Review Article

Perioperative Pulmonary Embolism Prevention and Treatment

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Abstract

All perioperative patients are at an increased risk of pulmonary embolism and venous thromboembolism. Perioperative massive Pulmonary Embolism (PE) is a significant cause of morbidity and mortality. Clinical outcomes have been shown to be improved by a high index of suspicion, prompt recognition, and aggressive intervention. It is important that healthcare providers recognize perioperative PE and know prevention and treatment options. Many medical societies have published guideline recommendations for management of PE. In this review, we will focus on perioperative acute PE treatment and prevention to implement guideline recommendations for optimizing management of acute PE.

Keywords: Pulmonary Embolism; Diagnosis; Thrombolytic agents; Prevention

Introduction

Massive perioperative Pulmonary Embolism (PE) is an uncommon event but significant cause of morbidity and mortality. It is estimated that PE is responsible for between 150,000 and 200,000 deaths per year in the United States [1]. 30% of the deaths from PE take place during the perioperative period [1]. PE is the third most common cardiovascular disease after myocardial infarction and cerebrovascular accident (stroke). Several studies have reported mortality rates ranging from 15% to 30%, while mortality rates in a massive PE can reach 30% to 50% [2-4]. A recent review of more than 3000 massive intraoperative thromboembolic events revealed an overall mortality of 41% [5].

Surgery increases the risks for perioperative PE. Healthcare providers, including anesthesiologists, are responsible for the diagnosis and treatment of perioperative PE. During surgery, PE often first presents with hemodynamic instability and if progressing quickly, can lead to death. It is important that healthcare providers recognize perioperative PE and know prevention and treatment options. Prompt diagnosis and treatment can save patient lives. In this review, we will focus on perioperative acute PE treatment and prevention.

Diagnosis of PE

Diagnosis of a PE in the perioperative period can be a challenge, but early detection can reduce morbidity. The American Heart Association (AHA) classified and defined PE into three classes: massive PE, submassive PE, and low-risk PE [6].

Definition for massive PE: Acute PE with sustained hypotension (systolic blood pressure <90 mm Hg) for at least 15 minutes or requiring isotropic support, not due to a cause other than PE, such as arrhythmia, hypovolemia, sepsis, or Left Ventricular (LV) dysfunction, pulselessness, or persistent profound bradycardia (heart rate<40 bpm with signs or symptoms of shock) [6].

Definition for submassive PE: Acute PE without systemic hypotension (systolic blood pressure ≥ 90 mm Hg) but with either RV dysfunction or myocardial necrosis [6].

RV dysfunction means the presence of at least 1 of the following: (1) RV dilation (apical 4-chamber RV diameter divided by LV diameter >0.9) or RV systolic dysfunction on echocardiography. (2) RV dilation (4-chamber RV diameter divided by LV diameter >0.9) on CT. (3) Elevation of BNP (>90 pg/mL). (4) Elevation of N-terminal pro-BNP (>500 pg/mL); or (5) Electrocardiographic changes (new complete or incomplete right bundle-branch block

Myocardial necrosis is defined as either of the following: (1) Elevation of troponin I (>0.4 ng/mL) or (2) Elevation of troponin T (>0.1 ng/mL).

Definition for low-risk PE: Acute PE and the absence of the clinical markers of adverse prognosis that define massive or submassive PE [6].

The Treatment of Acute Pulmonary Embolism

Systemic thrombolysis

Thrombolytic agents are indicated in patients who are normotensive but with evidence of RV failure or in cases of hemodynamic instability [7]. Several societies guidelines advocate the use of thrombolytic agent in patients with hemodynamic compromise and massive PE is acceptable [6,8].

A meta-analysis of clinical trials including patients with massive PE showed IV fibrinolytic agents reduced the composite of recurrent PE and death, but not in death alone [9]. The results of patients with submassive PE were better characterized in randomized trials. These studies showed the use of IV fibrinolytic therapy in patients with massive or submassive PE can improve hemodynamic stability and, possibly reduce the risk of recurrent PE and PE-attributed death [10].

The most commonly used thrombolytic agents approved by the
Catheter-based therapies

Catheter-based therapies can (1) rapidly reduce pulmonary artery pressure, RV strain, and Pulmonary Vascular Resistance (PVR), (2) increase systemic perfusion and (3) facilitate RV recovery [6]. This treatment is an alternative method to remove pulmonary emboli and is a less invasive approach compared to surgical embolectomy. Catheter-directed therapies include mechanical fragmentation of thrombus with a standard pulmonary artery catheter, clot pulverization with a rotating basket catheter, percutaneous rheolytic thrombectomy, or pigtail rotational catheter embolectomy [16]. Catheter-directed thrombolysis is considered in cases of unsuccessful systemic thrombolysis, contraindications to thrombolytic therapy, and when surgical embolectomy is unavailable or not feasible (Table 2) [7].

