Vascular Interventions for VTE Prophylaxis and Treatment

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Background

- In 2012, the Centers for Disease Control reported the rate of venous thromboembolism (VTE) in the United States as 0.1% to 0.2%.
    - Trauma patients are known to be among those at highest risk for VTE
- Trauma induces changes in the coagulation cascade due to stasis, vessel wall dysfunction, and alterations in the clotting mechanism (Virchow's triad), placing trauma patients at high risk for VTE.
    - Injured patients are often immobilized after high-energy trauma, causing venous stasis.
    - Endothelial damage caused by direct trauma to the vessels causes exposition of tissue factor bearing cells, propagating the coagulation cascade
- The reported incidence of VTE after trauma varies from 7 to 58% depending on patient demographics, nature of injuries, the method of detection, and type of VTE prophylaxis (if any) used.
    - The pooled estimate for DVT after injury is 11.8% and for PE is 1.5% .
    - The incidence of PE has increased more than 2-fold from 1994 to 2009 for trauma patients, although this increase may be related either to increased screening or to the increased sensitivity of cross-sectional imaging.
    - Without adequate thromboprophylaxis, the risk of developing DVT after trauma exceeds 50% with an ISS $\geq$ 9.
- Risk factors for increased DVT in the trauma population include increasing age, the presence of pelvic, spine, and long bone fractures, spinal cord injury, brain injury, venous injury, prolonged immobility, long duration of hospital stay, ventilator days > 3, blood transfusion, severity of trauma, and major surgical procedure.
- The mortality from VTE after trauma is as high as 50%.
    - PE is among the leading causes of death of trauma patients who survive beyond the first day of hospitalization.

Clinical Presentation

- Diagnosis of DVT and PE necessitates a high index of suspicion because clinical signs lack sensitivity and specificity.
- 50% of patients do not present with any symptoms.
- DVT of the lower extremities normally start in the calf veins. About 10-20% of thromboses extend proximally, and a further 1-5% go on to develop a fatal PE.
- Leg swelling is the most frequent symptom of DVT. Other symptoms include pain, tenderness, erythema, and pitting edema of the affected limb.
- Individual signs and symptoms are of little value, and Homan's sign (pain in the calf with active dorsiflexion of the foot) has low sensitivity and specificity in the diagnosis of DVT.
- PE presents with a variety of non-specific symptoms:
    - The most common clinical symptom is sudden onset dyspnea.

- Other symptoms include tachypnea, tachycardia, pleuritic or substernal chest pain, hemoptysis, and syncope.
- PE can present as sudden death.
- Most patients who die of PEs do so within 30 minutes of the acute event.
- Asymptomatic PE occur in 24% of moderately to severely injured patients.

Evaluation/Diagnostics/Imaging

- Early identification of DVT in trauma patients allows treatment to be initiated and decreases the frequency of complications.
- Scoring systems designed to identify risk factors for DVT development in non-trauma patients, such as the Wells scoring system, have limited utility in trauma patients.
- Venography is the gold standard for the diagnosis of DVT in trauma patients, but it is time-consuming, invasive, and has inherent risks and complications.
- Duplex ultrasound is the preferred diagnostic modality for DVT:
  - noninvasive
  - no contrast medium
  - performed at the bedside
  - ability to detect nonocclusive thrombus
- Venography may be used as a confirmatory study in those trauma patients who have an equivocal duplex ultrasound examination for DVT
- Pulmonary angiography is the gold standard investigation for PE.
  - Other less invasive modalities include CTPE and V-Q scanning.
  - CTPE is the preferred diagnostic modality for PE given the invasiveness of angiography.
  - CTPE is limited in individuals with impaired renal function or a severe allergy to contrast material.
  - V-Q scanning is limited in those with COPD, pneumonia, pulmonary edema, or other underlying pulmonary disease.
  - V-Q scanning can be considered in those without underlying pulmonary disease and in which administration of contrast material is contraindicated.

Screening for VTE in Trauma Patients

- There is controversy on the implementation of duplex ultrasound as a screening method for DVT in the trauma population.
  - Based on current evidence, routine screening of all trauma admissions is not recommended.
  - Serial duplex ultrasound imaging of *high-risk* asymptomatic trauma patients to screen for DVT may be cost-effective and may decrease the incidence of PE.

