



# 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) are a significant cause of morbidity and mortality. Clinical outcomes have been shown to be improved by a careful observation, 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.

Key words: Pulmonary embolism; perioperative; guideline

## 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). Thirty percent of the deaths from PE take place during the perioperative period (1). The third most prevalent cause of cardiovascular disease is PE after myocardial infarction and cerebrovascular accident (stroke). Several studies have reported the mortality rate of a PE 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 mas-

sive intraoperative thromboembolic events revealed an overall mortality of 41% (5).

Surgery increases the risks for perioperative PE. Healthcare providers 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 an acute PE

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

Criteria for *massive PE*: Acute PE with sustained systolic blood pressure < 90 mm Hg for at least 15 minutes or requiring inotropic support, pulselessness, or persistent heart rate <40 bpm with hemodynamic instability (6).

Criteria for *submassive PE*: Acute PE systolic blood pressure  $\geq$  90 mm Hg but with either RV dysfunction or myocardial necrosis (6).

RV dysfunction is diagnosed by the presence of at

**Table 1: AHA recommendations for systemic thrombolysis for acute PE**

Recommendations for Systemic Thrombolysis Utilization	Class	Level
Recommended for massive acute PE with acceptable risk of bleeding complications	IIa	B
Consider for submassive acute PE with clinical evidence of adverse prognosis (new hemodynamic instability, worsening respiratory insufficiency, severe RV dysfunction, or major myocardial necrosis) with low risk of bleeding complications	IIb	C
Not recommended for low-risk PE or submassive acute PE with minor RV dysfunction, minor myocardial necrosis, and if patient is not worsening clinically	III	B
Not recommended for undifferentiated cardiac arrest	III	B

Recommendation class: I: benefits >>>risks, IIa: benefits>>risks, IIb: benefits ≥ risks; III: risks ≥ benefits. Level of evidence: A: Multiple population evaluated; B: Limited population evaluated; C: Very limited population evaluated

least 1 of the following: RV dilation: apical 4-chamber RV diameter divided by LV diameter > 0.9 on echocardiography or on CT. BNP >90 pg/mL. N-terminal pro-BNP >500 pg/mL; or Electrocardiographic changes such as, new complete or incomplete right bundle-branch block, anteroseptal ST elevation or depression, or anteroseptal T-wave inversion.

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

Criteria for *low-risk PE*: Acute PE in the absence of criteria for 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 (6, 8).

A clinical study including patients with massive PE showed systemic thrombolysis therapy reduced the composite of recurrent PE and mortality, but no difference in mortality alone (9). The results of patients with submassive PE were categorized through random-

ized trials. These studies showed the use of systemic thrombolysis in patients with massive or submassive PE can enhance hemodynamic stability and, reduce recurrent PE and PE-attributed mortality (10).

The most commonly US Food and Drug Administration (FDA approved thrombolytic agents for acute PE include: tPA, alteplase, streptokinase (SK), and urokinase (UK). Other thrombolytic agents without FDA approval include tenecteplase, and reteplase.

All fibrinolytic drugs are enzymes that enhance the conversion of the patient's circulating plasminogen into plasmin. The contraindications include active bleeding; history of intracranial hemorrhage, intracranial cerebrovascular disease, possible aortic dissection, intracranial malignant neoplasm, ischemic stroke within 3 months, recent neurosurgery, recent head trauma(6), and 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. (12-15). AHA recommendations for systemic thrombolysis for acute PE (6) was shown in Table 1.

### Catheter-based therapies

Catheter-based therapies can (1) quickly ease pul-

**Table 2: AHA recommendation for catheter based therapies and surgical embolectomy for acute PE**

Recommendations for Catheter Based Therapies and Surgical Embolectomy	Class	Level
Recommended for massive PE with contraindications to fibrinolysis	IIa	C
Recommended for massive PE in patients who are unstable after systemic fibrinolysis	IIa	C
Recommended to safely transfer patient to an institution experienced in either catheter embolectomy or surgical embolectomy if these procedures are not available locally	IIa	C
Consider for patients with submassive acute PE with clinical evidence of adverse prognosis (new hemodynamic instability, worsening respiratory failure, severe RV dysfunction, or major myocardial necrosis)	IIb	C
Not recommend for low-risk PE or submassive acute PE with minor RV dysfunction, minor myocardial necrosis, and if patient is not worsening clinically	III	C

monary artery pressure, RV tension, and pulmonary vascular resistance (PVR), (2) improve systemic circulation, and (3) return RV function (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 fragmentation of thrombus by pulmonary artery catheter, clot reduction by basket catheter, thrombectomy by percutaneous rheolytic therapy, or pigtail catheter (16). Catheter-directed thrombolysis is considered in cases of unsuccessful systemic thrombolysis, contra-

indications to thrombolytic therapy, and when surgical embolectomy is unavailable or not feasible (7).