Potential complications from catheter directed therapies include pulmonary hemorrhage and right atrial or ventricular perforation leading to cardiac tamponade. Perforation or dissection of a major pulmonary artery branch may cause acute massive pulmonary hemorrhage and death [6].

There are no randomized trials or prospective cohort studies that have evaluated catheter based techniques for massive PE [16]. A systematic review of available cohort data included a total of 348

| Table 1: AHA recommendations for systemic thrombolysis for acute PE [6]. |
|-----------------------------|-----------------------------|-----------------------------|
| **Recommendations**         | **Class**                  | **Level**                  |
| Fibrinolysis is reasonable for patients with massive acute PE and acceptable risk of bleeding complications | Ila              | B                           |
| Fibrinolysis may be considered for patients with submassive acute PE judged to have clinical evidence of adverse prognosis (new hemodynamic instability, worsening respiratory insufficiency, severe RV dysfunction, or major myocardial necrosis) and low risk of bleeding complications | IIb              | C                           |
| Fibrinolysis is not recommended for patients with low-risk PE or submassive acute PE with minor RV dysfunction, minor myocardial necrosis, and no clinical worsening | III             | B                           |
| Fibrinolysis is not recommended for undifferentiated cardiac arrest | III              | B                           |

| Table 2: AHA recommendation for catheter based therapies and surgical embolectomy for acute PE [6]. |
|-----------------------------|-----------------------------|-----------------------------|
| **Recommendations**         | **Class**                  | **Level**                  |
| Depending on local expertise, either catheter embolectomy and fragmentation or surgical embolectomy is reasonable for patients with massive PE and contraindications to fibrinolysis | Ila              | C                           |
| Catheter embolectomy and fragmentation or surgical embolectomy is reasonable for patients with massive PE who remain unstable after receiving fibrinolysis | Ila              | C                           |
| For patients with massive PE who cannot receive fibrinolysis or who remain unstable after fibrinolysis, it is reasonable to consider transfer to an institution experienced in either catheter embolectomy or surgical embolectomy if these procedures are not available locally and safe transfer can be achieved | Ila              | C                           |
| Either catheter embolectomy or surgical embolectomy may be considered for patients with submassive acute PE judged to have clinical evidence of adverse prognosis (new hemodynamic instability, worsening respiratory failure, severe RV dysfunction, or major myocardial necrosis) | IIb              | C                           |
| Catheter embolectomy and surgical thrombectomy are not recommended for patients with low-risk PE or submassive acute PE with minor RV dysfunction, minor myocardial necrosis, and no clinical worsening | III             | C                           |

| Table 3: AHA recommendation for placement of IVC filter for acute PE [6]. |
|-----------------------------|-----------------------------|-----------------------------|
| **Recommendations**         | **Class**                  | **Level**                  |
| Adult patients with any confirmed acute PE (or proximal DVT) with contraindications to anticoagulation or with active bleeding complication should receive an IVC filter | I               | B                           |
| Anticoagulation should be resumed in patients with an IVC filter once contraindications to anticoagulation or active bleeding complications have resolved | I               | B                           |
| Patients who receive retrievable IVC filters should be evaluated periodically for filter retrieval within the specific filter’s retrieval window | I               | C                           |
| For patients with recurrent acute PE despite therapeutic anticoagulation, it is reasonable to place an IVC filter | Ila              | C                           |
| For DVT or PE patients who will require permanent IVC filtration (e.g., those with a long-term contraindication to anticoagulation), it is reasonable to select a permanent IVC filter device | Ila              | C                           |
| For DVT or PE patients who will require permanent IVC filtration (e.g., those with a long-term contraindication to anticoagulation), it is reasonable to select a permanent IVC filter device | Ila              | C                           |
| Placement of an IVC filter may be considered for patients with acute PE and very poor cardiopulmonary reserve, including those with massive PE | IIb              | C                           |
| An IVC filter should not be used routinely as an adjuvant to anticoagulation and systemic fibrinolysis in the treatment of acute PE | III              | C                           |

US Food and Drug Administration (FDA) for acute PE included: Recombinant tissue type Plasminogen Activator (tPA, alteplase), Streptokinase (SK) and recombinant human Urokinase (UK). Other thrombolytic agents not FDA approved include tenecteplase and reteplase.

