Cardio-vascular and thoracic surgery.

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Acknowledgements relating to this article

Assistance with the study: None.

Financial support and sponsorship: ESA

Conflicts of interest: The authors have no conflict of interest.
Abstract

None of the predictive models have been designed for and validated in patients undergoing cardiothoracic and vascular surgery. The presence of one or more risk factors (age > 70 years old, transfusion of > 4 units of RBC/FFP/Cryoprecipitate, mechanical ventilation > 24h, postoperative complication (e.g. acute kidney injury, infection/sepsis, neurological complication)) should place the cardiac population at high risk for VTE. In this context, we suggest the use of pharmacologic prophylaxis as soon as the satisfactory haemostasis has been achieved, in addition to IPC [GRADE 2C]. In patients undergoing AAA repair, particularly when an open surgical approach is used, the risk for DVT is high and the bleeding risk is high. In this context, we suggest the use of pharmacologic prophylaxis as soon as the satisfactory haemostasis is achieved [GRADE 2C]. Patients undergoing thoracic surgery in the absence of cancer could be considered at low risk for VTE. Patients undergoing thoracic surgery with a diagnosis of primary or metastatic cancer should be considered at high risk for VTE. In low-risk patients, we suggest the use of mechanical prophylaxis using IPC [GRADE 2C]. In high-risk patients, we suggest the use of medical prophylaxis in addition to IPC [GRADE 2B].
General Comments on Procedure related Risk Stratification

Venous thromboembolism (VTE) comprising deep venous thrombosis (DVT) and pulmonary embolism (PE) contribute to a high degree of perioperative mortality. Identifying patients at higher risk for perioperative venous thromboembolism (VTE) is crucial before instituting oriented preventative measures that seek to decrease the incidence of symptomatic events without increasing the risk for bleeding complications. Different predictive models have been developed in the surgical population, but none of them have assessed predictive factors in patients undergoing cardiovascular surgery. The Caprini “venous thromboembolism risk assessment model” was used in the 2012 ACCP guidelines to define the individual risk for VTE in patients undergoing general, non-cardiovascular, surgery. Although a recent investigation validated this model in critical ill surgical patients, this risk stratification is still missing in the sections of cardiovascular and thoracic surgeries. This is particularly true in the setting of cardiac surgery, where large differences in surgical techniques (e.g. internal thoracic arteries versus one arterial graft and additional venous grafts), surgical complexity (e.g. conventional valve replacement with sternotomy vs. minimal invasive lateral approaches) and the use of cardiopulmonary bypass (“on pump” procedures) vs. “off pump” procedures could significantly influence both the risk of VTE and haemorrhagic complications. As long as such models are not validated for these specific populations and procedures, the risk of VTE should be specifically assessed based on the existing literature and should not be generalized using non-specific predictive models. Additionally, due to the increasing age of the cardiothoracic surgical population and the increased number of comorbidities, a specific approach should be used to balance the risk of VTE with the risk of bleeding.

Risk Stratification in Cardiac Surgery

In the 2012 ACCP Guidelines patients undergoing cardiac surgery were evaluated to have an intermediate risk for VTE, with a high risk for perioperative bleeding.
A recent retrospective analysis reviewed more than 90,000 patients from the Premier Perspective Comparative database in the United States, the incidence of VTE varied between 0.70% in the absence of prophylaxis to 1.14% in patients that received fondaparinux. The incidence of major haemorrhagic complications was 1.43%. Another retrospective study recently reviewed more than 2 million patients from the American College of Surgeons National Surgical Quality Improvement Program database, and compared the incidence of DVT between general surgery and cardiac surgery. In this study, the incidence for DVT was 0.66% in general surgery and 2.07% in cardiac surgery.

