Introduction

Pulmonary resections like other operations have been encountered with a lot of postoperative complications. Acute pulmonary embolism is one of the fatal complications which present difficulties in understanding the mechanisms that triggers occurrence of embolism few hours to days after pulmonary resections. Diagnosing acute pulmonary embolism has presented some difficulties and confusion because of the unspecific symptoms. Most of the symptoms are also presented in other postoperative complications of the pulmonary resections. Early diagnosis and immediately appropriate treatment are the lifesaving options. Delaying the diagnosis and treatment from the time of symptoms presentation might take few minutes to hours to lose a life.\(^1,2\) The emergency of dealing with acute pulmonary embolism was also emphasized by Singh et al.\(^3\) when reported deaths of 18 patients ensued within 4 hours after presentation of the symptoms. With these concerns, a review was conducted by collecting data from different literatures which all together they tried to narrate the importance of understanding the emergency of preventing, diagnosing and treating acute pulmonary embolism.

Risk Factors

A clear cause of pulmonary embolism after pulmonary resections is still unknown. Physicians are largely relaying on predisposing risk factors on evaluating occurrence of pulmonary embolism. Assessment prior to operation is significant in detecting patients who have low, moderate...
and high risks in order to provide appropriate prophylactic treatment. Many literatures have mentioned cancer as a common and highly influential factor leading to acute pulmonary embolism due to presence of protein known as tissue factor (TF) that can account for the activation of the clotting system. Awareness should be raised to benign conditions which patient might had in his or her past medical history. Taking an example from a patient who was diagnosed having cirrhosis of the liver and treated using sclerotherapy with bucrylate or another who suffered from erosive gouty arthritis, both patients developed pulmonary embolism. Also body mass index (BMI) >25 Kg/m², longtime being bedridden, central venous catheter, varicose veins, pregnancy, oral contraceptive use or hormone replacement therapy, thrombophilia, previous history of pulmonary embolism, congestive heart failure, trauma, surgery without heparin and chronic respiratory failure are among the risk factors. Some literatures have tried to analyze the prevention of acute pulmonary embolism with a great success relaying on the best assessment of predisposing risk factors prior to the operation. The assessment has been used successfully in prospective studies with a large sample of 2856 patients between April 2002 and December 2006 and 6004 patients between January 1994 and November 2011.

Causes of Pulmonary Embolism

Pulmonary embolism mostly occurs from broken blood clots in the deep vein (deep vein thrombosis) of the legs which travel to the lungs and block pulmonary arteries. Rarely, pulmonary embolism can be caused by air bubbles, parts of tumor, fat from the bone marrow and other tissues travel to the lungs. The mechanism of deep vein thrombosis, air bubbles, fats from the bone marrow and parts of tumors have been explained in different literatures in how and when they cause pulmonary embolism. Apart from relying on predisposing risks prior to operation, there are theories which explain how pulmonary resections can lead to pulmonary embolism few minutes to hours after operation.

- For the patient having pneumonectomy, if the stamp of the pulmonary artery has been left too long after ipsilateral pneumonectomy, it might predispose to thrombus formation and cross embolization to the contra-lateral artery.
- Damage to the walls of the blood vessels during operation, it’s one of the acceptable theories to formation of blood clot preceding development of pulmonary embolism.
- Right decubitus position in patient undergoing thoracic surgery has been linked to be predisposing factor for the pulmonary embolism, especially to the operations lasting for more than 45 min under general anesthesia. Iliac compression syndrome and the decrease in venous velocity of the right femoral vein in the right lateral decubitus position may be a mechanism in the generation of thrombus.
- Reduction of the cross-section of pulmonary arteries after lung resection holds an increased chance of pulmonary embolism compared to the individual with normal lungs.
- Occurrence of chylothorax after lung resection due to injury of the thoracic duct or collateral lymphatic channels. Presence of chylothorax has been associated with significant increase loss of antithrombin which leads to significant decrease of antithrombin in the plasma.

