Dear Colleagues,

In this EMCREG-International Newsletter, Dr. Charles Cairns, Associate Professor of Surgery and Medicine and Associate Chief of Emergency Medicine at the Duke University School of Medicine discusses the important disease process venous thromboembolism (VTE) which includes deep venous thrombosis and pulmonary embolism. For the practicing emergency physician, VTE represents a common, life-threatening presentation to the emergency department (ED) with major challenges including early diagnosis and appropriate treatment. For patients with possible VTE, diagnosis often requires multiple testing modalities such as D-dimer biomarker testing, venous ultrasonography, Computer Tomographic angiography and ventilation/perfusion imaging using radionuclides. Clinical probability assessment tools have also been developed to enhance the clinician’s likelihood for diagnosing VTE. The complex interaction of pre-test likelihood for having VTE with positive and negative testing is well described to aid the reader in understanding the sometimes complex interaction of these diagnostic aids in the real clinical setting of the ED.

Similarly, the treatment of VTE is described detailing the use of anti-thrombotic agents such as heparin and low molecular weight heparin. For deep venous thrombosis and pulmonary embolism, low molecular weight heparin has proved to be safer and more effective than unfractionated heparin. Other anti-thrombin agents such as pentasaccharides have also been used for VTE. Direct thrombin inhibitors are indicated for the treatment of heparin-induced thrombocytopenia (HIT). The treatment of deep venous thrombosis and pulmonary embolism in hospital versus as an outpatient is also discussed with the advantages and disadvantages of these treatment settings. Treatment of special populations such as patients with pregnancy and impaired renal function is described. Finally, the indication for fibrinolytic therapy in sub-massive and massive pulmonary embolism is delineated.

Through this EMCREG-International Newsletter on Deep Venous Thrombosis and Pulmonary Embolism, we hope to provide cutting edge information for the clinician caring for these acutely ill patients. We strive through EMCREG-International Newsletters to continue to provide concise and practical approaches for you to give outstanding care for your patients.

Sincerely,

W. Brian Gibler, MD
President,
EMCREG-International

Andra L. Blomkalns, MD
Director of CME,
EMCREG-International

Objectives

1. To describe the diagnostic approach to developing a clinical probability score for acute venous thromboembolism.
2. To discuss the latest clinical practice guidelines on the treatment of acute venous thromboembolism.
3. To describe the sites of action of anticoagulation medications.
4. To describe the management approach to potential massive pulmonary embolism in the emergency department.

Introduction

Venous thromboembolism (VTE) is a clinical entity which includes deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE is a common medical condition affecting up to 117 patients per 100,000 population annually. The diagnosis of VTE is often difficult and frequently missed. Mortality in untreated PE is approximately 30%, but with adequate anticoagulant treatment, this can be reduced to 2–8%. The purpose of this Newsletter is to focus on the diagnosis and treatment of VTE, including PE and DVT in the emergency department (ED).

Diagnosis of Venous Thromboembolism

The approach to the diagnosis of DVT and PE is ultimately dependent upon the clinical suspicion of VTE. Specifically, the choice of diagnostic tests depends on the clinical probability of PE, condition of the patient, availability of diagnostic tests, risks of iodinated contrast material, radiation exposure, and cost. Recently, diagnostic recommendations based upon the results of the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) II trial and other studies have been published. These recommendations include both evidence-based recommendations and information related to radiation exposure, costs, and studies of the positive predictive values of clinical probability assessments.

Peer Reviewer for Industry Bias: Douglas M. Char, MD, Associate Professor and Residency Program Director, Department of Emergency Medicine, Director, Emergency Cardiac Evaluation Unit, Washington University, St. Louis, MO
Clinical Probability Assessment

The first step in approaching a patient with suspected VTE is to assess the probability of the presence of venous clots as low, moderate or high. This assessment should be made prior to any imaging tests and preferably using an objective method. While physicians experienced with PE management have shown similar results with either empirical assessment or clinical probability assessment scoring indexes, clinical probability assessment scoring indexes may be better for physicians who are less experienced with the assessment of PE.