In 2010, Schwann et al. reviewed 1070 adult cardiac surgical patients who underwent duplex venous scan (DVS) screening in the perioperative period of cardiac surgery. In this study, the authors reported a 13% incidence of “silent” deep venous thrombosis (DVT) within 30 postoperative days. The incidence of DVT was 12.9% after CABG, 20% after isolated valve surgery and 12.4% after combined CABG and valve surgery. Increased age (>70 years), blood product transfusion, prolonged mechanical ventilation (>24 hours) and the need for postoperative re-intubation were strong predictors for postoperative DVT. There was no difference with regard to the re-exploration rate (1.7% DVT vs. 1.9% no-DVT). The 30-day mortality in the patients with DVT was 6.9% compared to 1.7% in patients without DVT (p<0.003). Another recent study confirmed the relationship between blood product transfusion and the incidence of DVT in adults undergoing cardiac surgery. In this study, the authors reported that red blood cell transfusion is associated with a dose-dependent increase in the incidence of DVT (>1 unit RBC), and this deleterious effect is exacerbated with the co-administration of fresh frozen plasma and/or cryoprecipitate.

Current evidence regarding the incidence of DVT and VTE in patients undergoing cardiac surgery is somewhat conflicting. Although the incidence of symptomatic VTE is relatively low, between 0.70% and 2.07% depending on the prevention strategy, studies that used a systematic screening strategy using DVS reported high incidence of ‘silent’ DVT (=13%). According to these data, risk factors for postoperative VTE are: age >70 years old,
transfusion of blood products, postoperative mechanical ventilation >24h, and postoperative complications (e.g. re-intubation, renal failure, neurologic complications, infection and sepsis).

Most of these studies included both patients who underwent coronary artery bypass graft (CABG) surgery and valve replacement surgery. However, patients undergoing mechanical valve replacement surgery, implantation of a mitral or tricuspid valve, or a valvuloplasty should be considered as a specific population, since they require “bridging” anticoagulation before intermediate or long-term oral anticoagulation. 12 Patients after implantation of a bioprosthetic aortic valve may be considered as having the same risk category as CABG patients and will not require intermittent vitamin K antagonist therapy, but low dose aspirin therapy. 12-15 Patients with pre- and/or postoperative atrial fibrillation should equally be considered as a specific entity since they will require a specific approach.

Risk Stratification in Vascular Surgery

Due to the limited data available for vascular patients, the 2012 ACCP guidelines included vascular patients into the group of patients undergoing general surgery. This approach may be supported by the recent study published by Aziz et al. 9, where the incidence of DVT was 0.69% in general surgery patients and only moderately increased to 0.99% in vascular surgery patients. Ramanan et al. looked at the incidence of VTE in a cohort of 45,548 patients undergoing vascular surgery. 16 Venous thromboembolism was reported in 0.7% of patients, with an incidence of 0.2% for pulmonary embolism (PE). Patients with thoraco-abdominal aortic aneurysm (TAAA) repair had the highest rate of VTE (4.2%), followed by thoracic endovascular repair (TEVAR) (2.2%), open abdominal aortic surgery (1.7%), and EVAR (0.7%). The incidence of VTE in patients undergoing peripheral bypass surgery was 1% and for carotid endarterectomy 0.2%. Interestingly, the authors also reported that 41% of the VTE events were diagnosed after discharge, suggesting that high-risk patients could benefit from post-discharge prophylaxis.
In a large national survey comprising 12,469 patients, the incidence of DVT after repair of an unruptured abdominal aortic aneurysm (AAA) was 1.1%. The “in hospital” incidence was higher (1.6%) in patients who underwent “open surgery” compared to the EVAR (0.4%). In another study published in 2012, Scarborough et al. reviewed the incidence and predictors of VTE among 6,035 patients undergoing open aortic surgery, and defined a scoring system for predicting postoperative VTE complications in this population. The following parameters were identified as being independent predictors for postoperative VTE and were used to develop a simple scoring system: preoperative dyspnoea, chronic steroid usage, ruptured aneurysm, operative duration ≥ 5 hours, body mass index ≥ 30, postoperative pneumonia, postoperative mechanical ventilation > 48h, and re-operation.

In 2013, Davenport et al. developed a similar risk index in patients undergoing repair for non-ruptured AAA. The factors associated with the highest risk were the operative duration > 4 hours (4 points), followed by the administration of ≥ 5 units RBC and preoperative serum albumin ≤ 3 g/dl (3 points), and ASA classification IV or V, preoperative dyspnoea, open vs. endovascular repair, and/or the presence of wound infection (2 points). The incidence of VTE was 0.4% in patients with a score < 4, 1.2% with a score of 4-7, 2.6% with a score of 8-10, and 4.6% with a score ≥ 11.

