For the patients with impaired cardiorespiratory functions, epidural infusion supplies an efficient postoperative analgesia [33]. İn this type of analgesia, patients receiving anticoagulant drugs have high numbers of operations and hypotensive epidural anesthesia is becoming more important because of its blood loss-reducing effect [34]. Through the appropriate arrangements, the neuro-axial blockage can be easily performed for these patients. Especially antiplatelet therapy, used in patients having drug coated stents affects the type of anesthesia.

For the patients receiving antithrombotic agent, applying neuro-axial blockage is controversial because of high spinal-epidural hematoma risk. No absolute spinal bleeding risk is known under thrombophylaxis. Under LMWH, the risk of spinal apidural hematoma risks is 1/6600 for single epidural injection and 1/3100 for epidural catheter placement [35]. The anticoagulant drug arrangements for the patients, for whom the neuro-axial blockage is planned in thoracic surgery, can be listed as follows. Although the duration of action of fibrinolytic agents is short, plasminogen and fibrinogen inhibition may last up to 27 hours [36]. For the patients using fibrinolytic, there are questions about the safety of using neuro-axial blockage (33). Within first 10 days following the regional anesthesia, the neurological examination should be performed every 2 hours if there is any condition requiring the use of fibrinolytic, and certain tests should be performed before deciding for catheter.

Even though there is no limitation about the use of heparin,



**Citation:** Baygin O, Arslan DG, Saracoglu A (2018) The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery. Glob J Anesth 5(2): 019-026. DOI: http://doi.org/10.17352/2455-3476.000043

use of another anticoagulant should be avoided in cases such as Heparin Induced Trombocytopenia (HIT) complication. If the aPTT is normal after the dose of heparin, neuro-axial blockage can be performed after 4-6 hours, and then heparin can be implemented after 1 hour, and the level of local anesthetics should be at the minimum dose allowing the neurological examination [36]. In cases such as cardiopulmonary bypass, catheter implantation should be rescheduled to 12-24 hours earlier [33]. In cases, where the intraoperative anticoagulation is considered, postponing the surgery should be considered if bloody tap occurs [35].

Neuro-axial blockage is allowed for 12 hours after the LMWH thrombophylaxis dose and 24 hour after the therapeutic dose. For patients, requiring LMWH postoperatively, there are 3 important points with neuro-axial blockage; first postoperative dose, total daily dose, and dose schema [37]. In single daily postoperative dose, the first dose should be given after 6 hours and second dose after 24 hours, while catheter application can be performed 10-12 hours after LMWH or 2 hours before the next dose.

The use of warfarin should be terminated 5 days before, and the INR control can be performed for those patients. In urgent cases, it can be considered to give fresh frozen plasma. The use of catheter is possible with INR control, and neurological monitorization after 24 hours is required. If INR>3, then one should avoid from using catheter [33].

If no other anticoagulant medications are used, there is no specific contraindication with aspirin and NSAID derivatives [36-38]. One should wait for 5-7 days in clopidogrel and for 14 days in ticlodipin. It can be seen that these durations are shorter for GPIIb/IIIa inhibitors. While waiting for 8 hours is enough for tirofiban and eptifibatide, it would be appropriate to wait for 24-48 hours for absiksimab [36]. Among the patients using hirudin, waiting for 24 hours is recommended if the coagulation is normal, while waiting for 12 hours is enough for the patients using ximelagatran or melagatran [33]. There isn't enough data regarding fondaparinux. But, in general, it is believed that waiting for 5 half-lives is enough [36]. Apart from this, epidural catheter implementation can be performed for patients using idraparinux, dabigatran or rivaroxaban, and 36 hours after the last dose or 12 hours before the next dose for patients using fondaparinux.

### Perioperative bleeding

Perioperative blood loss and consequent blood transfusion are related with increased morbidity and mortality [39]. Blood conservation requires multidisciplinary approach, and its effects are seen in many points [40]. Identification and treatment of preoperative anemia constitute the first step. Using peroperative lysine-like agents was shown to decrease the blood loss, and the use of blood products [41]. Besides that, tranexamic acid was found effective in cardiac surgery without any thromboembolic complication [42].

Since the use of point-of care tests is useful for finding the reason of bleeding, they are widely used in many European countries. In general, the first seen one is mainly hypofibrinogenemia, while the fibrinogen is the main component of homeostasis. Even if the anemia is treated preoperatively, it should be kept in mind that acute anemias may occur due to massive bleeding.

