



# Deep vein thrombosis and pulmonary embolism following lung resection

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**Abstract:** Deep vein thrombosis (DVT) and pulmonary embolism (PE) are common complications in cancer. Patients with lung cancer have a risk of venous thromboembolism (VTE) of around 3% over 2 years. The incidence of DVT after thoracic surgery is estimated to be between 0.4% and 51% and the incidence of PE between 1% and 5%. The risk factors for VTE may be patient-related, cancer-related or treatment-related. Pneumonectomy is associated with a 3-fold increase in post discharge VTE events compared to lobectomy. The diagnosis of VTE may be challenging as it has few specific symptoms. For this reason, prophylactic treatment with low molecular weight heparin or unfractionated heparin and antiembolism stockings or intermittent pneumatic compression devices are widely recommended for patients at risk for VTE. Patients who undergo thoracic surgery are deemed at high risk for postoperative VTE as a significant proportion of them have cancer, underlying respiratory and cardiovascular comorbidities, and are of advanced age. Extended VTE prophylaxis may be considered as there is a risk of developing VTE post discharge. Risk-assessment models for VTE can be utilized in thoracic surgery and the Caprini risk-assessment model has been used successfully in the USA. Postoperative PE needs to be diagnosed and treated promptly as delay may be fatal. It is managed with anticoagulants but thrombolysis should be considered in compromised patients.

**Keywords:** Lung cancer; pulmonary embolism; deep vein thrombosis (DVT); lung resection

Received: 06 July 2020; Accepted: 22 September 2020; Published: 10 July 2021.

doi: 10.21037/shc-20-68

View this article at: <http://dx.doi.org/10.21037/shc-20-68>

## Introduction

Venous thromboembolism (VTE), which contains deep vein thrombosis (DVT) and pulmonary embolism (PE), is one of the most common complications in cancer as well as a major surgery-related complication (1). Malignancy has been associated with a 6 to 7-fold increased risk of DVT and a 3-fold increased risk of PE. The reported incidence of VTE among cancer patients is 10–20%, and up to 10% of patients with idiopathic VTE will be diagnosed with occult cancer or develop symptomatic cancer (2). However, the risk may vary considerably between different types of cancer. DVT rates may range between 2% and 34%

among patients with different types of localised cancer and the rates are higher in metastatic cancer. The incidence of VTE following lung resection is 2.3%. The highest levels are encountered in oesophagectomy with an incidence of 7.3% (3). The incidence of DVT after thoracic surgery is estimated to be between 0.4% and 51% and the incidence of PE between 1% and 5% with 2% being fatal (4). This variation may be due to differences in the detection method as in post-operative screening versus symptomatic detection and the type and/or duration of thromboprophylaxis (5).

VTE can still occur to 0.8–7.4% of patients who undergo thoracic surgery despite thromboprophylaxis

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(6,7). Dentali *et al.* (8), found a 1.7% incidence of VTE in patients who underwent thoracotomy for lung cancer despite administration of heparin. Agrazian *et al.* (9) screened patients operated for lung cancer and found 12.1% prevalence of VTE with 5.2% mortality rate. Most events were asymptomatic.

The patients who are diagnosed with lung cancer have a risk of DVT or PE estimated at around 3% over 2 years (10). Patients who undergo surgery have a two to three-fold increased risk of VTE compared to the patients who do not undergo surgery. Cancer patients who undergo the same thoracic surgical procedure have at least double risk of DVT and 3-fold risk of fatal PE compared to patients who do not have cancer (11).

VTE can cause increased bleeding, delay in chemotherapy, increased costs and risk of VTE recurrence. DVT can cause post-thrombotic syndrome due to damage of the venous valves which can affect quality of life. 10% of the patients who present with symptomatic PE will die in the first hour, and the patients who survive are at high risk for right heart failure and right heart strain (12).

VTE is the most common cause of death in postoperative cancer patients within 30 days of surgery, is associated with poorer longer-term prognosis, and can increase mortality from 1.2% to 8% (13). Yang *et al.* (14), found that the highest incidence of VTE was within one month after the procedure.