Diagnosis of Acute Pulmonary Embolism

In different patient’s conditions getting a true diagnosis in a right time, it is the key for the better outcome. Likewise in acute pulmonary embolism the ability to make early diagnosis of the condition will definitely improve the outcome. Regardless of the technological development and many researches which have been done, diagnosing acute pulmonary embolism after pulmonary resections has presented with some difficulties. There is a great need of knowing its clinical presentations and use of appropriate diagnostic methods and equipment.

The clinical severity of acute pulmonary embolism can be highly variable, ranging from asymptomatic to severe hypoxemia, right ventricular failure, cardiogenic shock, and death. Pulmonary embolism severity index (PESI) or simplified pulmonary severity index (sPESI) has been useful models in predicting the prognosis of the patients. These two models successfully can predict short and long term mortality. PESI is having 11 variables and can be stratified into low, moderate, high and very high risk while sPESI is having 6 variables and grouped as low and high risk. In clinical practice there is no significant difference between PESI and sPESI. sPESI has shown low efficiency in prediction of mortality in elderly patients.

Patients may present some of these signs and symptoms when they develop pulmonary embolism.

- Shortness of breath (Dyspnea) – which normally appears suddenly
- Pleuritic chest pain which may be worsened with deep breath
- Syncope
- Dry or moist rales
- Pleural friction rub may be audible
- Cough with blood streak sputum or blood
- Rapid or irregular heart rate (tachycardia)
- Patient may develop cyanosis (bluish skin discoloration) or clammy skin (cool, moist, and usually pale)
- Excessive sweating
- Light headedness and dizziness
- Leg pain or swelling or both usually in the calf
- Low blood pressure

Relaying only on these symptoms and signs in diagnosing pulmonary embolism is not good enough because they are not only specific to acute pulmonary embolism. Also not all these signs and symptoms can be seen to the patient as shown in Table 1. Most patients primarily develop dyspnea, pleuritic chest pain, syncope and cough which was reported also in a large scale study published in journal of the American College of Cardiology, European Journal of Internal Medicine and in Germany study combined results of a multicenter registry which included 204 centers. These unspecificities presentation most of the time has led to delay or misdiagnosis of acute pulmonary embolism.

In addition to clinical symptoms there are number of examinations which have been used to diagnose acute pulmonary embolism and reported in different literatures.

**Hematological abnormalities**

**Blood gas analysis**

Patient with acute pulmonary embolism mostly have been observed to decrease their arterial oxygen partial pressure (PaO₂), oxygen saturation (SaO₂) and increase in alveolar–arterial oxygen pressure gradient (P(A-a)O₂). Presence of PaO₂ <80 mmHg and P(A-a)O₂ >20 mmHg have been documented in some literature as the most common gas exchange abnormalities. Decrease of arterial carbon dioxide partial pressure (PaCO₂) has been detected in patients with acute pulmonary embolism but has shown low significance value in prediction of acute pulmonary embolism. Hypopcapnea develops in patient with acute pulmonary embolism due to increased total minute ventilation while hypercapnia may occur to reflects massive embolism accompanied by marked increases in physiological dead space.

**D-dimer**

D-dimer has been an important biomarker in prediction, exclusion and prognosis evaluation of acute pulmonary embolism. Increase of D-dimer levels has a direct relation with the increase in severity of pulmonary embolism. D-dimer also has been suggested to be a useful biomarker in determination of initial therapies and evaluation of patient’s prognosis. Different literatures documented that negative D-dimer test has effectively and safely excluded acute pulmonary embolism in patients presented with signs and symptoms of embolism. However D-dimer has low specificity leading to a high rate of false-positive results. D-dimer can be elevated in advanced age, pregnancy, trauma, inflammatory states, cancer and recent major surgery so it is very probable that a patient will have a positive D-dimer after lung resections.

**Cardiac markers**

Right ventricular pressure overload leading to right ventricular failure is the major complication of acute pulmonary embolism which causes many deaths. Right ventricular dysfunction triggers elevation of cardiac biomarkers mainly troponin (troponin I and troponin T) and natriuretic peptide (Brain-type natriuretic peptide (BNP) and N-terminal pro-BNP). The elevations of these biomarkers are associated with higher mortality and have become important markers for the risk stratification and appropriate management of acute pulmonary embolism.