Even though desmopressin is mainly used in deficiency of von Willebrand factor, it can also be used together with the point-of-care test for the patients using aspirin and ADP receptor inhibitor (clopidogrel). It can be reversed by using high dose of prothrombin concentrate for the patients using Factor Xa inhibitor agents. For the patients using idarucizumab and especially dabigatran, it is used as antagonist, and it was reported in RE-VERSE AD trial that it can be safely used [40].

The methods such as autologous transfusion, acute normovolemic hemodilution, intraoperative RBC salvage, controlled hypotension, topical hemostatic agents, and postoperative RBC salvage can be useful.

## Conclusion

First of all, risk classification of the patient and the surgical procedure should be performed. Patient-oriented planning should be considered for thrombosis and bleeding. It is recommended to continue antithrombotic agents in procedures with low risk of bleeding. But the dose should be kept below the therapeutic level. For the patients with high thromboembolic risk, if the antithrombotic agents will be terminated due to the bleeding risk, at least aspirin treatment should be maintained or the bridging treatment should be considered. When compared to VKA, the new generation anticoagulants have lower mortality, stroke, and systemic embolism risk. By using these drugs, lower rates of intracranial bleeding and major bleeding were reported. Besides, when compared to VKAs, similar incidence of recurrent thromboembolism may be observed.

## References


1. Vats A, Howell S (2013) Perioperative management of the patient with cardiovascular disease undergoing non-cardiac surgery. Surg 31: 410–415. Link: https://goo.gl/aVEj7B

2. Thiessen L, Grabowski D, Siragusa L, Young RS (2015) Bridging Protocol for Surgical Patients: One Clinic's Experience Facilitating a Safe Anticoagulation Intervention. J Perianesthesia Nurs 30: 476–86. Link: https://goo.gl/wuFeAP

3. Kristensen SD, Knuuti J (2014) New ESC/ESA Guidelines on non-cardiac surgery: Cardiovascular assessment and management. Eur Heart J 35: 2344–2345. Link: https://goo.gl/EJqSW3

4. Van Diepen S, Tricoci P, Podder M, Westerhout CM, Aylward PE, et al. (2015) Efficacy and Safety of Vorapaxar in Non–ST-Segment Elevation Acute Coronary Syndrome Patients Undergoing Noncardiac Surgery. J Am Heart Assoc 4: e002546. Link: https://goo.gl/kLSRB9

5. van Veen JJ, Makris M (2015) Management of peri-operative anti-thrombotic therapy. Anaesthesia 70: 58–67. Link: https://goo.gl/U6FsMk

6. Mahmoud KD, Sanon S, Habermann EB, Lennon RJ, Thomsen KM, et al. (2016) Perioperative cardiovascular risk of prior coronary stent implantation among patients undergoing noncardiac surgery. J Am Coll Cardiol 67: 1038–1049. Link: https://goo.gl/oq32fS




Citation: Baygin O, Arslan DG, Saracoglu A (2018) The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery. Glob J Anesth 5(2): 019-026. DOI: http://doi.org/10.17352/2455-3476.000043

7. Warshauer J, Patel VG, Christopoulos G, Kotsia AP, Banerjee S, et al. (2015) Outcomes of preoperative bridging therapy for patients undergoing surgery after coronary stent implantation: A weighted meta-analysis of 280 patients from eight studies. Catheter Cardiovasc Interv 85: 25–31. Link: https://goo.gl/Y1TMFE

8. Waçsowicz M, Syed S, Wijeysundera DN, Starzyk L, Grewal D, et al. (2016) Effectiveness of platelet inhibition on major adverse cardiac events in non-cardiac surgery after percutaneous coronary intervention: A prospective cohort study. Br J Anaesth 116: 493–500. Link: https://goo.gl/jFp4XA

9. Valle JA, Graham L, DeRussy A, Itani K, Hawn MT, et al. (2017) Triple Antithrombotic Therapy and Outcomes in Post-PCI Patients Undergoing Non-cardiac Surgery. World J Surg 41: 423-432. Link: https://goo.gl/XZMSh8

10. Salters C, Bradley B, Charnigo RJ, Shah Z, Meehan J, et al. (2015) Incidence, nature, and temporal trends of adverse events associated with noncardiac procedures among veterans with drug-eluting coronary artery stents. Catheter Cardiovasc Interv 86: 211–219. Link: https://goo.gl/XtxaBN

11. Saia F, Belotti LMB, Guastaroba P, Berardini A, Rossini R, et al. (2016) Risk of Adverse Cardiac and Bleeding Events Following Cardiac and Noncardiac Surgery in Patients with Coronary Stent: How Important Is the Interplay between Stent Type and Time from Stenting to Surgery? Circ Cardiovasc Qual Outcomes 9: 39–47. Link: https://goo.gl/fW9E9q