A number of clinical probability assessment tools for PE have been developed, but two of the best studied are relatively simple rules that provide dichotomous risk of either PE “likely or not” (Wells criteria, Table 1) or whether the risk of PE is “safe or not” (Charlotte rule, Figure 1). If the patient is deemed either “unlikely” or “safe”, then the patient is considered to have a low or moderate clinical probability of PE. Conversely, if the patient is deemed “likely” or “unsafe,” then the patient should be considered to have a high clinical probability of PE.

In addition, there is a similar clinical probability rule developed by Wells for the evaluation of DVT (Table 2). In outcome studies of untreated patients with normal CT angiography results and clinical assessment findings that ranged from low probability to “likely,” 1.5% of patients had VTE at 3-month follow-up. In the PIOPED II trial, if CT angiography results were negative, PE was present in 4% of patients with low probability clinical assessment. If both the CT angiogram and CT venogram were negative, PE was present in 8% of patients with moderate clinical probability assessment.

CT Imaging of Low Probability Patients with Abnormal D-dimer Results

An abnormal D-dimer indicates the need for further testing if PE is suspected. Popular imaging options include contrast-enhanced multidetector computerized tomography pulmonary angiography (CT angiography) and CT venous phase imaging of the proximal leg veins (CT venography).

The PIOPED investigators have recommended that no further testing be done if the D-dimer is normal in patients with both low and moderate probability clinical assessment (Figure 2). No further testing is required if the D-dimer is normal in a patient with a low probability clinical assessment.

The quantitative rapid ELISA, with a sensitivity of 95%, in general has shown the most clinically useful values among the various D-dimer assays. The post-test probability of PE ranges from 0.7% to 2% with a normal D-dimer rapid ELISA result and objective low probability clinical assessment for VTE. Thus, no further testing is required if the D-dimer is normal in a patient with a low probability clinical assessment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs and symptoms of deep vein thrombosis (minimum of leg swelling and pain with palpation of the deep veins)</td>
<td>3.0</td>
</tr>
<tr>
<td>Alternative diagnosis less likely than pulmonary embolism</td>
<td>3.0</td>
</tr>
<tr>
<td>Heart rate &gt; 100/min</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization (&gt;3 d) or surgery in the previous 4 weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous pulmonary embolism or deep vein thrombosis</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy (receiving treatment, treated in the last 6 months or palliative)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

≤ 4 points: Clinical probability of pulmonary embolism unlikely
> 4 points: Clinical probability of pulmonary embolism likely

**Figure 1:** Charlotte Criteria for “Safe” D-dimer Testing in ED Patients with Suspected PE. Adapted with permission from Kline, et al, Ann Emerg Med 2002;39:144-52.

**Figure 2:** Use of Quantitative D-dimer Testing in combination with clinical assessment. Adapted with permission from Stein, Radiology 2007;242:15-21.

**Table 2. Wells Criteria for Deep Venous Thrombosis**

<table>
<thead>
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<th>Variable</th>
<th>Points</th>
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<tr>
<td>Cancer (receiving treatment, treated in the past six months, or palliative care)</td>
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</tr>
<tr>
<td>Paralysis, paresis, or recent plaster immobilization of the lower extremities</td>
<td>1</td>
</tr>
<tr>
<td>Recently bedridden for three days or more, or major surgery within the previous 12 weeks requiring general or regional anesthesia</td>
<td>1</td>
</tr>
<tr>
<td>Localized tenderness along the distribution of the deep venous system</td>
<td>1</td>
</tr>
<tr>
<td>Entire leg swollen</td>
<td>1</td>
</tr>
<tr>
<td>Calf swelling at least 3 cm larger than that on the asymptomatic side (measured 10 cm below tibial tuberosity)</td>
<td>1</td>
</tr>
<tr>
<td>Pitting edema confined to the symptomatic leg</td>
<td>1</td>
</tr>
<tr>
<td>Collateral superficial veins (non-varicose)</td>
<td>1</td>
</tr>
<tr>
<td>Previously documented DVT</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis at least as likely as DVT</td>
<td>-2</td>
</tr>
</tbody>
</table>

