A Primer to Deep Venous Thrombosis and Management Strategies

Ratna Kunasani, MD
Incidence of Venous thrombosis: DVT and PE 1/1000/year in adult population.

2/3rds are DVT and 1/3rd are PE

Slightly more in males than females

1/10,000/yr in <45 y old to 5-6/1000/yr in 80 y olds

PE > in elderly than DVT

Major outcomes:
- Death- 6 of DVT and 10% PE within 1 month. PE:mortality of 30%
- Recurrence
- Post thrombotic syndrome (PTS)
- Major bleeding – secondary to anticoagulation
Acute DVT- spectrum: from asymptomatic calf vein thrombosis to
phlegmasia cerulea dolens (multisegment and involving the iliofemoral veins)
# Risk factors for VTE

**Unprovoked (Inherited)**
- Family history of thrombophilia
- Factor V Leiden
- Prothrombin G20210A mutation
- Protein C deficiency
- Protein S deficiency
- Antithrombin deficiency
- Sickle cell trait
- Antiphospholipid antibody syndrome
- May-Thurner syndrome

**Provoked (Acquired)**
- Age
- Obesity
- Smoking
- Cancer
- Heart failure (NYHA class III or IV)
- Pregnancy or postpartum period
- Trauma
- Immobility
- Surgery
- Hospitalization
- Oral contraception
- Personal prior history of VTE
- Inflammatory bowel disease
- Central venous catheter
Stratification of Common Risk Factors for Thromboembolism

**High Risk**
- Long bone fracture
- Major general surgery
- Trauma
- Spinal cord injury
- Major orthopedic surgery (major joint replacement)
- Active malignancy

**Moderate Risk**
- Indwelling central venous catheter
- Congestive heart failure
- Oral contraceptives
- Paralysis after stroke
- Pregnancy or postpartum period
- Known thrombophilia

**Low Risk**
- Laparoscopic surgery
- Obesity
- Smoking
- Varicose veins
- Immobility or bed rest > 3 days
VTE risk stratification*: Consider comorbidities, history of VTE, type of procedure, scoring systems (Rogers, Caprini)

- Very low/low-risk VTE
  - No need for bleeding risk assessment; aggressive early ambulation, mechanical VTE prophylaxis

- Moderate-risk VTE
  - Bleeding risk assessment
    - Low
      - Mechanical prophylaxis, early postoperative VTE chemoprophylaxis
    - High
      - Mechanical prophylaxis, monitoring of CBC, institution of chemoprophylaxis when bleeding risk diminishes

- High-risk VTE
  - Bleeding risk assessment
    - Low
      - Mechanical prophylaxis, early postoperative VTE chemoprophylaxis
    - High
      - Mechanical prophylaxis, monitoring of CBC, institution of chemoprophylaxis when bleeding risk diminishes; consider preoperative IVCF

*For patients undergoing general, vascular, gastrointestinal, urologic, bariatric, gynecologic, or plastic/reconstructive procedures. Adapted from the ACCP guidelines.
Until 2008, guidelines recommended only anticoag. Since then the ACCP and AHA suggest interventions for thrombus removal that include surgical and catheter-based techniques to reduce the incidence of PTS esp in pts with extensive venous thr.

Antithrombotic Therapy for VTE Disease
CHEST Guideline and Expert Panel Report

Clive Kearin, MD, PhD; Eli A. Akil, MD, MPH; Joseph Omelas, PhD; Allen Blavas, DO, FCCP; David Jimenez, MD, PhD, FCCP; Henri Bounameaux, MD; Menno Huisman, MD, PhD; Christopher S. King, MD, FCCP; Timothy A. Morris, MD, FCCP; Namita Sood, MD, FCCP; Scott M. Stevens, MD; Janine R. E. Wintch, MD, FCCP; Philip Wells, MD; Scott C. Wolter, MD; and COL Lisa Moore, MD, FCCP

BACKGROUND: We update recommendations on 12 topics that were in the 9th edition of these guidelines, and address 3 new topics.

METHODS: We generate strong (Grade 1) and weak (Grade 2) recommendations based on high- (Grade A), moderate- (Grade B), and low- (Grade C) quality evidence.

RESULTS: For VTE and no cancer, as long-term anticoagulant therapy, we suggest dabigatran (Grade 2B), rivaroxaban (Grade 2B), apixaban (Grade 2B), or edoxaban (Grade 2B) over vitamin K antagonist (VKA) therapy, and suggest VKA therapy over low-molecular-weight heparin (LMWH; Grade 2C). For VTE and cancer, we suggest LMWH over VKA (Grade 2B), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 2C), or edoxaban (Grade 2C). We have not changed recommendations for who should stop anticoagulation at 3 months or receive extended therapy. For VTE treated with anticoagulants, we recommend against an inferior vena cava filter (Grade 1B). For DVT, we suggest not using compression stockings routinely to prevent PTS (Grade 2B). For subsegmental pulmonary embolism and no proximal DVT, we suggest clinical surveillance over anticoagulation with a low risk of recurrent VTE (Grade 2C), and anticoagulation over clinical surveillance with a high risk (Grade 2C). We suggest thrombolytic therapy for pulmonary embolism with hypotension (Grade 2B), and systemic therapy over catheter-directed thrombolysis (Grade 2C). For recurrent VTE on a non-LMWH anticoagulant, we suggest LMWH (Grade 2C); for recurrent VTE on LMWH, we suggest increasing the LMWH dose (Grade 2C).

CONCLUSIONS: Of 54 recommendations included in the 30 statements, 20 were strong and none was based on high-quality evidence, highlighting the need for further research.