Potential complications from catheter directed therapies include pulmonary hemorrhage and the risk of cardiac tamponade if the right atria or ventricle are perforated. Similarly, massive pulmonary hemorrhage and death may result from the perforation or dissection of a major pulmonary blood vessel (6).

There are no prospective studies to evaluate catheter based techniques for massive PE (16). A systematic

Table 3: PE treatment options

	Treatment Options	
	Systemic Thrombolysis	Catheter Embolectomy and Fragmentation or Surgical Embolectomy
Low-Risk PE	Not Recommended (III-B)	Not Recommended (III-C)
Submassive PE	Recommended only if adverse prognosis present* (IIb-C)	Recommended only if adverse prognosis present* (IIb-C)
Massive PE	Recommended (IIa-B) with acceptable risk of bleeding complications	Recommended if fibrinolysis contraindicated or patient remains unstable after fibrinolysis (IIa-C)
Undifferentiated Cardiac Arrest	Not Recommended (III-B)	N/A
<p>Recommendation class: I: benefits &gt;&gt;&gt;risks, IIa: benefits&gt;&gt;risks, IIb: benefits ≥ risks; III: risks ≥ benefits.</p> <p>Level of evidence: A: Multiple population evaluated; B: Limited population evaluated; C: Very limited population evaluated</p> <p>*Acute Prognosis: new hemodynamic instability, worsening respiratory insufficiency, severe RV dysfunction or major myocardial necrosis</p>		

review with a total of 348 acute massive PE patients showed that success rate of clinical percutaneous therapy alone was 81%, and when combined with thrombolytic agents was 95% (17).

### Surgical embolectomy

Surgical embolectomy is considered the final treatment option for acute PE (18). The surgery requires a medi-

pulmonary hypertension, or severe hypoxia that could require the use of mechanical circulation supporting devices, and extracorporeal membrane oxygenation (ECMO) (7). AHA recommendation for catheter based therapies and surgical embolectomy for acute PE (6) was shown in Table 2.

PE treatment options were summarized in Table 3.

**Table 4: AHA recommendation for placement of IVC filter for acute PE**

Recommendations for placement of IVC Filter	Class	Level
Recommended for acute PE with contraindications to anticoagulation or with active bleeding complications	I	B
After placement of an IVC filter, anticoagulation should be resumed promptly when contraindications to anticoagulation or active bleeding complications have been resolved	I	B
After placement of retrievable IVC filters, patients should be assessed periodically for filter retrieval within the specific filter's retrieval window	I	C
Recommended to place an IVC filter for recurrent acute PE despite therapeutic anticoagulation	IIa	C
Recommended to place a permanent IVC filter for those with a long-term contraindication to anticoagulation	IIa	C
Consider to place an IVC filter for acute PE with very poor cardiopulmonary reserve	IIb	C
Not recommended to be used <i>routinely</i> as an adjuvant in the treatment of acute PE	III	C

an sternotomy and cardiopulmonary bypass. Surgical embolectomy is indicated for acute PE patients with a right atrial thrombus, paradoxical arterial embolism, or a closure of a patent foramen ovale (16). Surgical embolectomy is also indicated for patients who were unsuccessfully treated with thrombolytic agents (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

### Vena Caval Filters

An inferior vena cava (IVC) filter is inserted in patients with acute PE who can not receive systemic thrombolysis, in patients who experienced major bleeding events, and in patients who are confirmed recurrent PE after adequate anticoagulation therapy (23).

Data from the U.S. Nationwide Inpatient Sample suggest that cava filters may improve clinical outcome (24). In the PREPIC Trial (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave), patients with acute PE and lower extremities vein thrombosis were randomized into two groups, one group received anticoagulation only, the other group received anticoagulation with IVC filter (25). The results demonstrated that there were no differences in major bleeding,

postthrombotic chronic venous insufficiency, or mortality rate (25). These clinical data did not support the

Deep vein thrombosis (DVT) occurred in 348, 558 hospitalizations, pulmonary embolism (PE) occurred

**Table 5: Modified Caprini assessment model for general surgery thrombotic risk evaluation.**

1 Point	2 Points	3 Points	5 Points
Age 41-60 y	Age 61-74 y	Age ≥75 y	Stroke (<1 mo)
Minor surgery	Arthroscopic surgery	History of VTE	Elective arthroplasty
BMI >25 kg/m <sup>2</sup>	Major open surgery (>45 min)	Family history of VTE	Hip, pelvic, or leg fracture
Swollen legs	Laparoscopic surgery (>45 min)	Factor V Leiden	Acute spinal cord injury (<1 mo)
Varicose veins	Malignancy	Prothrombin 20210A	
Pregnancy or postpartum	Confined to bed (>72 h)	Lupus anticoagulation	
History of unexplained or recurrent spontaneous abortion	Immobilizing plaster cast	Anticardiolipin antibodies	
Oral contraceptive or hormone replacement	Central venous access	Elective serum homocysteine	
Sepsis (<1 mo)		Heparin-induced thrombocytopenia	
Serious lung disease, including pneumonia (<1 mo)		Other congenital or acquired thrombophilia	
Abnormal pulmonary function			
Acute myocardial infarction			
Congestive heart failure (<1 mo)			
History of inflammatory bowel disease			
Medical patient at bed rest			

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Score 0, very low risk; score 1-2, low risk; score 3-4, moderate risk; score ≥5, High risk

use of retrievable IVC filters in patients with acute PE.