A single centre study of 192 patients undergoing elective AAA repair assessed the incidence of DVT using preoperative and postoperative VDS. Despite mechanical prophylaxis, the incidence of DVT when early mobilisation and administration of LMWH was instituted (not among those with bleeding or in need of transfusion) was 10.2% in patients undergoing open surgical repair of the AAA and 5.3% among EVAR patients. As previously discussed for cardiac surgical patients, the observed incidence represents the incidence of “silent” DVT diagnosed by systematic screening with DVS.

Evidence regarding preventive strategies in cardiac and vascular surgery

Only a few older studies have assessed and compared the efficacy of different prophylactic strategies in patients undergoing cardiac and vascular surgery.
performed in the late 1980s, early 1990s, in an entirely different surgical population. Although recent meta-analyses have suggested that VTE prophylaxis could significantly reduce the risk of VTE without increasing the risk of bleeding and cardiac tamponade, the quality of these meta-analyses are limited by the weak quality of the studies included. In addition, these meta-analyses were unable to demonstrate that superiority or any signs of improved safety of one form of prophylaxis over another.

Due to its relatively short half-life (2-4 h) and the availability of a specific reversal agent, protamine, unfractionated heparin (UFH) remains the ‘gold standard’ for peri-operative anticoagulation in patients undergoing cardiac and major vascular surgery. On the other hand, low molecular weight heparins (LMWH), are usually used to "bridge" vitamin K antagonist therapy perioperatively, and are the primary agents for perioperative VTE prophylaxis in other surgical settings. The elimination half-life of LMWH is approximately 4-8 h, but pharmacokinetics varies between the agents due to the different composition. The elimination is predominantly via the renal system while only the effect of larger chains can be neutralized by protamine. Dosing protocols vary from fixed dosages to weight-adjusted protocols, from once to twice-daily administration, while some agents require lowering the dose in cases of severe renal impairment (CrCl < 30ml/min). Monitoring of the effect of LMWH is usually performed using a chromogenic anti Xa assay. The use of LMWH has been associated with an 80% reduction in the incidence of heparin-induced thrombocytopenia (HIT), a potentially severe thrombotic complication.

Due to the heterogeneity of different LMWHs used in clinical practice, the results obtained with one LMWH is not be extrapolated to the entire group of agents. To date, a limited number of studies have compared the safety and efficacy of UFH with LMWHs or fondaparinux in patients undergoing cardiac or aortic surgery. In a small retrospective investigation including approximately 200 patients following heart valve surgery, the administration of LMWH (dalteparin) was associated with a lower incidence of thrombotic
events (4% vs. 11%) when compared to UFH, in addition to a lower risk of HIT (3% vs. 6%),
HIT associated with thrombotic events (1% vs. 4%), and bleeding episodes (3% vs. 10%).

In two smaller studies performed in CABG patients, no difference in the incidence of bleeding
event was reported when fondaparinux was compared to LMWH. 28,29

In patients undergoing lower extremity arterial reconstruction, the efficacy and safety of UFH
was compared to LMWH after stratification for the risk of VTE. 30 The anticoagulation of low-
risk patients consisted of either two applications of 7,500 IU UFH subcutaneously (n=158) or
one daily application of 40 mg LMWH each up to discharge (n=169). High-risk patients
received either 25,000 IU UFH i.v. over 24 hours and 4 days (n=48), 2-times (n=51) or one-
time weight-adjusted LMWH (n=49) up to discharge (1 mg/kg body weight). This study
reported that the administration of LMWH significantly reduced the incidence of vascular re-
occlusion in both high and low risk patients without increasing the incidence of bleeding
complications. In a recent study performed in patients undergoing a large variety of vascular
surgical procedures, Durinka et al. reviewed the change in the incidence of VTE after the
implementation of a strict VTE prophylaxis protocol with early (within 24 h post OP) medical
DVT prophylaxis (UFH s.c. 3 times/day or enoxaparin). 31 The VTE prophylaxis protocol was
based on a multidisciplinary assessment of the risk with inclusion of mechanical prophylaxis.
The implementations of this standardized protocol reduced by 75% the overall incidence of
VTE.

