Venous Thromboembolism (VTE)
ACS Surgical Critical Care Review Course 2012

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VTE Epidemiology

- Pulmonary embolism (PE) and deep venous thrombosis (DVT)

- Affects between 600,000 and 2 million patients annually; death in 100,000 to 300,000 per year

- **PE remains the most common preventable cause of in-hospital mortality**

- **Fatal PE is the 3rd most common cause of death in trauma patients who survive the first 24 hours**
# VTE Incidence

<table>
<thead>
<tr>
<th></th>
<th>General Surgery</th>
<th>Trauma</th>
<th>Hip Fx</th>
<th>SCI</th>
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</thead>
<tbody>
<tr>
<td>Overall DVT</td>
<td>20-30%</td>
<td>58%</td>
<td>50%</td>
<td>70-90%</td>
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<tr>
<td>Proximal DVT</td>
<td>7%</td>
<td>18%</td>
<td>20%</td>
<td>15%</td>
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<tr>
<td>PE</td>
<td>0.5%-2%</td>
<td>2-22%</td>
<td>5-25%</td>
<td>5%</td>
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<tr>
<td>Fatal PE</td>
<td>0.1-0.8%</td>
<td>1%</td>
<td>4-7%</td>
<td>3-5%</td>
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*AHRQ - #1 strategy to improve patient safety in hospitals is prevention of VTE*
Diagnosis of DVT

- Compression duplex ultrasound
  - Most common method of detecting DVT
  - >90% sensitivity and specificity in detecting femoropopliteal DVT
  - 50% for calf DVT; poor visualization of pelvic veins
  - Sensitivity greater if symptomatic
    - Proximal DVT 97% vs. asymptomatic proximal 62%
    - Distal DVT 73% vs. asymptomatic distal 53%
- Indeterminant ➔ biomarkers (D-dimer); re-duplex in 24-48 hours
Which of the following EKG findings is most common in PE?

a. S1Q3T3
b. Normal sinus rhythm
c. Sinus tachycardia
d. Anterior T-wave inversion
e. Atrial fibrillation

RAS question
Diagnosis of PE

- Clinical examination
  - Dyspnea, hypoxia, hemoptysis, tachycardia, syncope, CV collapse
  - *Tachypnea most common sign*

- EKG
  - Normal, S1Q3T3, fib/flutter all uncommon as presenting sign
  - Non-specific ST or T-wave changes most common
    - *Anterior T-wave inversion most common (68%); appears early and is a marker of severity*
    - *T-waves normalize with effective thrombolysis*
Diagnosis of PE

- Contrast-enhanced spiral CT of the chest
  - Sensitivity >70%; >90% when clinical assessment and duplex added
  - Evaluate other pulmonary abnormalities as etiology
  - *Pre-test probability important*

- PIOPED II
  - 96% NPV if low pretest probability and negative CTA

- Combine with CTV of pelvis and deep thigh veins to evaluate for DVT
- Replaced V/Q (except in renal failure)
  - difficult to interpret with pre-existing lung disease
**Diagnosis of PE**

*Echo*

- Risk stratification by identifying PE and assessing cardiac function and hemodynamics
- Ideal in *hemodynamically unstable* patient
- Assess for other etiologies like MI, aortic dissection, and cardiac tamponade
- *RV dysfunction = increased mortality*

- *RV strain/dysfunction is a surrogate for PE (TTE)*
  - Associated but not specific
  - RV and PA dilatation, right-sided thrombus, hypokinesis, TR, abnormal motion of interventricular septum and bowing into the LV, lack of collapse of IVC during inspiration
Echo

- TEE
  - Direct visualization of PE; sensitive for central PE but loses accuracy in peripheral PE secondary to the left mainstem bronchus

- No HX of cardiopulmonary disease → echo may approximate degree of embolic burden

- HX of cardiopulmonary disease → RV dilatation common and echo not as effective in evaluation

- Absence of RV dilatation in unstable patient excludes PE as cause of shock
Diagnosis of PE