Patients who undergo pneumonectomy, have a peak incidence of VTE on the 6<sup>th</sup> or 7<sup>th</sup> postoperative day (15,16), when a significant amount of the patients will have been discharged from the hospital. The risk remains high until post-operative day 30; therefore, routine screening and extended prophylaxis in this cohort of patients may be considered.

## Risk factors

Rudolf Virchow suggested the three main causes of VTE in 1888: vascular endothelial damage, stasis and hypercoagulability (17). Hypercoagulability in cancer may be related to cytokine signalling, abnormal fibrinolysis, dysfunctional platelet adhesion and overexpression of tissue factor (18,19).

The risks that can contribute to VTE in lung cancer patients are multifactorial and can be patient-specific and/or related to biological parameters, related to the type of cancer or the presence of metastases, related to the treatment (surgery, chemotherapy, radiotherapy), or related

to all of them (13).

Patient-specific risk factors for VTE include age, gender, smoking history, race, BMI >25 kg/m<sup>2</sup>, prolonged immobility, higher performance status, past medical history, presence of varicose veins, serious lung disease or chronic respiratory insufficiency, pre-existing cardiac conditions, pregnancy, thrombophilia, previous history of PE, congestive heart failure, or trauma (14,18,20-23). Asian population may have a lower incidence of VTE which may be due to lower prevalence of factor V Leiden mutation and possibly lower levels of fibrinogen, factor VIIc and factor VIIIc (24). However, a recent study in China (22), found an overall incidence of VTE of 11.2% after lung surgery (without VTE prophylaxis which is not used routinely in China) and none of the patients had typical symptoms of VTE.

Tumour biology, histologic features and stage of the disease could be related to VTE (25). Postoperative VTE incidence is higher with late stage cancer (stage IV *vs.* stage I) which is an independent risk factor for postoperative VTE (14).

Radiotherapy and chemotherapy in lung cancer patients may lead to deficiency in protein C, protein S and antithrombin III, all of which contribute to thrombus formation (13). PICC catheter, which may lead to clot formation, postoperative use of antiangiogenesis drugs EGFR/TKI treatment, no EPO treatment, and preoperative increase in D-dimer levels (26) may all increase the risk of VTE (14).

Surgery for lung cancer is an independent risk factor. On the other hand, patients who have surgery for lung cancer with curative intent are most likely to have early-stage lung cancer and therefore they could express lower hypercoagulability (7). The patients who undergo lung resection may present a different VTE profile than the general oncology and orthopaedic patients with a higher rate of *denovo* PE; in this situation, DVT screening only may miss a significant proportion of PE.

Longer operative time, intraoperative bleeding and extent of surgical injury, increased ASA score, incomplete resection (14) and open surgery versus thoracoscopic surgery, 0.8% versus 0.6%, are all correlated to higher chance of VTE (25,27). The extent of the resection is also a risk factor for VTE; pneumonectomy is associated with 3-fold increase in the incidence of VTE post discharge compared to lobectomy, 2% versus 0.6%,  $P < 0.01$  (17). Factors related to the surgical technique, involving manipulation of the pulmonary arteries and division of arterial branches may have a role in formation of thrombi.

Daddi *et al.* (28) showed that 74% of PE events were found without DVT, potentially because of direct injury to the pulmonary vessels. Additionally, the risk could be higher due to prolonged periods of bed rest and reduced postoperative mobility due to pain (14).

The use of neuraxial and general anaesthesia instead of sole general anaesthesia in open lung surgery has been associated with increased risk of VTE possibly due to the reduced use of anticoagulants in the first group of patients for fear of neuraxial haematoma formation (29). Moreover, recent steroid use, blood transfusions, and postoperative complications such as wound infection, reintubation, peripheral nerve injury, postoperative sepsis and extended length of stay may increase the risk of DVT (3). PE is associated with recent radiation treatment, thrombocytosis (platelet count  $\geq 400,000$ ), and postoperative complications such as wound infection, reintubation, DVT, urinary tract infection, and cardiac arrest (3).

