VTE Prevention Strategies: Is a One Size Fits all Approach Correct?
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No disclosures...
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- Why do we care?
- Where is this in the realm of public health concerns?
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- **Incidence/Prevalence**
  - remains the most common preventable cause of hospital death, responsible for approximately 150k-200k deaths/yr in the U.S.
  - compare:
    - **CAD**: 610,000 deaths/yr (actual deaths attributable, calendar year 2017)
    - **lung cancer**: 154,050/yr (projected deaths in 2018 by ACS)
    - **VTE/PE**: 150-200k deaths/yr (CHEST, 2012), 60-100K deaths/yr (CDC, 2010)
    - **colon cancer**: 50,630/yr (projected deaths for 2018 by the ACS)
    - **pancreatic cancer**: 44,330/yr (projected 2018 deaths by the ACS)
    - **breast cancer**: high prevalence (1:8), 40,610/yr female deaths projected in 2018
    - **opioids**: 115 deaths in US/day = 41,630/yr (rapidly increasing)
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Of those affected by DVT/PE:

- 10-30% will die within one month of diagnosis
- sudden death is the first symptom in about 25% (40,000) of those having a PE
- of those with DVT, 50% will have long term complication (PTS), manifesting as limb swelling, pain, discoloration, and scaling
- 33% will have a recurrence of either DVT/PE within 10 years
- approximately 5-8% of the U.S. population has one of several (currently identifiable) genetic risk factors, (aka inherited thrombophilias)
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The Question: How to decide who, gets what, and for how long (extended duration)?

- primary prophylaxis (The **What**):
  - **prevention** of DVT/PE, utilizing methods that are preferably easy to administer, safe, with limited or no need for lab monitoring, clinically efficacious, cost effective
  - 1) early mobilization
  - 2) mechanical prophylaxis
    - intermittently pneumatic compression (IPC), (scds or foot pump)
  - 3) anticoagulation
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VTE prevention strategies:

3. anticoagulation
   a. unfractionated heparin, low dose (LDUH)
   b. low molecular weight heparin (LMWH): enoxaparin (lovenox), dalteparin (Fragmin), tinzaparin (Innohep)
   c. factor XA inhibitors: rivaroxaban (Xarelto), apixaban (Eliquis), fondaparinux (Arixtra), Edoxaban (Savaysa), betrixaban (Bevyxxa)
   d. Direct thrombin (Factor IIA) inhibitors:
      bivalent: hirudin, bivalirudin, desirudin, lepirudin
      univalent: argatroban, dabigatran (Pradaxa), inogatran, melagatran
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**Who**: (the Risk Factors)

for *Surgical* patients: immobility, type and extent of surgery or trauma, duration of hospital stay, history of previous VTE or cancer, recent sepsis, presence of central venous access device, pregnancy or the postpartum period, inherited or acquired hypercoaguable states.

for *Medical* patients: ICU stay, cancer, stroke, pregnancy, older age, male gender, immobility, prior VTE, sepsis, central access, CHF, acute resp. failure, IBD, known thombophilia
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How do we quantify risk of developing a VTE event?:

Risk stratification scoring systems for **Medical** patients:

**Padua Prediction Score:** Cancer (active or treated with chemo or XRT within the last 6 months (3 points), history of VTE (3 points), immobility for at least 3 days (3 points), preexisting hypercoaguable state (3 points), trauma or surgery within 1 month (2 points), age $\geq 70$ (1 point), cardiac or respiratory failure (1 point), cva or acute MI (1 point), acute infectious disease or rheumatic disease (1 point), BMI $> 30$ (1 point), HRT (1 point)

Results (90 day risk of symptomatic VTE if no prophylaxis during hosp):

0-3 points: 0.3% risk of symptomatic VTE
4-20 points: 11% risk of symptomatic VTE
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Medical:

IMPROVE risk score (International Medical Prevention Registry of VTE) Chest 2011:

four risk factors:

1. prior VTE*
2. active cancer*
3. age >60*
4. thrombophilia*

*risk of VTE within 92 days of admission was 0.4-0.5% if 0 risk factors

*risk of VTE within 92 days of admission was 8-11% if 3 of 4 factors present
Geneva risk score:

heart failure (2 points), respiratory failure (2 points), recent CVA (<3 months) (2 points), recent MI (<4 weeks) (2 points), acute infectious disease (2 points), acute rheumatic disease (2 points), acute cancer (2 points), myeloproliferative disorder (2 points), nephrotic syndrome (2 points), prior VTE (2 points), known hypercoaguable state (2 points), immobilization >3 days (2 points), recent travel >6 hr duration (1 point), age > 60 (1 point), BMI >30 (1 point), CVI (1 point), pregnancy (1 point), HRT (1 point), Dehydration (1 point)