- The rationale for surveillance screening duplexes is that the increased detection of DVT allows patients to receive early management of thrombotic disease and subsequently lower rates of PE.
    - There is no consensus as to what defines a patient as high-risk, but the current data show that detection of DVT in asymptomatic high-risk patients is feasible and might lead to reduced rates of PE.
    - High-risk patients include those with a Greenfield's Risk Assessment Profile (RAP) score > 10.
        - http://www.medicalalgorithms.com/risk-assessment-profile-rap-of-greenfield-et-al-for-venous-thromboembolism-in-adult-trauma-patients
    - Other risk factors that may justify screening include prolonged bed rest, GCS ≤ 7, spinal injury, lower extremity or pelvic fracture, ICU LOS > 4 days, age > 65 years, and delayed initiation of chemoprophylaxis.

Prophylaxis for VTE in the Trauma Patient

- VTE prophylaxis in trauma patients is a complex problem for three primary reasons: many are at very high risk for VTE, many have a high bleeding risk precluding the use of anticoagulant prophylaxis in the short term, and many have multiple dressings and orthopedic fixation devices precluding the use of sequential compression devices (SCDs).

Mechanical Prophylaxis

- External compression devices function by reducing the luminal diameter of a vein resulting in an increase in venous flow velocity, and they are commonly utilized in trauma setting because of ease of use and inherently low risk of associated bleeding.
- In a number of prospective randomized studies, pneumatic compression devices (PCDs) have been shown to reduce the incidence of both DVT and PE.
- But in a meta-analysis of pooled studies on the benefit of PCDs in trauma patients, no benefit of the use of PCDs over no prophylaxis was reported.
    - In the subset of head-injured patients, PCDs may have some benefit in isolated studies.
    - Variations in efficacy are likely related to poor compliance with the use of PCDs (30% in some studies)
- Mechanical VTE prophylaxis by graduated compression stockings or intermittent pneumatic compression provides suboptimal protection, and its use is recommended only in combination with LMWH prophylaxis or when anticoagulant DVT prophylaxis is contraindicated.

Pharmacologic Prophylaxis

- The risk of a PE after traumatic injury is highest during the first week of hospitalization and 37% to 50% of PE's are diagnosed early (<=4–7 days after injury). DVTs may also lead to chronic venous insufficiency and therefore preventing DVTs is important to prevent both short term and long term complications.
    - Thromboelastogram (TEG) evaluation has shown that a quarter of trauma patients present in a hypercoagulable state, even in the setting of a normal admission coagulation profile (INR and PTT), and that hypercoagulability after injury is most prevalent during the first 24-48 hours.
    - Therefore, it is imperative to begin pharmacologic prophylaxis in trauma patients within 24–48 hours after hospital admission and as soon as the risk of DVT/PE outweighs the risk of bleeding based on clinician judgment.
- Trauma patients with an ISS > 9, who can receive anticoagulants should receive LMWH (enoxaparin 30mg every 12 hours) as their primary mode of VTE prophylaxis.
    - A regimen of UFH every 8 hours *may be* noninferior to enoxaparin for the prevention of VTE following trauma.
- Use of chemoprophylaxis in TBI 24 hours after stable head CT is safe and decreases the rate of DVT formation.
- According to the American Society of Regional Anesthesia and Pain Medicine (ASRA), LMWH should not be used when epidural catheters are placed or removed.
    - In the setting of an epidural catheter, UFH (SC heparin 5000 units BID or TID) for DVT prophylaxis is recommended.

Prophylactic Vena Cava Filters

- Indications for prophylactic placement of an IVC filter are controversial.
    - A recent meta-analysis found an association between IVC filter placement and a lower incidence of PE in trauma patients, but it was not clear which patients experienced enough benefit to outweigh the risks associated with the procedure.
    - Also, high rates of prophylactic IVC filter placement have no effect on reducing trauma patient mortality and are paradoxically associated with an increase in DVT events.
- Most IVC filters are used for primary thromboprophylaxis within the first 7 to 10 days after major trauma when patients are at highest risk for bleeding
- According to the EAST clinical practice guidelines, insertion of prophylactic IVC filters should be considered in very high-risk patients:
    - who cannot receive anticoagulation because of increased risk of bleeding ***and***,
    - have an injury pattern rendering them immobilized for a prolonged period of time, including the following:

- Severe closed head injury (GCS < 8)
- Incomplete spinal cord injury with paraplegia or quadriplegia
- Complex pelvic fractures with associated long bone fractures
- Multiple lone bone fractures

Treatment of VTE in the Trauma Patient

Therapeutic Anticoagulation

- In patients with proximal DVT (thromboembolism in the popliteal, femoral, or iliac veins) or PE *and* no cancer, the American College of Chest Physicians (ACCP) recommend long-term (3 months) anticoagulant therapy with non-vitamin K antagonist oral anticoagulants (NOACs) such as dabigatran, rivaroxaban, apixaban or edoxaban over warfarin therapy.
- For those in whom NOACs are not used or is contraindicated (recent bleeding, high risk for bleeding), warfarin therapy is recommended over LMWH.

Use of Therapeutic Vena Cava Filters

- Vena cava filters are placed in patients with an acute proximal DVT or recent PE who have:
    - contraindication to receiving anticoagulation doses of heparin
    - developed a bleeding complication while on heparin
    - had a PE despite adequate anticoagulation.

Systemic Thrombolysis and Catheter-Assisted Thrombectomy

- Catheter-direct thrombolysis (CDT) or percutaneous mechanical thrombectomy (PMT) are indicated in patients with iliofemoral DVT (IFDVT) associated with limb-threatening circulatory compromise (phlegmasia cerulean dolens).
    - CDT and PMT can also be considered in patients with an IFDVT associated with rapid thrombus extension despite anticoagulation.
    - Surgical venous thrombectomy may be considered in these patients who have a contraindication to or failure of CDT or PMT.
    - Percutaneous transluminal venous angioplasty and stent placement can be used to treat venous lesions that obstruct flow in the iliac vein after preceding CDT, PMT, or surgical venous thrombectomy for acute IFDVT.
- Systemic thrombolytic therapy is recommended in patients with an acute PE with hypotension who do not have a high bleeding risk as well as patients with acute PE who deteriorate after starting anticoagulant therapy and who have a low bleeding risk.
    - EKG and bedside ECHO are adjuncts that can be used in the unstable patient to aid in diagnosis of massive or sub-massive PE.
    - S1Q3T3 (S wave in lead I, Q wave in lead III, and an inverted T wave in lead III) is an EKG findings suggestive of PE.
    - McConnell's sign is a distinct ECHO finding specific for massive PE. It is defined as a regional pattern of right ventricular dysfunction, with akinesia of the mid free wall and hypercontractility of the apical wall.

    - Other findings on ECHO that are suggestive of PE include right ventricular and atrial dilation, shifting of the interarterial septum to the left, tricuspid regurgitation, and decreased left ventricular filling.
- The recommended dose of fibrinolytic therapy is alteplase 100 mg as a continuous infusion over 2 hours through a peripheral intravenous catheter.
- Absolute contraindications to the use of thrombolytic therapy include active bleeding, bleeding diathesis, recent brain or spinal surgery within 3 months, history of intracranial hemorrhage, known intracranial neoplasm, arteriovenous malformation or aneurysm, significant head trauma, and cerebrovascular accident within 2 months.
- Relative contraindications include age greater than 75, pregnancy, current use of anticoagulation, prolonged cardiopulmonary resuscitation, recent bleeding, history or current severe uncontrolled hypertension, remote ischemic stroke with 3 months, and/or major surgery within 3 weeks.
- In patients with acute PE with hypotension and who have a) a high bleeding risk, b) failed systemic thrombolysis, or c) shock that is likely to cause death before systemic thrombolysis can take effect (e.g. within hours), catheter-assisted thrombus removal is recommended.
    - There are 3 general categories of percutaneous intervention for removing pulmonary emboli and decreasing thrombus burden: 1) Aspiration thrombectomy, 2) thrombus fragmentation, and 3) rheolytic thrombectomy.
    - The goals of catheter-based therapy include rapidly reducing pulmonary artery pressure, RV strain, and pulmonary vascular resistance, increasing systemic perfusion, and facilitating RV recovery.
- Emergency surgical embolectomy with cardiopulmonary bypass is also an effective strategy for managing patients with massive or submassive PE with RV dysfunction when contraindications preclude thrombolysis or whose condition is refractory to thrombolysis.

Suggested Readings

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