## Diagnosis

Diagnosing VTE may be challenging as it has few specific symptoms. Perioperative or postoperative VTE may be asymptomatic which could explain the low incidence of postoperative VTE reported in patients after thoracic surgery (22).

Postoperative VTE is defined as the presence of DVT and/or PE during the postoperative period.

DVT may be asymptomatic or present with calf pain. According to the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) (25,30), postoperative DVT is defined as a blood clot or thrombus in a deep vein of any limb identified up to 30 days after the operative procedure with both of the following: (I) new diagnosis of DVT confirmed by colour Doppler ultrasound examination, venogram, CT or any other definitive imaging modality including direct pathological examination such as autopsy and (II) the need for anticoagulation treatment or placement of an inferior vena cava filter or clipping the vena cava or indication in the patient's records that the patient required treatment but no additional option was available.

PE is most frequently attributed to DVT of the lower limbs where the clot travels to the pulmonary artery through the circulation. PE can occur rarely due to air embolism, tumour, or bone marrow fat.

The clinical presentation of PE may vary from asymptomatic to right heart failure, hypoxaemia, cardiogenic

shock and death. Pulmonary embolism severity index (PESI) and simplified PESI are models that have been suggested to predict short- and long-term mortality (31). Signs and symptoms that suggest pulmonary embolism are: sudden onset of shortness of breath, pleuritic chest pain, syncope, haemoptysis, rales, tachycardia/arrhythmia, cyanosis, light-headedness, hypotension, sweating, calf pain, persistent hypoxaemia. Additional signs are shock, RV dysfunction as evidence of RV dilatation on echocardiography, hypopokinesia or pressure overload, increase of BNP or N terminal pro-BNP, and raised right heart pressure at right heart catheterization, RV dilatation on CT, and positive cardiac troponin T or I (marking myocardial injury) (32). Arterial blood gas analysis shows decreased PaO<sub>2</sub>, SO<sub>2</sub>, and PaCO<sub>2</sub> and increase in the alveolar-arterial oxygen pressure gradient p(A-a)O<sub>2</sub>.

Postoperative PE is identified up to 30 days after the operation with both of the following: a) new diagnosis of a blood clot in a pulmonary artery with subsequent obstruction of blood supply to the lung parenchyma and b) V/Q scan which indicates a high probability of PE or a positive result identified on CT, TOE, pulmonary angiography, CT angiography with pulmonary embolism protocol or any other definitive imaging modality including direct pathological examination such as autopsy (25). CXR is non-specific. Echocardiography may demonstrate dilatation of the right ventricle, SPAP >40 mmHg, or tricuspid regurgitation. The gold-standard tool for diagnosis of PE is computed tomography chest angiography with pulmonary embolism protocol (CTPA), if immediately available and in a stable patient who is normotensive and with no shock. CTPA has a positive predicted value of up to 97% in the main or lobar pulmonary arteries and 68% in the segmental arteries (33). Ventilation/perfusion scan and MRI have been used with limited accuracy in detection of PE. According to the European Society of Cardiology, in patients with suspected PE and who present with shock or hypotension, if CT scan is not readily available or they are too unstable for a CT, echocardiography may be helpful. If there are no signs of RV overload or dysfunction on the echocardiogram in a patient who is hypotensive and in shock, PE can be excluded as a cause of haemodynamic compromise. D-dimer in combination with clinical assessment can rule out PE as diagnosis in 30% of the cases (32). However, increased d-dimer levels are not specific for PE as they can also be elevated in trauma, recent surgery, trauma, pregnancy, cancer, inflammation and advanced age. Elevated troponin I, troponin T and BNP are associated with increased

mortality, as they indicate right ventricular failure. WBC levels tend to be raised and INR tends to be low.

The presence of shock, hypotension, RV dysfunction and/or elevated troponin is associated with high mortality from PE (>15%) and thrombolysis or embolectomy may be indicated. If there are signs of RV dysfunction and/or myocardial injury, the mortality is 3–15%. When none of these risk factors are present, early mortality from PE is <1% (32).

Given that the diagnosis of DVT or PE is often subtle or subclinical, clinicians must be very vigilant and have a low threshold for investigations on clinical suspicion.

