acute venous disease

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thromboembolic disease

- deep vein thrombophlebitis
- superficial thrombophlebitis
- phlegmasia cereulea dolens
- pulmonary embolism
some facts

- over 250,000/yr die of pulmonary embolism
- 600,000 hospitalizations/yr for DVT
- 1-2% of hospitalized patients
- $1.2-2.4 billion per yr.
risk factors

- Hx of dvt, p.e.
- prolonged sitting, standing
- obesity
- recent surgery, trauma
- immobility paralysis
- malignancy
- hypercoaguable state
- smoking

- sepsis
- congestive heart failure
- age > 60
- BCPs
- pregnancy (>3)
- venous insufficiency
- copd
- venous incompetence
- nephrotic syndrome
congenital disorders

- atIII deficiency
- protein c, s deficiency
- apc resistance (leiden mutation)
- prothrombin 20210a
- homocystinemia
- heparin cofactor II deficiency
- dysfibrinogenemia
- inc. factor VII
- decreased pa; increased pai g4 gene
- abnormal plasminogen
acquired risk factors

- heparin induced thrombocytopenia
- warfarin induced thrombosis
- antiphospholipid syndrome
- estrogens
- pregnancy
- diabetes mellitus
antithrombin three deficiency

- antithrombin inhibits factors $\text{IX}_a$, $\text{X}_a$, $\text{Xi}_a$, and $\text{XII}_a$, thrombin
- risk of thrombosis increases when functional activity is less than 80%
- decreased in liver disease, sepsis, dic, bcps
- heparin, ffp, atIII replacement, warfarin
- prophylaxis in prothrombotic events
protein c and s deficiency

- vitamin k dependant liver proteins
- activated by thrombin, bound to endothelial cell thrombomodulin degrades factor $V_a$ and $XIII_a$, decreases tissue plasminogen activator
- protein s is a cofactor
- autosomal dominant 1:300
protein c and s deficiency

- Venous thrombosis at early age in heterozygotes (30-70% levels)
- Prophylaxis with warfarin, heparin
- Fresh frozen plasma to correct
- Life long warfarin for thromboses
- Warning!!! Cutaneous necrosis on warfarin more likely
activated protein c resistance (factor V Leiden)

- most common inherited cause of thrombosis (3-15% caucasians)
- factor V resistance to degradation by activated protein c
- 7 fold risk of venous thrombosis
- life long warfarin
homocystinemia

- increased risk of early onset dvt
- increased incidence of recurrent dvt
- platelet activation, increased factor VII and V, decreased protein c activity, mthfr mutation
- 39-50% of patients may have normal levels in fasting state
- folate (1-15mg/day), B₁₂, B₆
- elevated levels of prothrombin
- nucleotide change (g to a transition)
- arterial thrombosis (coronary and cerebral), warfarin for early and recurrent thromboses
5 fold increased risk of dvt

- increase in factors I, VII, VIII, IX, X, XII, platlets, pai-1,2
- decrease in protein c and antithrombin
- rule out thrombophillic states
- prophylaxis for 2nd pregnancy
antiphospholipid syndrome

- acquired, drug induced
- 1-5% of the population
- 50% of pts over 80
- lupus anticoagulants, anticardiolipin antibodies
- antibodies against B₂ glycoproteins, prothrombin, platlets, endothelial cells, protein C,S
antiphospholipid syndrome

- Test for both anticardiolipin and lupus anticoagulant
- Advise against oral contraception or pregnancy
- Lifelong warfarin INR 2.0-4.0
combination of two factors = 70-90% risk of vte
treatment goals

- prevent pulmonary embolism
- prevent propagation
- prevent postphlebitic sequellae
dvt diagnosis

- classic signs
  - tumor-swelling, unilateral edema
  - dolor-tenderness over the vein course in the thigh, calf muscles
  - calor-not usually found
  - rubor-if associated with svt

- Homans’ sign-present in 1/3 of patients with dvt and 1/2 of those without
diagnosis 2

clinical diagnosis is confirmed in 30-50%
differential diagnosis

- svt
- cellulitis/lymphangitis
- muscle or soft tissue injury
- achilles tendonitis
- asymmetric 2\(^0\) edema
- baker’s cyst
- arthritis
- post-phlebitic syndrome
svt and dvt