**Blood routine**

Patient with acute pulmonary embolism has been observed to have increased white blood cell (WBC) count. In clinical practice acute pulmonary embolism has been documented to increase the WBC count between 10–20 × 10⁹/L. There is a reported significant decrease of hemoglobin and platelet count in acute pulmonary embolism. This decrease of platelet, hemoglobin and increase of WBC count are not specific for the diagnosis of acute pulmonary embolism but can be useful when combined with other investigations.

**Coagulation test**

In acute pulmonary embolism, patient tends to have low international normalized ratio (INR). INR can be used for diagnosis of acute pulmonary embolism and controlling the use of anticoagulant. Also patient with acute pulmonary embolism tends to have low fibrinogen level thus why it is suggested that the high ratio of D-dimer to fibrinogen may help to rule in acute pulmonary embolism. While elevated plasma fibrinogen levels are associated with increased risk of acute pulmonary embolism.
<table>
<thead>
<tr>
<th>No</th>
<th>Year and Author</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis of Embolism</th>
<th>Types of operations</th>
<th>Onset of symptoms and signs of APE after operation</th>
<th>Diagnostic tools (Methods)</th>
<th>Prophylaxis</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2003 Kameyama et al.</td>
<td>F</td>
<td>51 yr</td>
<td>Adenocarcinoma of the lung</td>
<td>Left lower lobectomy</td>
<td>POD 5, chest pain, dyspnea, hypoxia and shock</td>
<td>Echocardiography</td>
<td>-</td>
<td>Intravenous heparin, r-TPA (Alteprase), Urokinase, Lastly Embolectomy and Omentopexy was performed</td>
<td>Discharged on 192nd day, No recurrence in 6 years follow up</td>
</tr>
<tr>
<td>2</td>
<td>2003 Kameyama et al.</td>
<td>F</td>
<td>49 yr</td>
<td>Adenocarcinoma of the lung</td>
<td>Right lower lobectomy</td>
<td>POD 1, sudden back pain, dyspnea and hypoxia</td>
<td>Echocardiography and Infused spiral CT</td>
<td>-</td>
<td>Intravenous heparin, r-TPA (Bolus infusion of alteprase), and Urokinase</td>
<td>Discharged on 28th day. Died due to recurrence of cancer 4 years later</td>
</tr>
<tr>
<td>3</td>
<td>2003 Kameyama et al.</td>
<td>M</td>
<td>65 yr</td>
<td>Adenocarcinoma of the lung</td>
<td>Left upper lobectomy</td>
<td>3 h postoperation developed sudden chest pain, dyspnea and hypoxia</td>
<td>Echocardiography</td>
<td>Subcutaneous heparin 5000 iu on the day of operation</td>
<td>r-TPA (Bolus infusion of monteplase), and LMWH</td>
<td>Discharged on 118th day. No recurrence in 1.5 years</td>
</tr>
<tr>
<td>4</td>
<td>2004 Shundo et al.</td>
<td>F</td>
<td>76 yr</td>
<td>Adenocarcinoma of the lung</td>
<td>Left pneumonectomy</td>
<td>POD 4, sudden syncope, dyspnea finally cardiopulmonary arrest</td>
<td>Autopsy</td>
<td>-</td>
<td>-</td>
<td>Died 1 hour after symptoms developed</td>
</tr>
<tr>
<td>5</td>
<td>2005 Chujo et al.</td>
<td>F</td>
<td>64 yr</td>
<td>Adenocarcinoma of the lung (Bronchoalveolar cell carcinoma)</td>
<td>Left upper lobe wedge resection</td>
<td>POD 1, chest pain and dyspnea</td>
<td>CT and Venography</td>
<td>-</td>
<td>Urokinase and heparin sodium, also IVC filter</td>
<td>Discharged on 25th day with anticoagulant</td>
</tr>
<tr>
<td>6</td>
<td>2007 Kilic et al.</td>
<td>M</td>
<td>57 yr</td>
<td>Squamous cell carcinoma</td>
<td>Left pneumonectomy</td>
<td>POD 1, sudden chest pain, dyspnea, tachycardia and hypoxia</td>
<td>CT Angiography</td>
<td>-</td>
<td>LMWH (Nadroparin calcium) for 2 months</td>
<td>Discharged and no recurrence in a 1 year follow up</td>
</tr>
<tr>
<td>7</td>
<td>2009 Ishikawa et al.</td>
<td>F</td>
<td>60 yr</td>
<td>Adenocarcinoma of the lung</td>
<td>Right middle and lower lobectomy</td>
<td>POD 20, dyspnea</td>
<td>Autopsy</td>
<td>-</td>
<td>-</td>
<td>Sudden death on POD 22</td>
</tr>
</tbody>
</table>