### Perioperative prevention

Low molecular weight heparin (LMWH) is widely recommended for VTE prophylaxis in patients undergoing surgery for cancer (34,35); however, the evidence for using it is mostly based on observational studies. VTE chemical prophylaxis regimen varies widely among centres regarding both duration and choice of pharmacological agent, which is likely due to the small amount of data specifically targeted to thoracic surgery patients (5). The majority of surgeons in the USA do provide pharmacological thromboprophylaxis to patients who undergo lung resection but they do not provide extended VTE prophylaxis post discharge. Most of the surgeons believe that VTE prophylaxis is safe and not related to any additional postoperative bleeding events (36). It is widely felt that the prevention of severe and potentially fatal PE outweighs the risks of postoperative bleeding.

Christensen *et al.* (6) performed a systematic literature review of 19 studies and 10,660 patients to assess the risk of VTE peri- and postoperatively in patients undergoing surgery for primary lung cancer with curative intent. The patients underwent either thoracotomy or VATS and either wedge resection, segmentectomy, lobectomy or pneumonectomy. The risk of VTE ranged between 0.2–19% with overall mean risk of 2%. The risk was 2.1% in the studies with 1 month follow up and 2.8% in studies with follow up greater than 1 month. This could suggest that the greatest risk for VTE is in the immediate postoperative period with reduced risk thereafter. The same group, in their randomised controlled trial (37), found no difference in the coagulation profile of VATS lobectomy patients who either received LMWH once daily or no LMWH at all.

Attaran *et al.* (7) suggested that thromboelastography could be used as screening for hyper-coagulopathic patients to provide thromboprophylaxis. Mulder *et al.* suggested

the use of rotational thromboelastometry (ROTEM), a viscoelastic test which can be used to assess coagulation and hypercoagulability (38) and is more sensitive in detection of coagulopathy than conventional coagulation. Hypercoagulability tends to be reversed after surgical resection; however, it tends to persist at least one to two weeks after surgery. This supports extended duration thromboprophylaxis regimens. ROTEM data may be useful for implementation in a risk assessment model.

Adverse side effects of LMWH may be thrombocytopenia, epistaxis, gastrointestinal bleeding and wound haematoma (20). Unfractionated heparin is effective in preventing post-operative VTE without adverse events related to epidural catheters or heparin-induced thrombocytopenia (39). The use of intermittent pneumatic compression has been shown to be effective in preventing pulmonary embolism post thoracic surgery (40). Fondaparinux may lead to more bleeding events post-surgery and hence the increased requirements for transfusions or re-exploration compared to enoxaparin (41), while it does not seem to provide a benefit to the risk of symptomatic postoperative PE.

Panucci *et al.* (42) studied whether the standard prophylactic dose of enoxaparin 40 mg once a day is adequate for patients undergoing thoracic surgical procedures. The anticoagulant effect of enoxaparin can be monitored by calculating anti-factor Xa (aFXa) levels, and it is considered adequate if the peak levels of aFXa are 0.3–0.5 IU/mL, as measured 4 hours after administration of enoxaparin once in steady state, usually after the 3<sup>rd</sup> dose. They found that only 30% of the patients had adequate peak aFXa levels and two thirds of the patients had undetectable level on anticoagulation 12 hours post dose. A weight-based dose as opposed to a fixed dose may be of benefit. This has been shown to be beneficial in patients who undergo surgery for trauma (43).

Dong *et al.* (1), compared LMWH combined with mechanical prophylaxis, with intermittent pneumatic compression and elastic stockings, against mechanical prophylaxis only for inpatients who underwent thoracotomy for lung or oesophageal cancer—with moderate risk of VTE—and they did not find that the first group had better results in VTE incidence or length of hospital stay. There were no bleeding events in the LMWH group.

The American College of Chest Physicians (ACCP, 9<sup>th</sup> edition) (12) and the American Society of Clinical Oncology (44) guidelines recommend LMWH for all patients undergoing surgical procedures for cancer starting either preoperatively or as soon as possible after the

procedure for at least 7–10 days, which may be extended for 4 weeks in high-risk patients with history of VTE, high BMI, or postoperative residual lesions (14). For patients who undergo thoracic surgery, mechanical and pharmacological prophylaxis, with low dose unfractionated heparin or LMWH is recommended as the benefit of prevention of VTE episodes outweighs the risk of bleeding (12).