Results (risk of developing VTE event):

- **low** risk (<3): 0.6% if receiving VTE prophylaxis, 0.8% if not receiving prophylaxis
- **high** risk (>3): 3.2% if receiving adequate VTE prophylaxis, 3.5% if not
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Medical patients, special circumstances:

HIT: Fondaparinux or argatroban

At higher risk of bleeding (i.e. GI bleed, intracranial hemorrhage): IPC, venous foot pump, compression stockings. add pharmacologic prophylaxis as soon as clinically able.

patients with stroke: LMWH>LDUH

patients with Neuroaxial anaesthesia*

patients: pregnancy (subject of HPT in Sentara currently)

patients with cancer

patients with spinal cord injury
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duration of prophylaxis (the *When*):

- in general, until ambulatory
- 3 major randomized trials (EXCLAIM 2010, 2013/ADOPT 2011/MAGELLAN 2013):
  - Regarding extended duration of prophylaxis: no reduction in VTE event rate or death, with *3x increase in bleeding risk if extended duration pursued*
  - in contrast to some high risk surgical patients (THR, TKR, etc.), extended duration prophylaxis has *not* been shown to be beneficial in pts admitted for acute medical illness.
Summary for *inpatient medical* patient population:

**Low risk**: (i.e. patient hospitalized with an acute medical illness and who are without obvious risk factors): early ambulation

**Moderate risk**: (i.e. patient hospitalized with an acute medical illness who has at least one risk factor for VTE and no increased risk of bleed): LMWH>LDUH, rather than mechanical prophylaxis

**High risk**: (i.e. patient hospitalized with an acute medical illness with high risk for VTE (ICU, cancer, stroke) and low risk of bleeding: LMWH>LDUH (higher dosing, UFH 5000 q8 or LMWH 30 mg q12) +/- IPC

**Extended duration** of administration (post discharge): no benefit shown to date

**Hx of HIT**: fondaparinux

**High bleeding risk**: IPC, anticoagulation as soon as able
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Risk Stratification for **Surgical patients**: Modified Caprini Score

(1 point)

- age 41-60, minor surgery, BMI >25, OC or HRT, pregnancy or postpartum, swollen legs, varicose veins, history of unexplained or recurrent spontaneous abortion, sepsis < one month ago, serious lung disease, including PNA <1 month ago, abnormal PFT, acute MI, CHF <1 month ago, history of IBD, medical patient at bed rest

(2 points)

- age 61-74 years, arthroscopic surgery, major open surgery (>45 minutes), laparoscopic surgery (>45 minutes), malignancy, bedrest (>72 hrs), immobilizing plaster cast, central line
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Surgical (Modified Caprini Score):

(3 points):

- age > 75 yrs, history of VTE, family Hx of VTE, Factor V Leiden, Prothrombin 20210A, Lupus anticoagulant, anticardiolipin antibodies, elevated serum homocysteine, heparin induced thrombocytopenia, other either congenital or acquired thrombophilia

(5 points)

- stroke (<1 month), elective arthroplasty, hip, pelvis, or leg fracture, acute spinal cord injury (<1 month)
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Risk of VTE of Surg. Pts using Modified Caprini Score:

**Very low:** 0 (general and abd-pelvic) or plastic and reconstructive surgery (Caprini 0-2) (risk of VTE: <0.5%)

**Low:** 1 to 2 (general and abd-pelvic surgery) or plastic and reconstructive surgery (Caprini 3-4) (risk of VTE: 1.5%)

**Moderate:** 3 to 4 (general and abd-pelvic) or plastic and recon surgery (caprini 5-6) (risk of VTE: 3.0%)

**High:** > 5 (general and abd-pelvic) or plastic and recon surgery (Caprini 7-8) (risk of VTE: 6%)

**this data was gleaned in the absence of either pharmacologic or mechanical prophylaxis**
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CHEST recommendations based on Caprini score:

- **Very low risk** (Caprini score 0): no specific prophylaxis other than early ambulation
- **Low risk** (Caprini score 1-2): mechanical prophylaxis, preferably Intermittant Pneumatic compression (IPC), over no prophylaxis
- **Moderate risk, and low risk of post operative bleeding** (Caprini score 3-4): LMWH, LDUH, or mechanical prophylaxis (IPC)
- **Moderate risk, and high risk for post operative bleeding** (Caprini 3-4): IPC
- **High risk, and low risk of post op bleeding** (Caprini ≥ 5): LMWH or LDUH, plus either IPC or elastic stockings
- **High risk, and high risk for post op bleeding** (Caprini ≥ 5): IPC, then LMWH or LDUH when able
CHEST recommendations based on Caprini score:

- High risk, surgery for cancer, not at risk for bleeding (Caprini > 5): **extended duration** pharmacologic prophylaxis (4 weeks) with LMWH over limited duration prophylaxis.