≤ 1 points: Clinical probability of DVT unlikely  
> 1 points: Clinical probability of DVT likely

Adapted with permission from Wells, et al, N Engl J Med 2003; 349:1227-35
The specificity of positive findings demonstrated on CT angiography can be related to the location of the pulmonary artery involved. In the PIOPED II study, if CT angiography results were positive in a patient with a low probability clinical assessment, PE was present in 58%.[3,4] However, if CT angiography showed PE in a main or lobar pulmonary artery, PE was present in 97%.[3,4] If the largest vessel showing PE was in a segmental branch, PE was present in 68% of patients, and if the largest vessel showing PE was in a subsegmental branch, PE was present in 25% of patients.[3,4]

The recommendations of the PIOPED investigators are that treatment is indicated in all patients with main or lobar pulmonary emboli on CT angiography. In low probability patients with segmental or subsegmental pulmonary emboli, the certainty of the CT diagnosis should be reassessed. Additional imaging options in these patients include venous ultrasound (either single or serial), MRI venography and pulmonary digital subtraction angiography.[3,4] Treatment with anticoagulants while awaiting the outcome of further diagnostic tests may be appropriate, particularly if the tests cannot be performed immediately.[14]

### Approach to Patients with a High Clinical Probability of VTE

#### D-dimer testing

A D-dimer test is not helpful because a negative D-dimer result does not exclude PE in more than 15% of patients with a high probability clinical assessment.[13]

#### CT Imaging

If results of CT angiography were positive in a patient with a high probability clinical assessment, PE was present in 96% in the PIOPED II study.[3,4] If CT angiography results were negative in a patient with a high probability assessment, PE was present in 40% of patients. If both CT angiography and venography results were negative, PE was present in only 18%.[3,4]

#### Alternative Diagnostic Pathways for VTE

##### Ventilation-Perfusion Scanning

Ventilation-perfusion (VQ) lung scans can be considered for further testing of PE. A perfusion lung scan alone can be considered in patients with normal or nearly normal chest radiographs.[15] The proportion of patients with nondiagnostic pulmonary VQ scans is lower in patients with normal versus abnormal chest radiographs.[15,16]

A low probability VQ scan result combined with a low probability clinical assessment showed PE in only 4% of patients in the PIOPED study.[9] A high probability VQ scan result combined with a high probability clinical assessment showed PE in 96% of patients.[3,9] With other combinations of clinical and VQ probabilities, PE was present in 16%–88% of patients and further evaluation was required. These other modalities included serial venous ultrasound examinations, CT angiography, or gadolinium-enhanced magnetic resonance imaging.[3]

Additional considerations for primary VQ scanning would include reduced radiation exposure compared to CT angiography. While female breast radiation is a concern, the risk of death from undiagnosed PE far exceeds the risk of radiation-induced malignancy.[3] In a recent survey, most (69%) of PIOPED II investigators still recommend CT angiography as the primary imaging modality in women of reproductive age, while pulmonary VQ scans are recommended as primary imaging by only 31% of the PIOPED II investigators.[3]

The absorbed dose to the breast with CT angiography has been calculated as 10–50 mGy.[3] The absorbed dose to the breast with a perfusion lung scan has been estimated to be 0.28 mGy. The absorbed dose to the breast with standard two-view mammography is 3 mGy. In the PIOPED study, a VQ scan in patients with a normal...
chest radiograph was diagnostic (high probability or normal/nearly normal) in 52% of patients suspected of having PE. More recently, a VQ scan was shown to be diagnostic in 91% of patients suspected of having PE with a normal chest radiograph.

**Venous Ultrasound**

Venous ultrasound detects DVT in 13%–15% of patients suspected of having PE and in 29% of patients with proved PE. Thus, a venous ultrasound examination prior to imaging with CT angiography or CT angiography and venography is optional and may guide treatment if results are positive.