- if you have svt in a patient with varicose veins, 4% chance of dvt
- without varicose veins, 40% chance of concomitant dvt
- with proximal svt risk of dvt is 10%
diagnostic tests

- duplex scan
- d-dimer
- venography
- mri/ct scan
acute dvt diagnosis
ascending phlebography

- gold standard
- > 95% accurate
- least accurate in femoral, iliac or foot
- risks of p.e., causing dvt are low

- superficial vein filling preferentially
- site, adherence, extent, age
- observer error

risks of p.e., causing dvt are low
may-thurner syndrome

left iliac venous occlusion by crossing rt. iliac artery
venography
infiltration
doppler

- wave:
  - continuous if hand held
  - pulsed on duplex
- 5 MHZ probe, 60 degree angle
- listen for:
  - spontaneous flow
  - respiratory variation
  - segmental augmentation
  - competency of valves
  - pulsatility
respiratory variation

![Diagram showing respiratory variation]

- **Inspiration:**
  - $P_{pv}$
  - "$P_{cv}$"
  - $P_{cv}$

- **Expiration:**
  - LEGS
  - ABDOMEN
  - THORAX
  - ARMS
  - HEAD
augmentation

- position important
- evaluate
  - tibials
  - popliteal
  - sfv
  - cfv
  - iliac
  - saphenous
reflux
duplex scan

- B mode 4-8 MHZ linear array probe
- color to demonstrate flow
- grey scale to assess chronic changes
- assesses the iliac / vena cava better
duplex femoral vein
duplex scan criteria

- compressibility
  - deep femoral
  - superficial femoral at adductor hiatus
  - posterior tibialis at ankle

- augmentation
  - competent
  - phasic
compressibility
venous hemodynamics
dvt acute vs. chronic

acute

- Less echogenic
- Vein distension
- Homogeneity
- Free floating
dvt acute vs. chronic
dvt acute vs. chronic

chronic
- echogenic
- vein retraction
- heterogeneity
- clot retraction
- collaterals
- recanalization
duplex
rationale

- duplex least accurate in infrapopliteal veins
- incidence of P.E. from infrapopliteal veins low
- often don’t treat calf thromboses
- incidence of progression >35% to popliteal in 24 hrs
## Duplex Scan Accuracy

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEMORAL POPLITEAL</td>
<td>89-100</td>
<td>98-100</td>
</tr>
<tr>
<td>POPLITEAL/UPPER CALF</td>
<td>63-91</td>
<td>83-100</td>
</tr>
<tr>
<td>TIBIOPERONEAL</td>
<td>73-100</td>
<td>86-100</td>
</tr>
</tbody>
</table>
Hey you!!

YEAH, YOU IN THE THIRD ROW!!!!!!!

WAKE UP!
**d-dimer**

- Products of degradation of cross linked fibrin by plasmin
- Up to 98% sensitive to diagnosis of DVT
- Low as 38% specific
  - Malignancy, recent surgery, hospitalized for >3 days
- High **Negative Predictive Value** (if it’s negative it ain’t there)
### Pre-testing Stratification

<table>
<thead>
<tr>
<th>Clinical Feature</th>
<th>Pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active cancer</td>
<td>1</td>
</tr>
<tr>
<td>Paralysis, paresis, immobilization</td>
<td>1</td>
</tr>
<tr>
<td>Bed ridden &gt;3 days/Surgery&lt;4 weeks</td>
<td>1</td>
</tr>
<tr>
<td>Tenderness along deep veins</td>
<td>1</td>
</tr>
<tr>
<td>Entire leg swollen</td>
<td>1</td>
</tr>
<tr>
<td>Swelling &gt;3 cm vs other leg (10 cm below tuberosity)</td>
<td>1</td>
</tr>
<tr>
<td>Pitting edema</td>
<td>1</td>
</tr>
<tr>
<td>Non-varicose superficial collateral veins</td>
<td>1</td>
</tr>
<tr>
<td>Alternative diagnosis likely</td>
<td>minus 2</td>
</tr>
</tbody>
</table>

**Probability:** Low $\leq 0$, Moderate $1\text{-}2$, High $\geq 3$  

*Lancet 350:1795, ‘97*
diagnostic algorithm for outpatients

Suspect Acute DVT

Determine Pre-test Probability

Low

D-Dimer

Neg

Excludes DVT

Pos

Excludes Duplex

Moderate

D-Dimer

Neg

Excludes DVT

Pos

Excludes Duplex

High

Excludes: inpts, previous DVT, anticoagulants, suspect PE
Prophylaxis-Hospitalized