Biomarkers

- Stratification in stable patients
  - Normal/low BNP and troponin $\Rightarrow$ low mortality
  - Elevated BNP and/or troponin $\Rightarrow$ higher mortality
According to the ACCP, which of the following is not appropriate VTE prophylaxis in the injured patient?

a. LDUH  
b. LMWH  
c. IVCF  
d. Fondaparinux  
e. No prophylaxis if high risk of bleeding

*RAS question*
Prophylaxis

- Preoperatively in patients undergoing major surgery secondary to venous stasis and relative hypercoagulability during the operation

  CONTROVERSIAL

  - Orthopedic surgery → large reduction in DVT when LMWH given at half dose in proximity (two hours before surgery or 4-6 hours after)
    - Two hours before with increased risk of major bleeding

  - Colorectal surgery
    - Two hours before abdominal surgery
Types of Prophylaxis

- Mechanical (IPC, GCS, venous foot pumps)
  - Mechanical prophylaxis alone not likely to be effective in ICU patients (bleeding a concern)
- IVCFs
IVCFs

- Not recommended as prophylaxis (ACCP)

- 2002 EAST guidelines → level III evidence in favor of
  - Prophylactic placement in very high risk trauma patients who are
    unable to be chemoprophylaxed

- More commonly placed for prophylaxis than for treatment
IVCFs

- **Conclusive data lacking that PE and death are reduced when used as prophylaxis, and may increase risk of DVT**

- **Retrievable**
  - Poor retrieval rates although improved to 60% with a dedicated filter registry in trauma patients
  - Most extensively utilized and studied in trauma patients, however there is a lack of high quality literature
    - Decrease in PE and fatal PE
    - Contraindication to chemoprophylaxis

- **Bariatric surgery**
  - Poor quality data supports use (with chemoprophylaxis)
Prophylaxis (Chemical)

- LDUH (5000 U’s q12 or q8)
  - Major abdominal or thoracic surgery
    - Meta-analyses reduced all DVT (20-40%), proximal DVT, PE and fatal PE

- 2002 EAST guidelines ➔ no support (level II)

- Arnold (Am Surg 2010) ➔ LDUH 5000 U’s q8 may be as effective as enoxaparin in trauma patients
  - Retrospective, decreased cost, protocol change mid-year

- RCT of LDUH vs. placebo in med-surg ICU patients reduced DVT from 29% to 13%
**Prophylaxis (Chemical)**

- **LMWH**
  - Derived from chemical depolymerization of UFH → reduced size, charge, weight with greater activity toward factor Xa and less activity for thrombin inhibition
  
  - Greater bioavailability, longer half-life, more predictable dose-response curves, better safety profiles with less bleeding, outpatient management, *reduced HIT*
  
  - Indicated in trauma and SCI, when compared to LDUH
  
  - 2008 ACCP guidelines recommended
Prophylaxis (Chemical)

- Fondaparinux
  - Factor Xa inhibitor; blocks thrombin generation by accelerating rate of factor IIa, VIIa, IXa, Xa, Xia, and XIIa inactivation by antithrombin
  - No HIT
  - No antidote, long half-life
  - Superior (or at least equivalent) to LMWH in ortho patients
  - Equivalent to dalteparin (LMWH) in major abdominal surgery (PEGASUS study)
  - Small pilot study in trauma patients found 1.2% incidence of DVT with no PE, HIT or major bleeding
Prophylaxis (Chemical)

- **VKA**
- **ASA**
- **DTIs**
  - Argatroban
  - Lepirudin
- **Oral agents**
  - Rivaroxaban (factor Xa inhibitor)
  - Dabigatran (direct thrombin inhibitor)
ASA

- 2012 ACCP guidelines for major general and abdominopelvic surgery in high risk patients (VTE 6%, Caprini ≥ 5, not at risk for bleeding) AND contraindication to LMWH or UFH (?HIT)
  - Low dose ASA or fondaparinux or IPC (2C)

- Re-evaluation of a subgroup analysis of the Antiplatelet Trialist Collaborative in general surgery patients by ACCP found reduced risk of asymptomatic proximal or distal DVT by 48%, symptomatic proximal DVT by 59%, and PE by 57%