All fibrinolytic drugs are enzymes that convert the patient’s native circulating plasminogen into plasmin. The contraindications include active internal bleeding; prior intracranial hemorrhage, intracranial cerebrovascular disease, suspected aortic dissection, intracranial malignant neoplasm, ischemic stroke within 3 months, recent intracranial or spinal cord surgery, recent closed-head or facial trauma with fracture or intracerebral injury [6], and severe uncontrolled hypertension [11].

Streptokinase should also not be used after 5 days to 12 months of initial use for possible anaphylactic reaction from anti-streptokinase antibodies or in patients with recent streptococcal infections due to possible drug resistance or reduced effects (Table 1) [12-15].

Catheter-based therapies

Catheter-based therapies can (1) rapidly reduce pulmonary artery
patients [17]. Clinical success with percutaneous therapy alone for patients with acute massive PE was 81%, and clinical success when combined with local infusion of thrombolytic agents was 95% [17].

Surgical embolectomy

Surgical embolectomy is considered the last treatment option for acute PE [18]. The surgery requires a median sternotomy and cardiopulmonary bypass. This operation is indicated for acute PE patients who need surgical excision of a right atrial thrombus, impending paradoxical arterial embolism, or a closure of a patent foramen ovale [16]. Surgical embolectomy can be used for patients in whom thrombolysis has been unsuccessful [16]. Significant advances in cardiac surgical techniques have reduced surgical mortality, which is about 6% currently [19,20]. In addition, there is evidence that pulmonary embolectomy can reduce long term mortality [21,22].

Major risks of surgical embolectomy include: injury to the distal branches of the PA during embolectomy that can lead to significant bronchoalveolar hemorrhage [7], inability to wean from cardiopulmonary bypass because of primary RV dysfunction, persistent severe pulmonary hypertension, or severe hypoxia that could require the use of mechanical circulatory support/Extracorporeal Membrane Oxygenation (ECMO) as a bridge to recovery [7].

Vena caval filters

Placement of an Inferior Vena Cava (IVC) filter is indicated in patients with acute PE who have absolute contraindications to anticoagulation, in those experiencing major bleeding events during the acute phase, and in patients with objectively confirmed recurrent PE, despite adequate anticoagulation treatment [23].

Data from the US Nationwide Inpatient Sample suggest that caval filters may be associated with an improved outcome [24]. In the PREPIC Trial (Pre vention du Risquéed’ Embolie Pulmonairepar Interruption Cave), hospitalized patients with acute symptomatic PE associated with lower-limb vein thrombosis were randomized into two groups, one group received anticoagulation only, the other group received anticoagulation with IVC filter [25]. The results showed that there were no differences in major bleeding, post thrombotic chronic venous insufficiency, or death during the study period [25]. These results did not demonstrate any advantages of the use of retrievable IVC filters in patients with acute PE.

Potential complications of IVC included penetration of the caval wall or embolization to the right heart cavities (Table 3).

Prevention

Deep Vein Thrombosis (DVT) occurred in 348, 558 hospitalizations, Pulmonary Embolism (PE) occurred in 277, 549 hospitalizations, and concomitant DVT and PE occurred in 78, 511 hospitalizations each year [26]. It was estimated that 15 percent, 24 percent, and 17 percent were at moderate, high, or very high risk for venous thromboembolism (VTE includes both deep vein thrombosis and pulmonary embolism) [27].

The National Quality Forum, the Surgical Care Improvement Project, the Centers for Medicine and Medicinal Services, the Joint Commission on Accreditation of Health Care Organizations, and the Office of the Surgeon General of the United States all have initiatives for VTE prophylaxis.

The American College of Chest Physicians (ACCP) published a series of VTE guidelines, and when comparing it with the previous guidelines, a very important change in the ACCP 2012 guideline is the emphasis in individualized assessment [28-30]. VTE perioperative evaluation should include the type and extent of surgery or trauma, duration of hospitalization, a history of previous VTE or cancer, immobility, recent sepsis, presence of a central venous access device, pregnancy or the postpartum period, and inherited or acquired hypercoagulable states. All clinical decisions should be made based on the balance between the risk of VTE and risk of major bleeding in the consideration of available literature reports (Table 4).
Perioperative patients can be divided into four different risks categories of VTE, patient with high risks, moderate risks, low risks and very low risks [28-30].