NICE (32,45) guidelines recommend initiating mechanical VTE prophylaxis (elastic stockings, intermittent pneumatic compression devices or foot impulse devices) upon admission and continuing their use until the patient is fully mobile. Pharmacological VTE prophylaxis with LMWH once daily or in divided doses twice daily, or unfractionated heparin in patients with renal failure, should be added in patients who have a low risk of major bleeding. For patients at high risk of bleeding, mechanical VTE prophylaxis is recommended. Additionally, the insertion or removal of epidural catheters should not occur within 12 h of heparin administration (46).

The Enhanced Recovery After Surgery (ERAS) guidelines (47) suggest that patients who undergo major lung resection should be given pharmacological and mechanical VTE prophylaxis. Extended administration of LMWH for up to 4 weeks is suggested for patients at high risk of VTE.

The European Society of Medical Oncology recommends that patients who undergo thoracotomy or thoracoscopy that lasts more than 30 minutes should be considered for LMWH (48).

The European Society of Anaesthesiology recommends that patients who undergo thoracic surgery for presumed benign disease should receive mechanical prophylaxis with intermittent pneumatic stockings as they have low risk for VTE (Grade 2C), whereas patients with the diagnosis of primary or metastatic cancer should be considered high-risk for VTE (with equally high risk of bleeding) and pharmacological as well as mechanical prophylaxis is recommended (Grade 2B) (49).

### ***Extended VTE prophylaxis and risk-assessment models***

Patients undergoing thoracic surgery are at risk of post discharge VTE (6,33,50) with the highest incidence appearing within 30 days after the procedure (20). In patients undergoing pneumonectomy for cancer, the incidence of VTE peaks on the 6<sup>th</sup> or 7<sup>th</sup> post operative day. Furthermore, the presence of VTE is a negative prognostic factor for long-term survival (16).

Thomas *et al.* (25) found that age >65 years, male sex, ASA of 4 and history of COPD were associated with an increased risk of post discharge VTE. Almost half of VTE events were reported post discharge. Patients with VTE that occurred before discharge were more likely to be readmitted, and patients with post discharge VTE had a fourfold increased risk for readmission. In a retrospective review of 232 lung resections for cancer, the rate of VTE was 5.2% with one-third occurring post discharge (51). In a recent prospective cohort study of 157 patients who were screened for VTE with CTPA and venous US Doppler one month postoperatively, VTE (symptomatic or not) was found in 12.1% of them (9).

Various studies have reported that the extension of pharmacological prophylaxis up to one month after surgery decreases the risk of VTE in major surgery for cancer (52,53). Currently, there is no evidence to support the use of oral pharmacological VTE prophylaxis. Despite this, administration of extended VTE prophylaxis in thoracic surgery patients varies widely between surgeons, centres and specialties (5). There is so far no prospective, randomized controlled trial in thoracic surgery to examine the potential benefit of extended, out-of-hospital postoperative VTE prophylaxis.

The introduction of a risk-assessment model or nomogram could be initiated in all patients so that they receive a tailor-made thromboprophylaxis, adjusted to their pre- and postoperative risk factors.

The Caprini risk assessment model (RAM) (54) (*Figure 1: Updated Caprini risk-assessment model*) which consists of patient risk stratification and extended postoperative VTE prophylaxis with LMWH has been suggested for lung cancer and has been used in the USA (20). Based on the score, patients are categorised as low risk (score 0–4) with no need of extended VTE prophylaxis, moderate risk (score 5–8) with recommendation for 10 days of extended prophylaxis and high risk (score  $\geq 9$ ) with need for 30 days of extended prophylaxis. Hackey *et al.* (51) found that thoracic surgery patients with a high Caprini score had a higher incidence of post-operative VTE events. They introduced (56) extended VTE prophylaxis according to the Caprini score. Patients demonstrated an excellent adherence (97.2%) to post-discharge enoxaparin prophylaxis, and the study reported an overall VTE rate of 2.3% with no post-discharge VTE or bleeding events. Similarly, Sterbing *et al.* (20) found that VTE rates dropped from 7% to 3% once the Caprini model was implemented with no adverse bleeding events.

