Thromboembolic Events

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1 Introduction

Venous thromboembolic (VTE) disease is the most feared complication of hospitalizations and is associated with a high degree of morbidity and mortality. Venous thromboembolism (VTE) is the third leading cardiovascular diagnosis after a heart attack and stroke. VTE refers to the interrelated diagnoses of deep vein thrombosis (DVT) and pulmonary embolism (PE).

2 Etiology

The predisposition to thromboembolic disease is multifactorial. Individual patient factors, current disease state, recent surgical procedures, and underlying hematologic disorders all add up to give a patient's risk of VTE at that particular time.

- Patient-related factors include age over 40 years, obesity, the presence of varicose veins, and immobility.
- The use of oral-contraceptive medications and smoking increases the risk of VTE, as well.
- Disease states generally known for increasing risk for VTE are malignancies, spinal cord injuries with paralysis, and nephrotic syndrome.
- The presence of pelvic, hip, or long-bone fractures, along with orthopedic surgeries involving the hip and knee, all increase the risk of VTE as well.

- Hematologic disorders that lead to hypercoagulability include activated protein C resistance (factor V Leiden mutation), protein C or protein S deficiency, antithrombin III deficiency, presence of lupus anticoagulant, dysfibrinogenemia, prothrombin mutation, polycythemia vera, and paroxysmal nocturnal hemoglobinuria. The physiologic state of pregnancy also confers a higher risk of VTE.

Multiple risk assessment models have now been developed to identify those at the highest risk of hospital-acquired VTE and to provide appropriate thromboprophylaxis for these patients.

3 Pathophysiology

According to **Virchow's triad**, the following are the main pathophysiological mechanisms involved in VTE:

- Damage to the vessel wall
- Blood flow abnormalities (either turbulence or **stasis**)
- Hypercoagulability

Venous thrombosis refers to the formation of a platelet and fibrin clot within the vascular lumen. Clinically significant thrombi are formed in vessels with large lumens, such as the deep veins of the legs, pelvis, and arms (deep vein thrombosis or DVT). The clot can then propagate with proximal extension. Clinical symptoms of the thrombus are seen when the clot propagates enough to have obstruction of vascular flow. If the clot dislodges, it can then embolize to a distant site. The most common site of embolization for these clots is in the pulmonary vasculature (pulmonary embolism of PE). Obstruction to pulmonary vascular flow can cause impaired gas-exchange, alveolar edema, or even pulmonary alveolar necrosis. Chronic repetitive pulmonary embolization can lead to increased pulmonary vascular resistance and, eventually, pulmonary hypertension.

4 Clinical presentation

The clinical presentation of acute **lower extremity DVT** varies with the anatomic distribution, extent, and degree of occlusion of the thrombus. Symptoms may range from no symptom at all to massive swelling and cyanosis of the limb. When present, signs and symptoms of acute lower extremity DVT may include pain, edema, erythema, tenderness, fever, prominent superficial veins, and peripheral cyanosis:

- Pain
- Redness
- Swelling
- Limb edema may be unilateral or bilateral if the thrombus extends to pelvic veins.
- Red and hot skin with dilated veins
- Tenderness

With **pulmonary embolism (PE)**, the most common presenting complaint is sudden dyspnea (that is sudden in onset). Patients may also have pleuritic chest pain, dry cough, and hemoptysis. Massive pulmonary embolism presents with syncope and signs of hemodynamic compromise such as hypotension and shock. Physical examination may reveal hypoxia, tachycardia, and fever. The most common symptoms of PE include the following:

- dyspnea
- pleuritic chest pain
- cough
- hemoptysis
- presyncope, or syncope.

5 Evaluation and diagnosis

Due to the poor sensitivity and specificity of clinical signs and symptoms for DVT and PE, clinical decision-making tools have been developed to identify those with a high pretest probability of VTE; this is possible using the Modified Well's criteria. The patient suspected of having venous thromboembolism is given points for the presence of predisposing criteria. This criteria gives us the probability to have a thromboembolic event. A medium or high chance will require definitive testing for VTE:

- Limb doppler-echography for DVT
- CT with intravenous contrast (or computed tomography pulmonary angiography)

The use of additional studies can help us to evaluate the severity of the VTE:

- Laboratory tests (such as arterial blood gas, troponin level, and serum brain-natriuretic peptide, D-dimer)
- Chest X-ray
- Electrocardiogram
- Echocardiography

6 Treatment and Management

Anticoagulation remains the primary treatment for VTE (DVT and PE). It is based on:

1. parenteral **heparin** therapy for at least 5 to 7 days
2. traditional **vitamin K antagonists** (warfarin, acenocumarol)
3. **direct-acting oral anticoagulants**, such as apixaban, dabigatran, edoxaban, and rivaroxaban

Thrombolytic therapy and intravenous filter placement are options reserved for specialized cases.

7 Prognosis and complications

Long term complications of adequately treated VTE are few. The most commonly reported long-term complication is **post-thrombotic syndrome** in patients diagnosed with DVT, which characteristically presents as pain and swelling of the limb with chronic venous insufficiency.

Longterm sequelae of recurrent PE include **pulmonary hypertension** and **cor pulmonale**, since pulmonary embolization can lead to increased pulmonary vascular resistance and, eventually, pulmonary hypertension.

There are also complications of the treatment of VTE:

- Bleeding. Patients with advanced age and underlying hepatic or renal dysfunction are at a higher risk of bleeding.
- Immune-mediated heparin-induced thrombocytopenia.
- Heparin induced osteopenia
- Warfarin-induced skin necrosis