APE: acute pulmonary embolism; M: male; F: female; POD: postoperative day; r-TPA: recombinant tissue plasminogen activator; C: confirmed; A: autopsy; LMWH: low-molecular weight heparin; CT: computed tomography; IVC: inferior vena cava; yr: years
Postoperative Acute Pulmonary Embolism Following Pulmonary Resections

Plain chest X-ray

Though it is not specific, it has been used in preliminary evaluation of the pulmonary embolism. In a prospective observational study which was done in 52 hospitals in seven countries, it was found to have normal findings in at least 25% to the patient who developed pulmonary embolism after surgical procedure.\(^{38}\) mostly it has been suggestive to suspect acute pulmonary embolism with the presence of cardiomegaly. Its appearance on the lung field has been misinterpreted with pneumonia or pulmonary infections which are among the most common pulmonary complications after pulmonary resections.

Echocardiography\(^{24,39,40}\) revealing

- Right ventricular dilatation
- Hypokinesis
- Presence of mean pulmonary arterial pressure of more than 40 mmHg
- Third tricuspid regurgitation.

Given the patients conditions at the presentation of acute pulmonary embolism, echocardiography can primarily be used for diagnosis. It was concluded to have 96% sensitivity and 83% specificity in a study which included 132 patients.\(^{40}\) Also Wang et al.\(^{41}\) reported the same sensitivity and specificity in their review.

Computed tomographic pulmonary angiography (CTPA)

With its high positive predictive value reported to be up to 97% in main or lobar pulmonary arteries and 68% in segmental arteries, it has been used widely as primarily diagnostic tool.\(^{42}\) CTPA will show filling defects within the pulmonary vasculature with acute pulmonary emboli. This has been described as the ‘polo mint’ sign on images acquired perpendicular to the long axis of a vessel and the “railway track” sign on longitudinal images of the vessel.\(^{43}\) Till now, CTPA has remained to be a gold standard in diagnosing pulmonary embolism, though in most acute case it has been difficult to be used due to the patients’ severity.

With those modalities mentioned above, there are others like ventilation-perfusion lung scanning, MRI and electrocardiograph which have been used in detecting pulmonary embolism but their accuracy in the incidence of postoperative acute pulmonary embolism is very limited.

After going through a number of studies which explain the emergency of early diagnosis for acute pulmonary embolism and difficulties which clinicians are facing in order to get a clear diagnosis, we analyzed the important criteria which can be considered as crucial factors to suspect or diagnose acute pulmonary embolism in an emergency situation. If the patient presents with at least three parameters out of five most common signs and symptoms as shown in Fig. 1, and with the inclusion of X-ray and echocardiography results which are supportive to pulmonary embolism as explained above can be a satisfactory evidences to make high suspicions of acute pulmonary embolism. All these investigations can be done on bedside and can help to get the results within few minutes. If the patient is hemodynamically stable, CTPA can be performed to confirm the diagnosis.