**Recommendations for Imaging Patients with Allergy to Iodinated Contrast Material**

Beyond D-dimer testing and clinical assessment, patients with mild iodine allergies may be treated with steroids prior to CT imaging. In patients with severe iodine allergy, venous ultrasound and VQ scans are recommended as alternative diagnostic tests. Other recently described approaches include CT angiography enhanced with 0.3–0.4 mmol gadolinium per kilogram of body weight and gadolinium-enhanced MR imaging.

**TREATMENT OF VENOUS THROMBOEMBOLISM**

Hemostasis and coagulation involves a sequence of interactions of coagulation factor interactions in two pathways called the intrinsic and extrinsic coagulation cascades (Figure 3). The final common pathway involves the transformation of prothrombin to thrombin by factor Xa. Thrombin (factor IIa) then serves to catalyze the activation of fibrinogen to fibrin, in addition to its role in feedback activation of several other clotting factors. Unfractionated heparin (UFH), low molecular weight heparin (LMWH) and the pentasaccharide fondaparinux all exert their anticoagulant effect by binding to and activating antithrombin which then neutralizes selected coagulation factors.

**Initial Management**

Prior to giving anticoagulation therapy, all patients should have baseline coagulation studies drawn including the activated partial thromboplastin time (aPTT), an international normalized ratio (INR), a complete blood count (CBC) including a platelet count, as well as a baseline renal studies (creatinine).

**Heparin – LMWH versus UFH**

**Deep Venous Thrombosis**

In the most recent American College of Physicians/American Academy of Family Physicians (ACP/AAFP) Clinical Guidelines, LMWH is preferred over UFH for the initial inpatient treatment of DVT. A recent analysis of 17 systematic reviews demonstrated that LMWH results in reduced mortality and less risk for major bleeding during initial therapy. In addition, LMWH was found to result in significant cost savings compared to UFH.
Pulmonary Embolism

Systematic reviews of existing trials indicate that LMWH is at least as effective as UFH for the initial treatment of patients with PE. For acute VTE treatment, limitations of UFH include an unpredictable anticoagulant response with the need for frequent monitoring, a relatively narrow therapeutic window, and the potential for severe toxicity, especially heparin-induced thrombocytopenia (HIT) in ≤3% of patients. Importantly, trials of UFH in PE show that many patients are subtherapeutic or supratherapeutic while receiving UFH. In contrast, LMWHs provide a more targeted approach to procoagulant complex inhibition, predictable pharmacokinetic and pharmacodynamic characteristics, and no need for anticoagulant monitoring.

Dosing considerations

Unfractionated Heparin

When UFH is used for treatment of VTE, a weight-based nomogram is the safest and most effective method to anticoagulate patients. The nomogram includes a heparin bolus of 80 units/kg IV followed by an IV heparin infusion of 18 units/kg/h. In general, the recommended range of an aPTT for therapeutic heparin levels is 1.5 to 2.5 times the control aPTT and assessed starting four to six hours after the initial UFH infusion. Reagents used in individual hospital laboratories have different sensitivities to heparin, and must be calibrated based on therapeutic heparin levels to a reagent-specific range for aPTT. Thus, laboratories using different reagents have different therapeutic aPTT ranges, and heparin should be dosed according to the hospital’s reagent-specific range.

Low-Molecular-Weight Heparin

The three LMWH preparations currently approved for use in the United States are enoxaparin, dalteparin, and tinzaparin. They are all administered subcutaneously at intervals of either once or twice daily for both prophylaxis and treatment doses. There was no increase in bleeding in once-daily versus twice-daily dosing of LMWH. Because LMWHs have more predictable pharmacokinetics than UFH, routine coagulation monitoring is not performed.

Because LMWHs are excreted by the kidneys, caution must be used when administering LMWHs for treatment of VTE in patients who have a creatinine clearance of less than 30 mL/min. Enoxaparin can still be used in patients with renal failure, but at a reduced dose of 1 mg/kg SC once daily. Another group of patients for whom LMWH dosing is unclear is obese patients with weights over 150 kg. In obese patients with body mass index greater than 30, there is evidence that once-daily enoxaparin (1.5 mg/kg) is less effective than twice daily enoxaparin (1 mg/kg).