Aspirin is routinely administered after cardiac surgery and vascular surgery to increase graft
patency, and low dose aspirin may also reduce the incidence of VTE. 32 In patients following
orthopaedic surgery, a recent meta-analysis classified aspirin as being as powerful as LMWH
to prevent VTE. 33 The analysis of the INSPIRE study showed an approximately 30% reduction in the recurrence of venous thrombosis when aspirin was given 34, while the
ASPIRE trial did not report any benefit of aspirin administration. 35 Studies in cardiothoracic
and vascular surgery are missing. Hence, in these scenarios, the role of low-dose aspirin
mono-therapy in the prevention of venous thromboembolism is unclear. In a recent study,
Morhosseini et al. randomized 120 patients undergoing elective OPCABG surgery to receive heparin (5000 units s.c. every 8 hours) or aspirin (80 mg daily) plus heparin (5000 units s.c. every 8 hours). In this study, the incidence of postoperative DVT was significantly reduced (16.6% vs. 3.3%) when aspirin was administered in addition to subcutaneous heparin. These data suggest a potential role of low-dose aspirin in reducing the risk of DVT in this specific patient population.

Risk Stratification in Thoracic Surgery

The incidence of VTE in patients undergoing thoracic surgery remains unclear, and varies based on the underlying disease (e.g. cancer), the type of procedure (e.g. thoracotomy vs. minimally invasive), the comorbidities, the screening strategy, and the prophylactic approach. As reported in the study published by Gomez-Hernandez et al., lung cancer, lung metastasis, or pulmonary nodules represent the vast majority of the indication for thoracic surgery. Although the incidence of VTE was relatively low in the general thoracic population (0.18%), the incidence was significantly higher in patients presenting with two or more of the following risk factors: advanced age, obesity, cancer, and history of DVT. Lung cancer patients undergoing thoracic surgery have at least a two fold increased risk for DVT and a threefold increased risk of PE compared to those without surgery. In a study that explored the long-term incidence of VTE among 1001 surgical patients with lung cancer, the cumulative incidence of VTE was 2% at 1 month, 3% at 3 months, with a maximum incidence of 5.3% at 30 months. In a recent systematic review assessing 19 studies, Christensen et al. reported a pooled risk of VTE of 2.0%, but with a large inter-study variation (0.2%-19%). The authors were not able to draw any firm conclusions regarding a potential benefit of minimally invasive procedures versus open thoracotomies due to the very limited number of patients that had minimally invasive procedure in the included studies. Although one might expect a lower incidence of VTE in patients undergoing minimally invasive thoracic surgery, a recent study reported an incidence of 1.9% (47/2445) in patients who underwent thoracotomy vs. 1.2% (33/2831) in patients with minimal access surgery. The incidence of
VTE was 2% in a population of 3208 patients undergoing esophagectomy. After stratification for timing (pre- versus post-discharge), the authors reported that 17% of VTE occurred after discharge. High ASA classification, diabetes mellitus, preoperative dyspnoea, history of cardiovascular disease, arterial hypertension and preoperative anaemia were associated with pre-discharge VTE, while advanced age was the only item associated with post-discharge VTE.

In a recent study from Hachey et al., the Caprini score was used for preoperative risk stratification in a cohort of 253 patients undergoing lung surgery for cancer. A high risk Caprini score > 9 was associated with a negative predictive value of 98.5% for VTE prediction in this specific population. In a cohort of 97 patients undergoing esophagectomy, a Caprini risk score > 15 showed a negative predictive value of 100%.

**Evidence regarding preventive strategies in thoracic surgery**

As discussed in the cardiovascular section, only a few studies have compared different prophylactic strategies in patients undergoing thoracic surgery. Among six studies published before 2000, none showed any statistically significant difference between pharmacological strategies to reduce the incidence of VTE, or an increase in bleeding risk.

In a before-and-after study, Nagahiro et al. reported the efficacy of IPC in preventing pulmonary embolism in 706 patients undergoing thoracic surgery between 1995 and 2000. Among 344 patients not receiving any prophylactic treatment, 7 (2%) had postoperative PE while IPC was found to prevent PE among 362 patients in the interventional group.