High risk patients - Patients undergoing general and abdominal-pelvic surgery with a Caprini score of 5 or more, or those undergoing plastic and reconstructive surgery with a Caprini score of 7 to 8 are considered as high risk patients [29-31]. The estimated baseline risk of VTE in the absence of prophylaxis is estimated to be approximately 6 percent. Examples of patients in the high risk group are those undergoing hip/knee arthroplasty, pelvic/hip fracture surgery, colorectal surgery, major trauma, spinal cord injury or cancer surgery [28-30].

The VTE prophylaxis protocol for patients with high risk patients, recommends the use of either drugs or physical methods that are effective for preventing DVT and is considered as a primary prevention approach. Secondary prevention involves the early detection and treatment of subclinical venous thrombosis. Primary prophylaxis is preferred and is more cost effective than treatment after a VTE [27].

With all primary VTE prevention in patients with high risks without major bleeding risk, pharmacology prevention is preferred [30,31]. These agents include low-molecular-weight heparin; fondaparinux; dabigatran, apixaban, rivaroxaban, endoxaban; low-dose unfractionated heparin; adjusted-dose vitamin K antagonist; aspirin (all Grade I B) for a minimum of 10 to 14 days [28].

Patients at high risk for VTE undergoing abdominal or pelvic surgery for cancer, ACCP recommends extended-duration, postoperative, pharmacologic prophylaxis for 4 weeks with LMWH over limited-duration prophylaxis (Grade IB) [30].

Patients with high risk of VTE undergoing orthopedic surgery are suggested to be on VTE prophylaxis for up to 35 days (Grade II B) [28]. In patients at increased bleeding risk, ACCP suggests an IPCD or no prophylaxis [28].

For patients with isolated lower extremities injuries requiring leg immobilization, ACCP suggests no thromboprophylaxis (Grade IIIB). For patients undergoing knee arthroscopy without a history of VTE, no thromboprophylaxis is suggested (Grade IIB) [28].

Patients with a high risk for VTE who are at high risk for major bleeding complications or those in whom the consequences of bleeding are believed to be particularly severe, ACCP the recommends the use of mechanical prophylaxis, preferably with IPC, over no prophylaxis until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade IIC) [30].

Moderate risk patients - Surgical patients undergoing general and abdominal-pelvic surgery with a Caprini score of 3 to 4, or those undergoing plastic and reconstructive surgery with a Caprini score of 5 to 6 carry a moderate risk of thrombotic events. Their estimated baseline risk of VTE in the absence of prophylaxis is estimated to be approximately 3 percent. Examples of these groups of patients include patients with general gynecologic, urologic, thoracic, ankle fracture, or neurosurgical procedures [28-30].

For patient with moderate risk of VTE without major risk of bleeding: Low-Molecular-Weight Heparin (LMWH) (Grade IIB), low-dose unfractionated heparin (Grade IIB), or mechanical prophylaxis with IPC (Grade IIC) is recommended over no prophylaxis [30]. For patients at moderate risk for VTE who are at high risk for major bleeding complications or those in whom the risk of bleeding is severe, the ACCP recommends mechanical prophylaxis, preferably with IPC until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade IIC) [31].

Low risk patients - Patients undergoing general and abdominal-pelvic surgery with a Caprini score of 1 to 2, or those undergoing plastic and reconstructive surgery with a Caprini score of 3 to 4 are included in the low risk group for thrombotic events. Their estimated baseline risk of VTE in the absence of prophylaxis is estimated to be approximately 1.5 percent. Clinical data on this group is scarce but the recommendation by the ACCP includes mechanical prophylaxis, preferably with intermittent pneumatic compression (IPC) over no prophylaxis (Grade IIC) [30].

Very low risk patients - patients undergoing general and abdominal-pelvic surgery with a Caprini score of zero, and those undergoing plastic and reconstructive surgery with a Caprini score of zero to two carries very low risk of thrombotic events with estimated risk less than 0.5 percent without prophylaxis. There is no clinical data to demonstrate the efficacy of VTE prophylaxis in this group. No specific pharmacologic (Grade I B) or mechanical (Grade II C) prophylaxis are recommended to be used other than early ambulation [30].

An important update in the 2012 ACCP guideline is for patients in all risk groups, that recommend that an inferior vena cava filter should not be used for primary VTE prevention (Grade II C) and that surveillance with venous compression ultrasonography should not be performed (Grade II C) [28-30].

VTE Prophylaxis should be started either before or shortly after surgery, and continued at least until the patient is fully ambulatory based on FDA approved labeling.

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