Pentasaccharides

Fondaparinux is based on the pentasaccharide region of the heparin molecule specific for antithrombin binding. Fondaparinux selectively inhibits factor Xa by binding to antithrombin. Because fondaparinux lacks the longer saccharide chains that bind to thrombin, it has no ability to neutralize thrombin and is entirely specific for factor Xa.

Fondaparinux is at least as effective as enoxaparin 1 mg/kg twice daily for the initial treatment of acute DVT and as effective as UFH for the initial treatment of acute, nonmassive PE, without increased risk for major bleeding. As with LMWHs, fondaparinux on an outpatient basis is safe and effective. Fondaparinux exhibits 100% bioavailability and has a long half-life (~17-20 h) and little interpatient variability, allowing for once-daily dosing without dose adjustment or monitoring. The dosing of fondaparinux is weight-dependent: 5.0 mg once daily for <50 kg, 7.5 for 50-100 kg, or 10.0 mg for >100 kg. Importantly, fondaparinux is contraindicated in patients with severe renal impairment (creatinine clearance <30 mL/min).

Direct Thrombin Inhibitors

The direct thrombin inhibitors lepirudin and argatroban are indicated for acute VTE treatment in the setting of HIT. Because these drugs have no structural similarity to heparin, they do not cross-react with heparin-induced antibodies. These therapies significantly reduce the incidence of new thrombosis and death related to thrombosis without increasing major bleeding in patients with HIT. The broader use of these agents in VTE patients is limited by their high drug-acquisition costs and the need for frequent monitoring.
Inpatient vs. Outpatient Treatment of VTE

Deep Venous Thrombosis

A recent systematic review of VTE trials that compared inpatient and outpatient treatment for VTE concluded that the rates of recurrent DVT, major bleeding, and death during follow-up were similar for inpatient and outpatient treatment strategies.22

Across all groups, the percentages of patients having recurrent DVT ranged from 0% to 9%, with minimal differences according to treatment. Pulmonary embolism rarely occurred in any group in any study. The incidence of major bleeding ranged from 0% to 4%, and the percentage of patients dying during follow-up ranged from 0% to 18%, with minimal differences between inpatient and outpatient treatment groups.22 In addition, there appeared to be significant cost savings with outpatient treatment.21,22

All of these studies were conducted among highly selected groups of patients and in clinical systems with the required support services in place. Most of these studies, however, excluded patients with concomitant PE, previous VTE, thrombophilic conditions or significant comorbid illnesses, pregnant patients, and those deemed unlikely to adhere to outpatient therapy.22

Pulmonary Embolus

There is little evidence regarding the outpatient treatment of PE. The one cohort study that exclusively enrolled patients with PE found no significant difference in event rates.22 All these studies, however, may have been underpowered to detect a difference in event rates between inpatient and outpatient strategies.22

Thus, the consideration of outpatient treatment of DVT patients in the ED must account for the possibility of concomitant PE as well as those exclusion factors listed above. In addition, several of these studies allowed a brief inpatient admission for stabilization of the patients before randomization to the outpatient group.22

Longer-term Management of VTE Beyond the ED

Compression Stockings

The ACP/AAFP recommend that compression stockings should be used routinely to prevent post-thrombotic syndrome, beginning within 1 month of diagnosis of proximal DVT and continuing for a minimum of 1 year after diagnosis.21 There was a marked reduction in the incidence and severity of post-thrombotic syndrome among patients wearing compression stockings if use was initiated within 1 month of diagnosis of proximal DVT.22

Duration and Type of Anticoagulation

The ACP/AAFP guidelines recommend anticoagulation should be maintained for 3 to 6 months for VTE secondary to transient risk factors, and for more than 12 months (up to 4 years) for recurrent VTE. Conventional intensity therapy (INR 2.0 – 2.8) is optimal. LMWH is safe and efficacious for the long-term treatment of VTE in selected patients, and may be preferable for patients with cancer.21