- High risk, but both LMWH and LDUH are contraindicated (HIT), not at high risk for post operative bleeding: **asa, fondaparinux, or IPC**

- Cardiac surgery patient, uncomplicated post op course: **IPC**

- Cardiac surgery patient, prolonged post op course, non hemorrhagic complications: add LMWH or LDUH to **IPC**
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CHEST recommendations based on Caprini score:

- Thoracic surgery pt, not at high risk for periop bleed, *moderate* risk for VTE (Caprini 3-4): LDUH, LMWH, or IPC.
- Thoracic surgery pt, not at high risk for periop bleed, *high* risk for VTE (Caprini $\geq 5$): LDUH, LMWH, plus IPC.
- Thoracic surgery pt, *high* risk for bleeding, (any Caprini score): ICP until can employ either LMWH or LDUH.

Craniotomy pt: IPC

Craniotomy pt, high risk for VTE (i.e. for cancer): IPC + LMWH or LDUH when able
CHEST recommendations based on Caprini score:

- Spinal surgery pt: IPC
- Spinal surgery pt, at high risk for VTE (i.e. cancer or combined ant/post approach): IPC + LMWH or LDUH as soon as able post operatively

- Major Trauma pt: LDUH, LMWH, or IPC
- Major Trauma pt with high risk for VTE (acute spinal injury, TBI, spinal surgery as a result of the trauma): LDUH, LMWH, plus IPC if no LE contraindication
- Major trauma pt, contraindication to LMWH or LDUH: IPC; add LMWH or LDUH when able
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CHEST recommendations based on Caprini score:

- For no patient population is an IVC filter recommended for primary VTE prevention.
- For no patient population is routine periodic surveillance with Venous ultrasound recommended.
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Finishing thoughts:

Very low risk deserves mobilization only, Low risk IPC.

That means that everything higher than this in the scoring systems would appear to benefit from the administration of an anticoagulant, +/- IPC.

LMWH/LDUH are employed in the majority of cases for prophylaxis, with use of increasing doses in higher risk populations, +/- addition of IPC.

exceptions to the rule:

Fondaparinux is superior (to LMWH) in THR, TKR, hip FX; may be used with major abdominal surgeries as well, but higher risk of major postoperative bleed (vs. LMWH)

Rivaroxaban likewise more efficacious for VTE reduction in THR, TKR (vs. LMWH)
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exceptions:

- for ortho, Rivaroxaban superior to fondaparinux and LMWH, with lower rates of symptomatic VTE, lower rates of severe bleeding, shorter hospitalization stays...prospective study needed (ORTHO-TEP registry)

- apixaban: may be used in TKR, THR extended prophylaxis, as has significantly lower rates of VTE without increased bleeding (vs. LMWH). (ADVANCE 2)

However: conflicting recommendations due to likely differences among the studies in the agent used, dose, timing of initiation, total duration of prophylaxis. *Meta analysis, on balance suggests benefits of direct thrombin inhibitors and Xa inhibitors for the prevention of VTE are marginal and may be offset by an increased risk of bleeding*
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Other Considerations:

cost of product (average in Sentara system):
- heparin: 5000 IU vial=$1.00/dose
- enoxaparin: 40 mg= $3.45/dose

issues outside of upfront cost alone:
- pt comfort: 2-3 doses (LDUH) vs. 1 (LMWH)
- materials: one prefilled syringe (LMWH) vs. three syringes and needles, disposal thereof (LDUH)
- nursing time: one dose daily (LMWH) vs. 2-3 times daily (LDUH)
- elimination several times daily of potential medication error with LMWH (vs. LDUH)
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New challenges:

iv opioid shortage: will likely necessitate increased use of spinal/epidural anesthesia for pain control. Will this alter our experience with dosing/timing of anticoagulant administration?

This is not a stagnant topic:

- new agents continue to come to market
- new payor models/ACOs (potentially with burden of longer stewardship on outpatient basis for patients),
- continued observation of VTE outcomes based on adjustments made to care regimen (in the absence of a double blind prospective trial)

For now, be mindful..you can make a big difference