Prevention of Acute Pulmonary Embolism

Prevention of any disease is better than its treatment. Prevention of postoperative acute pulmonary embolism has been a challenging task. Thoroughly assessment of the patient before the operation is of high importance. There is a need of understanding risk factors prior to operation. Different literatures have categorized risk factors as shown in Table 2.\(^{44}\)

In 2004, the Chest published an article which elaborated categorizations of risks into 4 levels as low, moderate, high and very high in considerations to types of surgeries whether they are minor or major surgeries, age of the patients, previous history of venous thromboembolism and type of procedure done in the operation.

Thoroughly preoperative workup is very important as admitted in one of the retrospective studies as one of their limitation in drawing a conclusion on their results.\(^{12}\) The understanding of appropriate patients’ risk levels generated a good guidance for prophylaxis suitable to those patients. Two large retrospective studies which included...
8860 patients, were conducted by giving prophylaxis to patients based on their risk factors for venous thromboembolism.\(^4,5\) In both studies their results were statistically significant and favored the protocol they used for prevention of postoperative embolism.

Failure to do proper risk assessment and use of appropriate prophylaxis prior to the operation has been related to the increased chances of developing pulmonary embolism. Table 1 shows that, there was no documentation of using prophylaxis prior or post operation in 6 cases which developed pulmonary embolism, and 1 remained case which prophylaxis was used, his risk levels were not clearly narrated.

<table>
<thead>
<tr>
<th>Level</th>
<th>Presentation</th>
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<tbody>
<tr>
<td>1st</td>
<td>Low risk</td>
</tr>
<tr>
<td>2nd</td>
<td>Moderate risk</td>
</tr>
<tr>
<td>3rd</td>
<td>High risk</td>
</tr>
<tr>
<td>4th</td>
<td>Very high risk</td>
</tr>
</tbody>
</table>

The use of intermittent pneumatic compression has been strongly supported in a study which included 706 patients.\(^12\) In this study, they concluded that there was a statistical significant correlation between the occurrence of pulmonary embolism and the use of intermittent pneumatic compression. Though they had some limitations to reach their conclusion, they had convinced results to use it in clinical practice. Since in the group which received intermittent pneumatic compression, there was no patient developed pulmonary embolism while there were seven patients who developed acute pulmonary embolism in the group which did not receive intermittent pneumatic compression.

Use of anticoagulant therapy has been worried to cause more bleeding and epidural hematoma. Intensive monitoring of the patients is crucial to help minimize the complications. Unfractionated heparin was studied to observe its effects on controlling pulmonary embolism and the use of subcutaneous injection of UFH received either 5000 or 2500 units twice daily was recommended to be safe.\(^45\) In many hospitals, clinicians prefer low molecular weight heparin (LMWH) over unfractionated heparin. Costantino et al.\(^46\) and Erkens et al.\(^47\) reported that LMWH has lower chance of causing major bleeding compared to unfractionated heparin but Kanaan et al.\(^48\) conducted a meta-analysis which concluded similarities in bleeding outcomes.

**Treatment of Acute Pulmonary Embolism**

The mortality rate of acute pulmonary embolism after pulmonary resections has gained appreciated controlled level due to advanced medical technology and skills to control the condition. Before these advancements, there are studies which reported high fatality incidences of acute pulmonary embolism after pulmonary resections. In a study which was done between 1975 and 1993, Kalweit et al.\(^49\) reported death of 21/1735 patients (1.21%) due to confirmed acute pulmonary embolism which accounted for mortality of nearly 20% among the complications in the patients who underwent pulmonary resections.

Proper evaluations of the patient prior to the operation, appropriate prophylactic approach and advanced therapies have created a new and proper way of fighting postoperative acute pulmonary embolism. There are different treatments approaches published in literatures which have been employed to resolve acute pulmonary embolism. These approaches have been categorized in two groups which are medical and surgical approach. Table 1 shows five patients survived after receiving treatment on time and two patients who died didn’t receive any treatment for pulmonary embolism and their diagnosis were confirmed through autopsy.