Vena Cava Filters

In a single randomized study, filter placement with anticoagulation was associated with a slight reduction in symptomatic PE compared with anticoagulation alone. However, filters were associated with a significant increase in recurrent DVT compared with anticoagulation alone.22

In an observational cohort study, filter placement did not reduce PE but was associated with a 2-fold increase in the relative hazard of subsequent DVT among patients with initial PE.22

SPECIAL PATIENT POPULATIONS

Patients with Impaired Renal Function

If the creatinine clearance is moderately elevated, the decision to proceed with CT imaging depends on clinical judgment.3 Nonionic contrast material may be less nephrotoxic than ionic contrast material.3 Prophylactic hydration with sodium bicarbonate before contrast material exposure reduces the risks of renal dysfunction in patients with renal insufficiency.25 Administering an isotonic solution of sodium bicarbonate 3 mL/kg/h for 1 hour before and 1 mL/kg/h for 6 hours after the infusion of contrast material has been recommended.25

Alternative pathways to CT scanning in patients with renal insufficiency include D-dimer testing with clinical assessment, venous ultrasound, and VQ scans.3
Treatment Implications

Because LMWHs and fondaparinux are eliminated primarily via the kidneys, their half-lives are prolonged in patients with renal impairment. Reduced creatinine clearance may result in drug accumulation, potentially increasing bleeding risk and other adverse events. Fondaparinux is contraindicated in patients with creatinine clearance less than 30 mL/min. A dose decrease of enoxaparin to 1 mg/kg given every 24 hours is recommended for these patients with severe renal insufficiency.24

Pregnant Patients

Pregnant women have a 5-fold increased risk for VTE compared with nonpregnant women.21 D-dimer testing with clinical assessment should still be performed in pregnant women even though results may be inherently positive due to pregnancy.26 If D-dimer results are positive, venous ultrasound is recommended before imaging tests with ionizing radiation are performed.3 If radiographic imaging is necessary, there is controversy on whether pulmonary VQ scans or CT angiography is preferred. Studies suggest that the radiation dose to the fetus from 16-slice CT angiography is the same or less magnitude than that from a pulmonary VQ scan or pulmonary perfusion scan alone.6,27 Yet most (69%) PIOPED II investigators recommend pulmonary VQ scans with 31% recommending CT angiography as the radiographic imaging modality of choice in pregnant women.3 Vitamin K antagonists, such as warfarin, should be avoided in pregnant patients because these drugs cross the placenta and are associated with embryopathy during development and fetal bleeding at delivery.21 LMWH and UFH would be alternatives given that neither LMWH nor unfractionated heparin crosses the placenta, and neither is associated with impaired embryonic development or fetal bleeding.21

Unfortunately, there are few data on the use of either LMWH or UFH to treat VTE in pregnant patients. While LMWH as a prophylactic therapy for pregnant women has been extensively studied, fewer than 200 pregnant women have been treated with LMWH in observational studies of treatment of DVT or PE.22 There has been a case series describing the use of vena cava filters for VTE in 18 pregnant patients, but any comparisons to heparin therapy are challenging.22

Suspected massive PE

Suspected massive PE, which could occur in a patient presenting with shock, or hypotension, represents a distinct clinical problem. The clinical suspicion for PE is usually high, and the differential diagnosis includes cardiogenic shock, tamponade and aortic dissection. The most useful initial test in this setting is echocardiography, which will usually show indirect signs of acute pulmonary hypertension and right ventricular overload if acute PE is the cause of the hemodynamic consequences.2 A positive venous ultrasound result in the appropriate clinical setting could also indicate PE.3

The sensitivity of transthoracic echocardiography for right ventricular enlargement or dysfunction in 33 patients with massive PE or unstable patients was 100%.3,28 If any two of three assessments (high clinical probability, echocardiography, ultrasound) are positive, the sensitivity for massive PE is 97% with a negative predictive value of 98%.29

In a highly unstable patient, fibrinolytic treatment or even surgery for PE may be initiated based on compatible echocardiographic findings alone.3 If the patient is stabilized by supportive treatment, a definite diagnosis should be sought.

