Review of VTE Management

Lower extremity DVT

- All proximal DVTs (popliteal, femoral or iliac) should be treated due to higher risk of embolization/death regardless of symptoms.
- Distal DVT (below the knee in the calf veins, not involving popliteal)
    - Symptomatic: consider anticoagulation if low bleeding risk
        - High risk of bleeding or low risk of embolization (muscular veins << calf veins), negative DD, no risk factors -> consider surveillance US
    - Asymptomatic: Considerations for treatment include extension into or towards proximal veins on surveillance, unprovoked, elevated Ddimer>500, extensive (length>5cm, diameter>7mm, multiple veins), close to proximal veins persistent risk factors, mobility status
    - Evidence for recommendations of management of distal DVTs is low quality
    - Recommendations: distal DVT without severe symptoms or risk factors for extension can be monitored with serial imaging (every week for 2 weeks)
        - Anticoagulate if extension, increase duration of imaging if stable
- Duration of therapy
    - Risk of recurrence after surgery-provoked DVT much lower than nonsurgical trigger (estrogen, immobilization, surgery)
        - Surgery: 1% after 1 year, 3% after 5 years
        - Nonsurgical reversible trigger: 5% after 1 year, 15% after 5 years
        - Unprovoked: 10% after 1 year, 30% after 5 years
        - Cancer: unknown
    - American college of chest Physicians, International society of Thrombosis and hemostasis guidelines suggest:
        - First episode (provoked/unprovoked): 3 months minimum
        - Unprovoked or recurrent or provoked with minor/irreversible risk factor: consider indefinite

Choice of anticoagulation

- Standard treatment: UFH, LMWH or Fondaparinux bridged to warfarin x 5 days and INR>2-3 x 24hours -> warfarin monotherapy afterwards
- Xa inhibitors: Rivaroxaban, apixaban, edoxaban
    - Only Rivaroxaban and Apixaban studied as monotherapy
      EINSTEIN DVT 2010: rivaroxaban vs LMWH/VKA, similar rates of recurrent thrombosis and major hemorrhage
        - EINSTEIN PE 2012: xarelto noninferior to LMWH+VKA for recurrent VTE and had lower rate of major bleeding

    - EINSTEIN-extension: after 6-12 mos of anticoagulation, rivaroxoban 10mg or 20mg decreased risk of recurrent VTE compared to aspirin without increasing in bleeding rate
    - AMPLIFY 2013: apixaban vs LMWH/VKA. Apixaban noninferior in terms of recurrent VTE or death from VTE, had decreased major bleeding
    - AMPLIFY-extension: patients treated with 6-12mos of anticoagulation and uncertain about continuing therapy -> on apixaban 2.5 or 5mg bid, decreased recurrent VTE and all cause mortality compared to placebo, no increase in major bleeding
    - Edoxaban/LMWH + UFH or LMWH/VKA: edoxaban noninferior for recurrent VTE and with significantly less clinically relevant bleeding
- Direct thrombin inhibitors Dabigatran
    - RE-COVER: Dabigatran/LMWH v LMWH/warfarin, dabigatran noninferior to warfarin with similar bleeding rates, but significantly more expensive
    - RE-COVER II: replicated results, included more Asian patients
    - RE-MEDY: Dabigatran vs warfarin long term after treatment for VTE. Dabigatran noninferior to warfarin, associated with lower bleeding but higher incidence of acute coronary event
    - RESONATE: dabigatran vs placebo long term after treatment for VTE. Dabigatran reduced recurrent VTE but significantly increased bleeding

Superficial Vein thrombosis

- Less than 5cm, remote from the saphenofemoral/saphenopopliteal junction, no medical risk factors: supportive treatment with extremity elevation, warm/cold compresses, nsaids
- Anticoagulation if >5cm, approaching the deep venous system (saphenofemoral junction), demonstrates propagation or other risk factors for thrombosis
    - PPX Fondaparinux SC 2.5mg qday or LMWH x 45 days
        - Rivaroxaban 10mg noninferior to fondaparinux (SURPRISE)

Upper extremity thrombosis

- Primary (unprovoked) vs Secondary (CVC, pacemaker, cancer)
    - Mostly due to CVC. No data regarding whether anticoagulation is needed prior to removal. If catheter is functioning and still needed, do not need to remove.
        - No recommendation for immediate or deferred removal
- 5% lead to symptomatic PE
- Axillary or proximal veins: Recommend 3mo anticoag for uncomplicated cases, may need extension if continued need for catheter/cancer
    - Isolated brachial vein: limited data about whether to anticoagulate, alternative is to use US surveillance or treatment w/ ppx dose
        - Treatment suggested if symptomatic, associated with catheter that cannot be removed, or associated with cancer

- Suggest warfarin or LMWH for therapy, data lacking for the DOACs

VTE in Malignancy

- Initial therapy: LMWH preferred over UFH due to metaanalysis showing mortality benefit at 3 months
    - Data insufficient for fondaparinux and DOACs
- Long term therapy
    - LMWH preferred (CLOT/CATCH trials)
    - Edoxaban noninferior to Dalteparin in terms of composite outcome of recurrent VTE and major bleeding
        - Higher rate of major bleeding with edoxaban
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Episode	Location	Trigger	Treatment Duration
1st	Proximal	Surgery	3 months
1st	Proximal	Nonsurgical transient risk factor	3 months
1st	Distal*	Surgery or nonsurgical transient risk factor	3 months
1st	Proximal	Unprovoked	3 months with extension if bleeding risk is low/moderate (no scheduled stop date)
1st	Distal*	Unprovoked	3 months
2nd	Proximal or Distal*	Unprovoked	Extended anticoagulation, 3 months if bleeding risk is high
2nd	Proximal or Distal*	Provoked	Unclear benefit of extended anticoagulation
N/A	N/A	Cancer	Extended anticoagulation