Complications of IVC could include the caval wall penetration or the right side heart embolism. AHA recommendations for placement of IVC filter for acute PE (6) was shown in Table 4.

### Prevention

in 277, 549 hospitalizations, and concomitant DVT and PE occurred in 78, 511 hospitalizations each year (26). In surgical patients, it was estimated that 15 percent were at a moderate risk, 24 percent were at a high risk, and 17 percent were at a very high risk for venous thromboembolism (VTE includes both deep vein thrombosis and pulmonary embolism) (27).

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

The American College of Chest Physicians (ACCP) published a series of VTE guidelines. A very important change in the ACCP 2012 guideline for the risk of PE with surgery is the emphasis in individualized assessment (28-30). VTE perioperative evaluation should include the category and scope of surgery or trauma, length 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 medical 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.

Perioperative patients can be divided into four different risk categories of VTE, patient with high risks, moderate risks, low risks and very low risks. (28-30) (Table 5).

**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 without prophylaxis is estimated to be approximately 6 percent. Examples of patients in the high-risk group are those undergoing major joint 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 medication or physical methods that are effective for DVT prophylaxis and is considered as a primary prevention approach. Early detection and treatment of subclinical venous thrombosis are classified as secondary prevention. 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 I B). (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 (Intermittent Pneumatic Compression Device) or no prophylaxis. (28)

For patients with isolated lower extremity injuries requiring leg immobilization, ACCP suggests no thromboprophylaxis (Grade IIB). For patients undergoing knee arthroscopy without a history of VTE, thromboprophylaxis is not suggested either (Grade IIB). (28)

Patients with a high risk for VTE who are at high risk for major bleeding complications, the ACCP recommends the use of mechanical prophylaxis, preferably with IPC, over no prophylaxis until the risk of bleeding diminishes and prophylaxis with medication can 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 group 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

**Table 6: VTE prevention**

	Classification	Primary Prevention	Prevention with high risk for major bleeding complications
High Risk	General/Abdominal-Pelvic Surgery with Caprini score of $\geq 5$  OR  Plastic/Reconstructive Surgery with Caprini score of 7-8	Pharmacology with LMW Heparin, fondaparinux, dabigatran, apixaban, rivaroxaban, endoxaban, low dose unfractionated heparin, adjusted-dose vitamin K antagonist, aspirin (Grade IB) for a minimum of 10-14 days	Mechanical Prophylaxis, preferably with IPC, over no prophylaxis until risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade IIC)
Moderate Risk	General/Abdominal-Pelvic Surgery with Caprini score of 3-4  OR  Plastic/Reconstructive Surgery with Caprini score of 5-6	Pharmacology with LMWH (Grade IIB), low-dose unfractionated heparin (Grade IIB), or mechanical prophylaxis with IPC (Grade IIC) are recommended over no prophylaxis.	Mechanical prophylaxis, preferably with IPC until the risk of bleeding diminishes and pharmacologic prophylaxis may be initiated (Grade IIC)
Low Risk	General/Abdominal-Pelvic Surgery with Caprini score of 1-2  OR  Plastic/Reconstructive Surgery with Caprini score of 3-4	Mechanical prophylaxis, preferably with IPC over no prophylaxis (Grade IIC)	Mechanical prophylaxis, preferably with IPC over no prophylaxis (Grade IIC)
Very Low Risk	General/Abdominal-Pelvic Surgery with Caprini score of 0  OR  Plastic/Reconstructive Surgery with Caprini score of 0-2	Early Ambulation recommended. No specific pharmacologic (Grade IB) or mechanical (Grade IIC) recommended	Early Ambulation recommended. No specific pharmacologic (Grade IB) or mechanical (Grade IIC) recommended

LMWH : low-molecular-weight heparin

(Grade IIC) are 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 II C). (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 without any prophylactic treatment is estimated to be approximately 1.5 percent. Clinical data on this group is scarce but the recommendation by the ACCP include mechanical prophylaxis,

preferably with intermittent pneumatic compression (IPC) over no prophylaxis (Grade II C). (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. Early ambulation is recommended. (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 as the primary VTE prevention method (Grade II C) and that venous compression ultrasonography should not be

executed (Grade II C)(28-30).

VTE Prophylaxis should be started either preoperatively or promptly postoperatively, and continued at least until the patient is fully ambulatory based on FDA approved labeling. VTE prevention was summarized in Table 6.

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