In another retrospective study, a group of 169 patients with IPC was compared with a group of 154 patients that received IPC and UFH (2500-5000 s.c. twice daily). Pulmonary embolism was reported in only one of the 169 patients included in the IPC group, while no pulmonary embolism was reported in the group of patients that received both IPC and UFH. The small number of patients included, the retrospective nature of the study, and the single centre design limited the extrapolation of the results to a larger cohort of patients.
retrospective study, enoxaparin 40 mg/day was compared to fundaparinux 2.5 mg/day in medical and thoracic surgical patients. 46 Although the authors report no significant difference in the incidence of VTE, a lower incidence of bleeding was observed in the enoxaparin group. In another study including 117 patients undergoing esophagectomy, nadroparin once daily was associated with a higher incidence of VTE (9.1%) when compared to a twice-daily administration (0%). 47 The results of this small “pseudo-randomized” study should be interpreted with caution, and needs to be confirmed in a further large and well-designed prospective study.
Cardiac and Vascular surgery surgery

- In the absence of risk factors, we suggest to consider the risk of VTE as moderate in patients undergoing CABG and bioprosthetic aortic valve implantation surgery [GRADE 2C]. The risk of bleeding is to be considered high. In this population, we suggest the use of mechanical prophylaxis using intermittent pneumatic compression (IPC) [GRADE 2C].

- The presence of one or more risk factors (age > 70 years old, transfusion of > 4 units of RBC/FFP/Cryoprecipitate, mechanical ventilation > 24h, postoperative complication (e.g. acute kidney injury, infection/sepsis, neurological complication)) should place the cardiac population at high risk for VTE. In this context, we suggest the use of pharmacologic prophylaxis as soon as the satisfactory haemostasis has been achieved, in addition to IPC [GRADE 2C].

- Patients undergoing other valve surgery and those with atrial fibrillation should be considered a specific entity at high risk of VTE, since they will mostly require postoperative therapeutic medical “bridging” prior to long-term anticoagulation.

- Patients undergoing peripheral vascular surgery are considered to have a low risk for VTE and low risk for bleeding. Stringent medical prophylaxis appears to reduce the event rate significantly. In this population, we suggest medical therapy [GRADE 2C].

- In patients undergoing AAA repair, particularly when an open surgical approach is used, the risk for DVT is higher with a high bleeding risk. These patients should be considered as having a moderate risk. Patients with additional risk factors including, body mass index ≥ 30, preoperative dyspnoea, chronic steroid usage, ruptured aneurysm, open surgery, operative duration ≥ 5 hours, transfusion of ≥ 5 units, postoperative mechanical ventilation > 48h, postoperative complication (acute kidney injury, infection/sepsis), and re-operation, should be considered as moderate to high risk. In this context, we suggest the use of pharmacologic prophylaxis as soon as the satisfactory haemostasis is achieved [GRADE 2C].

- We suggest that low-dose aspirin could be used to decrease the incidence of VTE in cardiac and vascular patients, but should not be considered as the sole agent in high-risk patients. [GRADE 2C].

- UFH are associated with the highest risk to develop the prothrombotic condition of HIT. Therefore, in an attempt to minimize the risk for HIT, we suggest that UFH should be used as briefly as possible and replaced by LMWH as soon as the bleeding risk decreases [GRADE 2C].

- In patients with severely impaired renal function (CrCl < 30 ml/min) and a high risk for haemorrhagic complications, we suggest to closely monitor the administration of UFH and LMWH and to adapt the dosage [GRADE 2C].

Thoracic surgery

- Based on the current literature, patients undergoing thoracic surgery in the absence of cancer could be considered at low risk for VTE. However, since the vast majority of patients undergoing thoracic surgery have a diagnosis of primary or metastatic cancer, they should be considered at high risk for VTE with an equally high bleeding risk.

- In the absence of evidence regarding patients undergoing minimally invasive procedure, the same risk stratification should be applied as described above.

- In low-risk patients, we suggest the use of mechanical prophylaxis using IPC [GRADE 2C]. In high-risk patients, we suggest the use of medical prophylaxis in addition to IPC [GRADE 2B].
References