The European Society of Cardiology approach to the management of suspected massive PE, including hemodynamic support is highlighted in Table 3.

Fibrinolytic Therapy for Massive PE

The increase in right ventricular (RV) afterload observed in patients with massive PE may induce RV failure, systemic hypotension and shock.2,30 In patients with pulmonary hypertension and low cardiac output due to PE, fibrinolytic therapy induces a 30% reduction in mean pulmonary arterial pressure (PAP) and a 15% increase in cardiac index within two hours of treatment. In addition, fibrinolytic therapy can cause a significant reduction in mean RV end-diastolic area within 3 hours.2,30 In contrast, heparin alone did not produce any change in cardiac index, PAP or echocardiographic findings at 2 or at 72 h after the beginning of therapy.2

There appears to be a survival benefit from fibrinolytic therapy in patients with massive PE, such as those with shock and/or hypotension, defined as a systolic blood pressure <90 mmHg or a pressure drop of > 40 mmHg for >15 min if not caused by new-onset arrhythmia, hypovolemia or sepsis.2 Several contraindications exist for fibrinolytic therapy in an unstable patient with a massive PE, most of these are considered only relative contraindications.2
Pulmonary Embolism and Deep Venous Thrombosis: Evaluation and Treatment in the Emergency Department

**Table 3. Emergency Management of Suspected Massive Pulmonary Embolus**

Dobutamine and dopamine may be used in patients with PE, low cardiac index and normal blood pressure.

Vasopressive drugs may be used in hypotensive patients with PE.

Monitored oxygen therapy is beneficial in patients with PE and hypoxemia.

The usefulness of fluid challenge is controversial and should not exceed 500 ml.

Fibrinolytic therapy is indicated in patients with massive PE, as shown by shock and/or hypotension.

Most contraindications for fibrinolytic therapy in massive PE are relative.

Fibrinolytic therapy should be based on objective diagnostic tests, including echocardiography.

The use of fibrinolytic therapy in patients with sub-massive PE (isolated RV hypokinesia) is controversial.

Fibrinolytic therapy is not indicated in patients without right ventricular overload.

Acute pulmonary thrombectomy has a limited role in massive, life-threatening PE.

Adapted with permission from the European Society of Cardiology Task Force Guidelines on diagnosis and management of acute pulmonary embolism. Eur Heart J. 2000;21:1301-36

**REFERENCES**


There appears to be a survival benefit from fibrinolytic therapy in patients with massive PE, such as those with shock and/or hypotension defined as a systolic blood pressure <90 mmHg or a pressure drop of > 40 mmHg for >15 min if not caused by new-onset arrhythmia, hypovolemia or sepsis.


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CME Post Test

After you have read the monograph carefully, record your answers by circling the appropriate letter answer for each question.

1. The mortality rate in untreated pulmonary embolism is approximately:
   a. 5%
   b. 10%
   c. 30%
   d. 50%

2. The primary consideration in the assessment of a patient with suspected venous thromboembolism is:
   a. Cost of diagnostic procedures
   b. Risks of ionizing radiation
   c. Clinical probability of pulmonary embolism
   d. Chest x-ray appearance

3. Fondaparinux selectively inhibits which coagulation factor:
   a. Factor XII
   b. Factor Xa
   c. Factor IX
   d. Factor IIa

4. The appropriate dose of enoxaparin in patients with severe renal insufficiency (creatinine clearance < 30 mL/min) is:
   a. 1 mg/kg SC twice a day
   b. 1 mg/kg SC once a day
   c. 30 mg SC once a day
   d. 40 mg SC once a day

5. Which of the following radiological studies results in the highest radiation exposure to the developing fetus:
   a. CT angiography
   b. CT venography
   c. Ventilation/perfusion scan
   d. Perfusion scan

CME EXPIRATION DATE: July 1, 2008

On a scale of 1 to 5, with 1 being highly satisfied and 5 being highly dissatisfied, please rate this program with respect to:

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What topics would be of interest to you for future CME programs?

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Pulmonary Embolism and Deep Venous Thrombosis: Evaluation and Treatment in the Emergency Department

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