- Data with moderate heterogeneity, no blinding in two studies, inconsistent outcomes, imprecision in RR of bleeding, and six studies used fibrinogen scanning for surveillance
LDUH and Trauma

- **LDUH** or LMWH or IPC (2012 ACCP - 2C)
  - Low quality evidence in support of asymptomatic proximal DVT which is reduced by 58% with LMWH and by 90% with LDUH plus continuous passive motion (ortho and skeletal trauma patients)
Traumatic Brain Injury
(Timing of Prophylaxis Highly Controversial)

- Incidence of VTE 3-5% when started within 24-48 hours
  - Up to 15% when delayed beyond 48 hours

- Risk of hemorrhage requiring craniotomy (0.5%) or change in management or outcome (1.1%)

- LMWH > LDUH
  - Norwood 2008; Dudley 2010; Koehler 2011; Minshall 2011
Traumatic Brain Injury
(Timing of Prophylaxis Highly Controversial)

- **Brain Trauma Foundation** (*J Neurotrauma* 2007)
  - Level III recommendation for LMWH or LDUH + mechanical
  - Insufficient evidence to support preferred agent, dose, or timing

- **Phelan and** *The Delayed Versus Early Enoxaparin Prophylaxis I study*
  - Low risk TBI patients with progression rates equal to placebo after starting enoxaparin at 24 hours after injury
Extended Prophylaxis

- Following THR/hip fracture surgery
  - 28-35 days with LMWH
  - Coumadin effective but with higher rates of bleeding
  - Fondaparinux for 3 weeks ➔ decreased asymptomatic and symptomatic VTE

- Major abdominal/cancer surgery
  - ASCRS ➔ 2-4 weeks after discharge
  - Four weeks of dalteparin compared to 1 week
    - pRCT reduced venographically-detected DVT from 16.3% to 7.3%
  - LMWH for 1 month after surgery (pelvic also) reduced DVT from 14.3% to 6.1%
Extended Prophylaxis

- SCI
  - 2012 ACCP guidelines
  - 3 months with LMWH
    - >90% of all VTE occurred within first 91 days after injury
**VTE Treatment (Anticoagulants)**

- *All patients suspected of PE should receive anticoagulation during their evaluation unless contraindicated*

- Intravenous UFH may be preferable in the critically ill as variability of absorption of SQ LMWH, potential for bleeding complications that can be reversed with protamine, shorter half-life

- Warfarin duration depends on thrombogenic risk factors, type of thrombosis (idiopathic), recurrence, and **D-dimer** level one month after therapy completed
**D-dimer**

- Degradation product of cross-linked fibrin formed after clots degraded by plasmin
- Reflects systemic activation of clot as well as degradation
- If positive and clinical suspicion, DVT in 70%
- If negative, no DVT (*high NPV*)

*Useful predictor of recurrent VTE; if still elevated after discontinuing anticoagulation ➔ restart anticoagulation*
**VTE Treatment**  
*(IVCF/Caval Interruption)*

- Routine use for treatment of DVT not recommended
- **Indications:**
  - VTE with contraindication to anticoagulation in proximal DVT
  - VTE with complications of anticoagulation in proximal DVT
  - VTE with failure of anticoagulation in proximal DVT
  - Free-floating iliofemoral/caval thrombus > 5 cm
  - HX of PHTN or poor cardiopulmonary reserve and patient unable to withstand another event
  - Massive PE resulting in hemodynamic instability and inability to withstand another event
  - Morbid obesity with BMI > 55 and undergoing gastric bypass
IVCF

  - *Only RCT of IVCFs in proximal DVT shown to prevent PE*

- 400 patients with proximal DVT, randomized to permanent filter or no filter *AND* to LMWH or LDUH

- Initial non-significant reduction in PE and at 8 years (63% risk reduction), but no difference in mortality

- At 2 years and 8 years → increased DVT, no change in mortality, PTS similar

- *LMWH = LDUH*
Anticoagulation in setting of IVCFs (once safe) indicated to decrease risk of recurrent DVT, IVC thrombosis, and PTS

Beneficial in patients undergoing surgical embolectomy
Thrombolytics
(DVT)

- Not routinely recommended secondary to bleeding potential and inability to predict complete lysis

- Complete lysis more likely if acute iliofemoral DVT, no previous HX, and popliteal vein for access

- Patency at 12 months 79% if lysis complete vs. 32% if lysis < 50%

- Anticoagulation after thrombolytics reduces PTS and maintains venous patency after DVT compared to anticoagulation alone
Which of the following is an absolute indication for the use of thrombolytics in PE?