Medically, the use of anticoagulant therapy (LMWH, fondaparinux, warfarin and unfractionated heparin), thrombolytic therapy (Recombinant tissue plasminogen activator and Urokinase) and oxygen inhalation therapy has significantly improved the outcome on patient’s conditions. Many literatures have reported similarities in the effectiveness and safety of LMWH and unfractionated heparin in treatment of embolism.\(^50–54\) The worry of aggravating bleeding has been of great concern. Bleeding as a major obstacle to these therapies, as the case reported by Sayeed et al.\(^55\) which necessitated the infusion of 21 units of blood. There are studies which showed these therapies can be used safely. Sakuragi et al.\(^56\) reported a successful treatment of seven patients with acute pulmonary embolism developed after pulmonary resections using anticoagulants.
and thrombolytic therapy, also summarized 20 patients of postoperative acute pulmonary embolism which were reported before 2003. In those cases, 12 patients survived after being treated. 10 patients were treated with anticoagulants and thrombolytic therapy while in two patients embolectomy was performed. The remained eight patients died; in which five patients did not receive any treatment for acute pulmonary embolism and their diagnosis were confirmed through autopsy. While two patients were treated with anticoagulant and thrombolytic drugs and one patient underwent embolectomy. And Spohr et al. 57) reported a successfully thrombolysis after a failure of complete removal of emboli by pulmonary embolectomy. Also Table 1 show, four patients survived after receiving anticoagulant and thrombolytic therapy as the first treatment choice for acute pulmonary embolism.

Surgical approach (embolectomy and inferior vena cava filter placement) for acute pulmonary embolism has shown to be a lifesaving in some cases. In a review conducted at St. Joseph Mercy Oakland Hospital to evaluate the outcome after embolectomy, reported 30% mortality in a report which included 1300 patients in their study. 58) Despite of the high mortality rate reported in their review, embolectomy served lives in conditions which anticoagulants and thrombolytic therapy failed. Surgical approach is indicated in the presence of:

- Persistent systemic hypotension with features of shock that is likely to cause death before thrombolysis can take effect.
- Massive or sub-massive pulmonary embolism with right ventricular dysfunction and worsening respiratory failure.
- Contraindication to use thrombolytic or anticoagulation therapy with high risk of bleeding.
- Poor response to systemic thrombolysis or failed thrombolysis.

Surgical approach is contraindicated when there is multiple organ failure due to massive embolism and risk of massive bleeding during operation.

**Conclusion**

Before operation, surgeons are expected to perform a thorough workup on their patients to identify risks which might lead to embolism. A clear understanding of their patients and assigning to the respective risks category will be the best way of providing appropriate preventive measures. As we have cited out some literature which successfully prevented the occurrence of acute pulmonary embolism. So it’s possible to walk through the same path and achieve a success they achieved.

Despite the complications which have been worried to happen due to medications commonly known to be used in prevention, Yoshida et al. 45) strongly supported the use of medications in prevention of pulmonary embolism. We also advise more research and studies should be done to improve the diagnosing skills, since most of the known criteria used for diagnosis are not specific to acute pulmonary embolism. A number of complications which occur after pulmonary resection have some similarity in their presentation with pulmonary embolism.

Anticoagulant therapy and thrombolytic therapy have been proved to be the best option in treating acute pulmonary embolism as many studies have shown successful results. 55, 56) After critical assessment of literatures, it is suggested that anticoagulant and thrombolytic therapy can primarily be an option for treatment of acute pulmonary embolism after pulmonary resections. Patients should be closely monitored during the administration of these drugs to avoid severe complications which might be induced by these drugs. Embolectomy can be reserved when there is failure on the medical therapy. And inferior vena cava filter can be used when there is sign or detection of venous thromboembolism or deep vein thrombosis. Therefore clinicians are urged to work hard on preoperative assessment and prevention instead of waiting the condition to develop.

When the condition develops treatment should be started as soon as possible.

**Disclosure Statement**

Authors have no conflict of interest.

**References**

42) Lapner ST, Kearon C. Diagnosis and management of pulmonary embolism. BMJ 2013; 346: f757.