12. Yamamoto K, Wada H, Sakakura K, Ikeda N, Yamada Y, et al. (2014) Cardiovascular and bleeding risk of non-cardiac surgery in patients on antiplatelet therapy. J Cardiol 64: 334–338. Link: https://goo.gl/SRRUwb

13. Wylie BJ, Singh MP, Coull BA, Quinn A, Yeboah- K, et al. (2015) Association between wood cooking fuel and maternal hypertension at delivery in central East India. HHS Public Access 34: 355–368. Link: https://goo.gl/zMYNR9

14. Witt DM, Clark NP, Kaatz S, Schnurr T, Ansell JE (2016) Guidance for the practical management of warfarin therapy in the treatment of venous thromboembolism. J Thromb Thrombolysis 41: 187–205. Link: https://goo.gl/vrv3vf

15. Wakabayashi Y, Wada H, Sakakura K, Yamamoto K, Mitsuhashi T, et al. (2015) Major adverse cardiac and bleeding events associated with non-cardiac surgery in coronary artery disease patients with or without prior percutaneous coronary intervention. J Cardiol 66: 341–346. Link: https://goo.gl/hFZvnD

16. Strosberg DS, Corbey T, Henry JC, Starr JE (2016) Preoperative antiplatelet use does not increase incidence of bleeding after major operations. Surgery [Internet] 160: 968–976. Link: https://goo.gl/7dMvaY

17. Luni FK, Riaz H, Khan AR, Riaz T, Husnain M, et al. (2017) Clinical outcomes associated with per-operative discontinuation of aspirin in patients with coronary artery disease: A systematic review and meta-analysis. Catheter Cardiovasc Interv 89: 1168-1175. Link: https://goo.gl/p2p5tE

18. Capodanno D, Angiolillo DJ (2013) Management of antiplatelet therapy in patients with coronary artery disease requiring cardiac and noncardiac surgery. Circulation 128: 2785–2798. Link: https://goo.gl/6nu8xm

19. Armstrong EJ, Graham L, Waldo SW, Valle JA, Maddox TM, et al. (2017) Patient and lesion-specific characteristics predict risk of major adverse cardiovascular events among patients with previous percutaneous coronary intervention undergoing noncardiac surgery. Catheter Cardiovasc Interv 89: 617-627. Link: https://goo.gl/8Rvzvb

20. Rechenmacher SJ, Fang JC (2015) Bridging Anticoagulation Primum Non Nocere. J Am Coll Cardiol 66: 1392–1403. Link: https://goo.gl/GiysNU

21. Pipanmekaporn T, Punjasawadwong Y, Charuluxananan S, Lapisatepun W, Bunburaphong P, et al. (2014) Incidence of and risk factors for cardiovascular complications after thoracic surgery for noncancerous lesions. J Cardiothorac Vasc Anesth 28: 948–953. Link: https://goo.gl/3dsBWg

22. Flaker GC, Theriot P, Binder LG, Dobesh PP, Cuker A, et al. (2016) Management of Periprocedural Anticoagulation: A Survey of Contemporary Practice. J Am Coll Cardiol 68: 217–226. Link: https://goo.gl/r6EYAa

23. Koenig-Oberhuber V, Filipovic M (2016) New antiplatelet drugs and new oral anticoagulants. Br J Anaesth 117: 74–84. Link: https://goo.gl/DV7h2p

24. Schulman-Marcus J, Pashun RA, Feldman DN, Swaminathan R V (2016) Coronary Angiography and Revascularization Prior to Noncardiac Surgery. Curr Treat Options Cardiovasc Med 18: 1–11. Link: https://goo.gl/tL76Fy

25. Rossini R, Angiolillo DJ, Musumeci G, Capodanno D, Lettino M, et al. (2017) Antiplatelet therapy and outcome in patients undergoing surgery following coronary stenting: Results of the surgery after stenting registry. Catheter Cardiovasc Interv 89: 13-25. Link: https://goo.gl/uAKM2G

26. Gerstein NS, Schulman PM, Gerstein WH, Petersen TR, Tawil I (2012) Should More Patients Continue Aspirin Therapy Perioperatively? Ann Surg 255: 811–819. Link: https://goo.gl/r5iMrQ

27. Douketis JD, Spyropoulos AC, Spencer FA, Mayr M, Jaffer AK, et al. (2012) Perioperative management of antithrombotic therapy. Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 141: 326-350. Link: https://goo.gl/P7qCtX