• Low Risk  Early and continuous ambulation, graduated stockings

• Moderate Risk  Compression Device, s.c. low dose UFH or LMWH

• High Risk  low dose UFH or LMWH once or twice daily, or oral anticoagulant, and/or IPCD
dvt treatment

- tibio-peroneal
- fem-pop/iliofemoral
- recurrent
- phlegmasia cereulea dolens
tibio-peroneal dvt

- controversial
  - to heparinize or not
  - if you do, use outpt therapy with LMWH
  - if you don’t, use nonsteroidals

- ambulation
- support hose
- restudy for propagation
ilio-fem-pop dvt

- 20% of popliteal untreated propagate
- LMWH or unfractionated heparin
  - rate of propagation and p.e. same
- ambulation early
  - bed rest increases propagation 20 to 1
  - swelling diminished sooner with ambulation and....
- support hose-class II
- early warfarin
recurrent dvt

- look for HCS or other reason
- if already on coumadin, add ASA/plavix
- retreat if not on anticoagulants
- consider lifelong coumadin
- Up to 20% recurrence
Differential Effects of UFH and LMWH on Factor Xa and Thrombin

<table>
<thead>
<tr>
<th>Feature</th>
<th>UFH (high mw 15,000)</th>
<th>LMWH (low MW 4500-6000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bioavailability</td>
<td>&lt;30%</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>Half-life</td>
<td>short $t_{1/2}$</td>
<td>longer</td>
</tr>
<tr>
<td>Anti-Xa/IIa ratio</td>
<td>low</td>
<td>high</td>
</tr>
<tr>
<td>Drug interactions</td>
<td>fewer</td>
<td></td>
</tr>
<tr>
<td>Administration</td>
<td>continuous/inpatient</td>
<td>intermittent/outpatient</td>
</tr>
<tr>
<td>Event</td>
<td>UFH</td>
<td>LMWH</td>
</tr>
<tr>
<td>------------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>recurrence</td>
<td>6.7-8.5 (%)</td>
<td>5.3-6.9</td>
</tr>
<tr>
<td>bleeding</td>
<td>1.2-2.0 (%)</td>
<td>0.5-2.0</td>
</tr>
<tr>
<td>death</td>
<td>6.3-8.0 (%)</td>
<td>4.0-6.9</td>
</tr>
<tr>
<td>HIT</td>
<td>1-2 (%)</td>
<td>1-2</td>
</tr>
</tbody>
</table>
patients not suitable for outpatient therapy

- severe liver disease
- thrombocytopenia
- renal disease
- high risk of falling
- acute p.e.
- other reasons for hospitalization
inpatient therapy

- LMWH or
- continuous iv heparin by nomogram
- loading dose of 80-100U/kg
- 15-20 U/kg/hr
- check aPTT
  - <35 sec  rebolus and 4U/kg/hr
  - 45-70 sec  ok
  - >70 sec  decrease or stop for 2 hrs
long term therapy

- start coumadin when aPTT therapeutic or after 2 days of LMWH
- overlap of at least 5 days or until therapeutic
- INR of 2-3
- 3-6 mo. reduces the frequency of recurrence over 1-2mo (6% vs 11-18%)
- check venous hemodynamics
alternatives to coumadin

- **ximelagatran** (oral iia)
  - max level 1.5-2.5 hrs
  - vte prophylaxis, decreased recurrent dvt vs lmwh + warfarin
  - acute coronary syndrome with asa
  - transient liver toxicity

- **dabigatran** (oral iia)
  - vte prophylaxis phase iii
  - equivalent to enoxaparin
  - peak = 2hrs; t½ = 15 hrs
alternatives to coumadin

- razaxaban
  - factor xa inhibitor
  - s.c. administration
  - liver metabolized
  - randomized knee replacement
    - dose dependant reduction in vte compared to lmwh
    - dose dependant increase in bleeding
HIT

- ufh acts as a hapten between platelet membrane and pf-4
- uncommon in dialysis pts-why?
- monitor pt ct every other day for 14 days
- lmwh 1/10th incidence of hit
- 50% fall in platelets or below 150,000/ul
- argatroban (2.0 ug/kg/min)
argatroban