- a. Severe hypoxemia
- b. Hemodynamic instability
- c. Large perfusion defect on V/Q scan
- d. Extensive embolic burden on CT scan
- e. Free-floating right atrial or ventricular thrombus

RAS question
Thrombolytics (PE)

- Indicated in hemodynamically unstable patient without major contraindication to bleeding

- Higher bleeding rates (retroperitoneal and intracranial)

- Improvements in end-tidal CO2 → success of thrombolytics

- Not successful in 8%
  - Mortality 7% when embolectomy performed vs. 38% when repeated thrombolysis attempted (recurrent PE also higher in latter group)

- Compared to heparin alone, greater percentage of clot resolution/lysis with thrombolytics by 7 days
Thrombolytics (PE)

- Clot-directed may be superior (clot fragmentation better with decreased bleeding)
- *Not indicated in treatment of PE in hypotensive surgical patients because of risk of hemorrhage*
  - Embolectomy

- Do not delay if considering as irreversible cardiogenic shock may ensue
- Best outcomes if young patient, embolus < 48 hours old, and embolus is large
  - Most beneficial in patients with massive PE at risk for death within the first hour (10%)
Thrombolytics (PE)

- Other potential indications besides RV dysfunction without instability
  - Severe hypoxemia
  - Large perfusion defect on V/Q scan
  - Extensive embolic burden on CT
  - Free-floating right atrial or ventricular thrombus
  - PFO
  - CPR

- Consider embolectomy if contraindication to thrombolytics or failure of thrombolysis

In cardiac arrest patients, 30% still survive → Paramount to continue resuscitation and chest compressions to fracture embolism
Thrombolytics (PE)

- RV dysfunction/strain in hemodynamically stable patients with PE
  - Controversial

- Biomarkers may allow stratification
  - Troponin indicates myocardial ischemia from increased wall tension from PE
  - BNP indicates RV stress and dilatation
  - No elevation → excellent outcomes and may be discharged or period of brief observation
  - Elevations → higher mortality → thrombolytics
PATIENTS WITHOUT CARDIOPULMONARY DISEASE
+ HEMODYNAMICALLY UNSTABLE + RV
DILATATION + HIGH PROBABILITY OF PE ➔
CONSIDER THROMBOLYSIS AND/OR
EMBOLECTOMY WITHOUT CONFIRMATION
Embolectomy (DVT)

- Rescue therapy for failed thrombolytics or high risk of bleeding and to prevent venous gangrene

- Successful in 42-93%

- Embolectomy + anticoagulation compared to anticoagulation alone
  - 2008 ACCP recommend against percutaneous embolectomy alone
  - Iliofemoral and femoropopliteal patency better
  - Patency at 10 years betters
  - Less popliteal reflux
Embolectomy
(PE)

- Surgical embolectomy with massive, central PE and hypotension on vasopressors (usually when thrombolytics or percutaneous embolectomy not successful)
  - Expand to patients with instability and not necessarily a large clot burden

- High morbidity and mortality, however improved outcomes (operative death 6%) noted recently when
  - Performed prior to cardiogenic shock/cardiac arrest
  - Performed on warm, beating heart without cross-clamping, cardioplegia, or fibrillation
  - Routinely placing an IVCF
  - Not operating on patients with out-of-hospital arrest without first restoring spontaneous circulation
  - Not operating on the elderly (>80yo)
**Embolectomy**

(PE)

- Percutaneous trans-catheter embolectomy
  - Aspirates thrombus after destroying it with high-pressure saline
  - Successful in 87% with major complications in 8%
  - Majority did not receive thrombolytics
  - Consider as first line therapy