CHEST 2016; 149(2):315-352

KEY WORDS: antithrombotic therapy; evidence-based medicine; GRADE approach; venous thromboembolism
40% had Venous claudication, 15% developed venous ulceration in 5 y – all these pts have a dec QoL. Recurrence is high in pts with high thrombus burden.

US can detect valve reflux from valve closure times- but not the contribution of obstruction to the pathology. Hemodynamics are affected long before imaging techniques detect obstruction, and imaging is usually performed in resting pts.

Luminal venous obstruction causes the most severe form of PTS.

Even when the distal valves are not initially involved in the thrombus, presence of sig valve dysfunction due to persistent thrombus burden- can involve them.

When spontaneous lysis occurs (within 30 d)- valve function is frequently preserved. Successful thr lysis preserves valve and endothelial function.
PTS is defined as the S/S resulting from ac DVT – usually as a result of venous HTN from valve reflux +/- luminal obstruction.

Severity of ac DVT and the inv of IF segment & Anticoag Rx alone results in sev PTS morbidity. Ambulatory venous HTN- elev venous pr during exercise – lead to swelling and pigmentation Microcirculatory changes lead to dermal break down.

Labropoulos et al- monitored venous pressures in pts with PTS after DVT- noted that pts Rxed with anticoag alone had the highest pressures.

Strategies for thrombus removal:

- Venous thrombectomy

- Systemic thrombolysis

**CDT : replaced systemic lysis**

National Venous Registry – largest to date – CDT – 71% pts had IF DVT
At 1 yr 78% of pts who had complete clot resolution had patent veins compared to 37% pts who had < 50% clot lysis
96% of 1st time IF DVT who had 100% lysis – had patent veins at 1 y
72% of pts with 100% lysis had competent valves vs 38% who had <50% lysis
CDT had better QoL vs AC alone, and pts with complete/successful lysis had better QoL

**Pharmacomechanical : In Pts with C/I to anticoag**

- Endovascular mech thrombectomy: Vedantham et al 1st– CDT vs PMT – used diff catheters- 28 limbs -Amplatz (Ev3), Angiojet (Possis), Tretola (Arrow), and Oasis (Bos Sci) catheters. CDT removed 26% of the thr vs PMT which removed 82% (on venographic scoring).

**US accelerated thr lysis:**

Parikh et al – EKOS EndoWave (Ekos corp): UE and LE DVT- variety of lytic agents. Historical controls (weakness of the study) >90% lysis in 70% pts. Partial and complete lysis in 91%, median infusion time 22 hrs, major complications 4%- puncture site hematomas

**Isolated segment PMT : Trellis catheter.**

Double balloon, tpa infused in the isolated segment- catheter spins at 1500 rpm for 15-20 minutes- fragmented thrombus is aspirated
Martinez et al 52 limbs- 1st 25 with CDT, the next 27 pts with ISPMT. Complete lysis (>90%) was achieved in 28% of ISPMT vs 11% of CDT (p= 0.077). Rx time was shorter (23.4hrs vs 55.4 hrs – p< 0.01). rt-PA dose was less (33.4mg vs 59.3mg, p = 0.009). Bleeding Cx – 5% in both groups.
Compartment pressures (surrogate for venous pr) which were elevated - normalized after operative thrombectomy.

CDT – is beneficial in IF DVT – improves QoL

Pharmacomechanical Thr lysis- reduces lytic dose, short Rx and ICU /hospital stay, less bleeding

**CaVent trial - CDT vs Anticoag for Ac IF DVT:**
Alteplase fused with a Unifuse catheter at 0.01mg/kg/hr for 96 hrs (mean -24 hrs): complet lysis -43%, partial in 37%, unsuccessful in 10%. Sig improved IF patency at 6 months and thus less PTS at 2 y. Absolute risk reduction in PTS of 14.4%, major bleeding complications in 3.3%

The **ATTRACT** Study is an NIH-funded, Phase III, multicenter, randomized, open-label, assessor-blinded, parallel two-arm, controlled clinical **trial**.  
Started enrollment in 2009- completed enrollment in 2014- sample 692 pts. Pts with IF and fempop DVT- CDT vs Anticoag alone, also compare CDT vs PMT and cost analysis
Images obtained by venous intravascular ultrasound (IVUS).

1. Intraluminal septa.
2. Trabeculation with multiple lumina.
3. In-stent restenosis precisely identifying the stent, neointimal hyperplasia, and remaining lumen.
4. Compression of the vein by the artery at the iliac vessel crossing, creating an hourglass appearance. The adjacent artery is marked with an A. The black circle inside the vein represents the inserted IVUS catheter.
The extensive thrombus was demonstrated by a catheter phlebogram of the femoral vein. The bulk of the thrombus from the proximal popliteal vein to the common iliac vein was treated with the Trellis catheter via an ultrasound-guided popliteal vein approach. The clot in the posterior tibial and popliteal veins was treated with the EKOS EndoWave system. Liquefied and fragmented thrombus resulting from isolated segmental pharmacomechanical thrombolysis was aspirated via the Trellis catheter.
A 65-year-old white man was referred with phlegmasia cerulea dolens of his left leg, 36 hours after major abdominal laparotomy. Venous duplex demonstrated clot in the posterior tibial veins extending to the external iliac vein.

At 16 months the patient was asymptomatic, had no postthrombotic symptoms, maintained lower extremity venous patency with normal valve function.
Stent extends below inguinal ligament into CFV

CFV

GSV

Profunda femoris
Conclusions

DVT is associated with increased morbidity and mortality

PTS- is associated with significant reduced QoL

Interventions to decrease clot burden recommended in pts with proximal DVT to decrease PTS

PMT and CDT preferred choice of treatment in prox IF DVT with lifestyle limiting symptoms

Proximal vein stenosis / scarring can be treated in the chronic phase with endovascular intervention