<p>1 point for each risk factor that apply now or within the past month</p> <ul style="list-style-type: none"> <li>• Age 40-60 years</li> <li>• Minor surgery (&lt;45 minutes) planned</li> <li>• BMI <math>\geq 30</math> kg/m<sup>2</sup></li> <li>• Major surgery (&gt;45 minutes) within the last month</li> <li>• Swollen legs (current)</li> <li>• Visible varicose veins</li> <li>• Sepsis</li> <li>• COPD</li> <li>• Acute myocardial infarction</li> <li>• Congestive heart failure</li> <li>• History of Inflammatory Bowel Disease</li> <li>• Bed rest or restricted mobility</li> </ul>	<p>2 points for each risk factor</p> <ul style="list-style-type: none"> <li>• Age 61-74 years</li> <li>• Major open or keyhole surgery (&gt;45 minutes)</li> <li>• Prior or present cancer (excluding non melanoma skin cancer, breast and thyroid cancer)</li> <li>• Immobilising plaster cast</li> <li>• Central venous access</li> <li>• Confined to bed for <math>\leq 72</math> hours</li> </ul>	<p>3 points for each risk factor</p> <ul style="list-style-type: none"> <li>• Age <math>\geq 75</math> years</li> <li>• History or family history of VTE</li> <li>• Current chemotherapy</li> <li>• Positive Factor V Leiden/ Prothrombin 20210A/Lupus anticoagulant</li> <li>• Elevated anticardiolipin antibodies or serum homocysteine HIT</li> <li>• Other congenital or acquired thrombophilias</li> </ul>	<p>5 points for each risk factor that apply now or within the past month</p> <ul style="list-style-type: none"> <li>• Major surgery lasting more than 6 hours</li> <li>• Stroke</li> <li>• Elective hip or knee arthroplasty</li> <li>• Hip, pelvis, leg fracture</li> <li>• Acute spinal cord fracture or paralysis</li> <li>• Multiple traumas</li> </ul>								
<p>For women only (1 point each)</p> <ul style="list-style-type: none"> <li>• Pregnant or post-partum</li> <li>• History of unexplained or recurrent spontaneous abortion</li> <li>• Oral contraceptives or HRT</li> </ul>	<p>Caprini risk category based on total risk score</p> <table border="1"> <thead> <tr> <th>Total score</th> <th>Category</th> </tr> </thead> <tbody> <tr> <td>0-4</td> <td>Low</td> </tr> <tr> <td>5-8</td> <td>Moderate</td> </tr> <tr> <td><math>\geq 9</math></td> <td>High</td> </tr> </tbody> </table>			Total score	Category	0-4	Low	5-8	Moderate	$\geq 9$	High
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**Figure 1** Updated Caprini risk-assessment model (55).

Other suggested risk assessment models for VTE include Rogers RAM (57) for surgical patients excluding orthopaedic surgery, Padua RAM (58) for medical patients and Khorana RAM (59) for oncology patients. The Chao-Yang VTE RAM (26) is a RAM which has been suggested for patients undergoing thoracic surgery in China. This model found that age  $\geq 60$ , ASA  $\geq 2$ , open surgery, operative time  $>180$  min, intraoperative bleeding  $>200$  mL, D-dimer  $>0.55$  mL/L, RBC  $<4.0 \times 10^{12}$ /L and BMI  $>30$  kg/m<sup>2</sup> were independent risk factors for VTE.

Shah *et al.* (60) suggested nomograms that allow individualised risk assessment for postoperative VTE and post discharge VTE in patients post abdominal or thoracic surgery, to identify those patients who are at higher risk for postoperative VTE, given the significant variation in the incidence of VTE depending on patient and procedural factors.

Novis *et al.* (61), implemented a computerised DVT risk-assessment tool for surgical patients and they found that the number of patients who received appropriate thromboprophylaxis more than doubled and that there was an 80% decrease in the incidence of postoperative DVT rate, when the tool was used.