28. Tanaka A, Ishii H, Tatami Y, Shibata Y, Osugi N, et al. (2016) Unfractionated heparin during the interruption of antiplatelet therapy for non-cardiac surgery after drug-eluting stent implantation. Intern Med 55: 333–337. Link: https://goo.gl/w1pHxx

29. Ghadimi K, Thompson A (2015) Update on perioperative care of the cardiac patient for noncardiac surgery. Curr Opin Anaesthesiol 28: 342–348. Link: https://goo.gl/17Gd6L

30. Ripollés-Melchor J, Espinosa Á, Martínez-Hurtado E, Abad-Gurumeta A, Casans-Francés R, et al. (2016) Perioperative goal-directed hemodynamic therapy in noncardiac surgery: A systematic review and meta-analysis. J Clin Anesth 28: 105–115. Link: https://goo.gl/cNojGf

31. Wang T, Luo L, Huang H, Yu J, Pan C, et al. (2014) Perioperative Blood Transfusion Is Associated With Worse Clinical Outcomes in Resected Lung Cancer. Ann Thorac Surg 97: 1827–1837. Link: https://goo.gl/6VwWC4

32. Oprea AD, Noto CJ, Halaszynski TM (2016) Risk stratification, perioperative and periprocedural management of the patient receiving anticoagulant therapy. J Clin Anesth 34: 586–599. Link: https://goo.gl/kkSyp4

33. Vandermeulen E (2010) Regional anaesthesia and anticoagulation. Best Pract Res Clin Anaesthesiol 24: 121–131. Link: https://goo.gl/sBSuAw

34. Sambandam B, Batra S, Gupta R, Agrawal N (2013) Blood conservation strategies in orthopedic surgeries: A review. J Clin Orthop Trauma 4: 164–170. Link: https://goo.gl/egyJ2h

35. Gogarten W, Vandermeulen E, Van Aken H, Kozek S, Llau JV, et al. (2010) Regional anaesthesia and antithrombotic agents: recommendations of the European Society of Anaesthesiology. Eur J Anaesthesiol 27: 999–1015. Link: https://goo.gl/xPTNnW

36. Narouze S, Benzon HT, Provenzano DA, Buvanendran A, De Andres J, et al. (2015) Interventional Spine and Pain Procedures in Patients on Antiplatelet and Anticoagulant Medications. Reg Anesth Pain Med 40: 182-212. Link: https://goo.gl/APNpVP

37. Li J, Halaszynski T (2015) Neuraxial and peripheral nerve blocks in patients taking anticoagulant or thromboprophylactic drugs: Challenges and solutions. Local Reg Anesth 8: 21–32. Link: https://goo.gl/VSBbYY

38. Horlocker TT, Wedel DJ, Schroeder DR, Rose SH, Elliott BA, et al. (1995) Preoperative antiplatelet therapy does not increase the risk of spinal hematoma associated with regional anesthesia. Anesth Analg 80: 303–309. Link: https://goo.gl/X88d2h




**Citation:** Baygin O, Arslan DG, Saracoglu A (2018) The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery. Glob J Anesth 5(2): 019-026. DOI: http://doi.org/10.17352/2455-3476.000043

39. Timpa JG, Meara LCO, Goldberg KG, Phillips JP, Crawford JH, et al. (2016) Implementation of a Multidisciplinary Bleeding and Transfusion Protocol Significantly Decreases Perioperative Blood Product Utilization and Improves Some Bleeding Outcomes. J Extracorpor Technol 48: 11–18. Link: https://goo.gl/1AEriV

40. Theusinger OM, Spahn DR (2016) Perioperative blood conservation strategies for Major Spine Surgery. Best Pract Res Clin Anaesthesiol 30: 41–52. Link: https://goo.gl/GdyuN6

41. Simonazzi G, Bisulli M, Saccone G, Moro E, Marshall A, et al. (2016) Tranexamic acid for preventing postpartum blood loss after cesarean delivery: A systematic review and meta-analysis of randomized controlled trials. Acta Obstet Gynecol Scand 95: 28–37. Link: https://goo.gl/pVUnAw

42. Reed MR, Woolley LT (2015) Uses of tranexamic acid. Contin Educ Anaesthesia, Crit Care Pain 15: 32–37. Link: https://goo.gl/FFBP3N





**Citation:** Baygin O, Arslan DG, Saracoglu A (2018) The delicate balance between bleeding and thrombosis in cardiac patients undergoing thoracic surgery. Glob J Anesth 5(2): 019-026. DOI: http://doi.org/10.17352/2455-3476.000043