- direct thrombin (IIa) inhibitor
- synthetic analog of hirudin (smaller molecule)
- $t_{1/2} = 30-60$ mins.
- hepatic clearance
- i.v. administration
- monitor aPTT
primary axillary/subclavian vein thrombosis (Paget-Schroetter)

- 2º to hypertrophy of the scalenus muscles or an abnormal rib
- duplex and venography, MVOV
- heparinization thrombolysis look for causes repair anticoagulation
- without repair-chronic problems and recurrence
- repair of anomalies should be done within a wk after lysis
Paget-Schroetter Syndrome TOS

- thoracic outlet
- dilated superficial veins
- cervical rib
Paget-Schroetter
secondary axillary/subclavian vein thrombosis

- prevention-use I.J. preferentially
- avoid long termed central lines, pic lines
- surveillance
- thrombolysis early followed by anticoagulation
- catheter removal depends on necessity vs symptoms
phlegmasia

- iliofemoral thrombosis
- thrombectomy vs thrombolysis
  - contraindication to lysis
  - viability of limb (alba)
  - popliteal approach for lysis
  - with or without fistula
- post thrombotic sequellae
- anticoagulation
phlegmasia cereulea dolens
phlegmasia cereulea dolens

- if no “P’s” anticoagulate, elevate/ambulate, stockings
- “P”
  - Pain - Pulseless
  - Pallor - PARESTHESIA
  - Poikilothermia - PARALYSIS
- even in the presence of arterial flow if the two big “P’s” are present, thrombectomy and fasciotomy are necessary
thrombectomy
Thrombolysis

- **systemic/regional**
  - better venous patency and less post thrombotic syndrome
  - bleeding, long treatment times

- **catheter directed**
  - patency and function improved over systemic
  - possibly decreased bleeding
  - life function better

- **mechanical**
  - often needs thrombolytic therapy after
Thrombolysis

- pharmacomechanical
  - seed with tpa
  - mechanical thrombectomy
  - increases clearing of clot
  - fewer pts need regional or catheter thrombolysis for shorter times
phlegmasia-thrombolysis
Phlegmasia-thrombolysis

popliteal access
adjunctive measures may-thurner
may-thurner after stent

90% 1 yr patency
Maximum Venous Outflow Velocity

- Evocative test measuring venous outflow velocity using a standardized thigh blood pressure cuff and duplex obtained femoral vein velocities upon release to detect venous outflow obstruction.

- Lebow et al (UTMCK): MVOV is significantly decreased on the left side in a sample of normal female volunteers and can be used as a preliminary test to Dx functional venous outflow obstruction.
Left Venous Outflow Obstruction

MVOV 82 cm/sec

MVOV 40 cm/sec
a myth

“bed rest in acute dvt reduces the risk of pe, alleviates pain, and decreases swelling”
no difference in pe between lmwh and bed rest and lmwh and 4 hrs ambulation a day and compression

clinically asymptomatic pe was found by scan in ½ of pts at the time of dvt diagnosis

ambulation and compression reduces stasis and thrombus propagation (26% vs 1%)

ambulation and compression leads to faster pain relief and less swelling

Reduces the frequency and severity of post thrombotic syndrome
ivc filters

Indications (classical)

- major p.e.
- p.e. on adequate anticoagulation
- loose clot
- respiratory insufficiency
- can’t anticoagulate

1-4% recurrence
ivc filters

- not so classical reasons
  - cancer
  - surgery and dvt
  - hit
  - trauma
  - free floating
  - morbid obesity surgery
  - venous reconstruction, endovascular procedures
removable filters
removable filters

Opt-Ease
rationale

- higher incidence of dvt after filter
- iver thrombosis
- migration
- strut fracture (→)
- Penetration (→)
  - Duodenum, ureter, aorta
- infection

- trauma
- pregnancy
- short termed prophylaxis

- Penetration (→)
removable filter

as yet, no clear-cut indications for use
summary—what’s new since I last gave grand rounds on this subject over two years ago

- d-dimer
- LMWH outpt therapy
- replacement for heparin-argatroban
- replacement for coumadin
- thrombolysis
- ct diagnosis of PE
- removable filters
- MVOV
SO LONG AND THANKS FOR ALL THE FISH