This suggests that implementing a standardised DVT risk assessment computerised tool can increase the

appropriate use of thromboprophylaxis accordingly with a subsequent decrease in VTE events.

### Management of postoperative DVT/PE

In cancer patients with VTE, ACCP guidelines (62,63) suggest LMWH over vitamin K antagonists, dabigatran, rivaroxaban, apixaban, or edoxaban. For patients with DVT the routine use of compression stockings is not recommended to prevent post-thrombotic syndrome.

The recommended period of anticoagulation for proximal DVT or PE of provoked by surgery is 3 months and it is preferred over a shorter period.

Acute PE needs to be diagnosed and treated promptly as delay may be fatal (23,64). Haemodynamic and respiratory support is necessary in patients with confirmed or suspected PE and shock or hypotension (32).

Once PE is diagnosed or there is a high suspicion of PE, the use of any anticoagulant therapy with either LMWH, unfractionated heparin, or fondaparinux must be initiated (65). Supplementary oxygen should be given as well. Bleeding may be of concern, therefore the patients should be monitored closely, as blood transfusions may be necessary. If there is evidence of DVT in the lower limbs, an inferior vena cava filter may be considered.

Thrombolysis with urokinase or recombinant tissue plasminogen activator is advised as first-line treatment in patients with PE and persistent hypotension and/or cardiogenic shock, as it has been shown to be effective in resolving thromboembolic obstruction and improving haemodynamic parameters (32,62,63). However, thrombolysis should be avoided in patients with low risk of PE and considered with caution in patients with intermediate risk for PE and in pre-existing factors for increased risk of bleeding, as history of haemorrhagic stroke, ischemic stroke the last 6 months, central nervous system damage or neoplasm, recent major trauma, surgery or head injury within preceding 3 weeks, gastrointestinal bleeding within the last month, known bleeding.

Embolectomy can be lifesaving and indicated in the failure of medical therapy, as in persistent systemic hypotension with shock that can lead to death before thrombolysis can act (66), massive PE with RV dysfunction and worsening respiratory failure, contraindication to use anticoagulation/thrombolysis with high risk of bleeding, failed thrombolysis or poor response. Mortality can be as high as 30% (23,67). Usually pulmonary endarterectomy is applied to patients with chronic thromboembolic pulmonary hypertension (CTEPH) (68).

## Conclusion

Patients who undergo thoracic surgery patients are deemed at high risk for DVT and/or PE. Pharmacologic thromboprophylaxis (69) with LMWH, unfractionated heparin or fondaparinux is recommended for patients who undergo major thoracic surgery and have no increased risk of bleeding. Patients with increased risk of bleeding should have mechanical thromboprophylaxis. Extended pharmacologic prophylaxis for up to 28 days should be considered in patients with risk factors who undergo major surgery for cancer.

Patients with high probability or confirmed PE should be started on anticoagulation without delay. Thrombolysis should be considered in PE with cardiogenic shock or persistent hypotension.

There is a need for universal guidelines specifically targeted to thoracic surgery patients to prevent postoperative VTE and its complications. Randomized controlled trials and the introduction of risk assessment models to assess the potential benefit of extended post-discharge VTE prophylaxis may be beneficial.

## Acknowledgments

*Funding:* None.

## Footnote

*Provenance and Peer Review:* This article was commissioned by the Guest Editor (David Waller) for the series “Complications of Thoracic Surgery – aetiology, management and prevention” published in Shanghai Chest. The article has undergone external peer review.

*Conflicts of Interest:* The author has completed the ICMJE uniform disclosure form (available at: <http://dx.doi.org/10.21037/shc-20-68>). The series “Complications of Thoracic Surgery – aetiology, management and prevention” was commissioned by the editorial office without any funding or sponsorship. The author has no other conflicts of interest to declare.

*Ethical Statement:* The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/shc-20-68

**Cite this article as:** Kolokotroni SM. Deep vein thrombosis and pulmonary embolism following lung resection. *Shanghai Chest* 2021;5:30.