ANTITHROMBOTIC THERAPY FOR UPPER EXTREMITY DVT AND PE

BACKGROUND

- Thromboembolism encompasses two interrelated conditions that are part of the same spectrum, deep venous thrombosis (DVT) and pulmonary embolism (PE).
- PE and DVT can occur in the setting of disease processes, following hospitalization for serious illness, or following major surgery.
- 90% of all clinically important PEs result from DVT occurring in the deep veins of the lower extremities, at or above the popliteal veins.
- However, emboli also can originate from the pelvic veins, the inferior vena cava, and the upper extremities.
- 75% of patients with UE DVT have secondary thrombosis due to:
    - hypercoagulability
    - indwelling central venous catheters
    - use of permanent cardiac pacemakers
    - mediastinal tumors/radiation/surgery/trauma (e.g. fractured clavicle).
- The main complication of DVT is PE.
- Approximately 5 million cases of DVT and about 600,000 cases of PE occur per year, and one third of PE cases are fatal.

RISK FACTORS AND ESTIMATED RELATIVE RISK FOR VENOUS THROMBOEMBOLISM:

Inherited conditions	Acquired conditions

• Antithrombin deficiency - 25
• Protein C or Protein S deficiency – 10
• Factor V Leiden mutation:
   o Heterozygous - 5
   o Homozygous - 50
	• Major surgery or trauma - 5-200
	• History of venous thromboembolism - 50
	• Cancer - 5
	• Major medical illness with hosp - 5
	• Age:
	   o older than 50 years - 5
	   o older than 70 years - 10
	• Obesity - 1-3

MANAGEMENT

The Seventh American College of Clinical Pharmacy (ACCP) Consensus Conference on Antithrombotic Therapy, using published data, recommends for:

- Initial and Long-term Treatment of Upper Extremity DVT:
    - Initial treatment should be with IV UFH or SC LMWH for at least 7 days. In patients with a low risk of bleeding and symptoms of new onset, a short course of thrombolytic therapy is suggested for initial therapy.

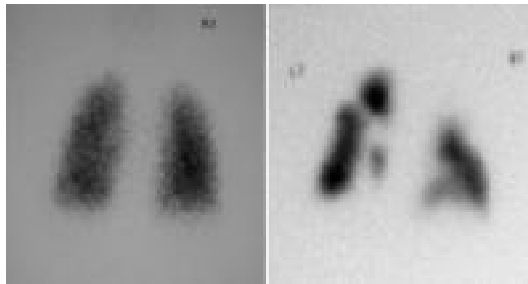
    - In patients with acute UEDVT and failure of anticoagulant or thrombolytic therapy and persistent symptoms, surgical embolectomy is suggested.
    - In patients with acute UEDVT and who have contraindications to anticoagulant therapy, a SVC may also be considered for initial treatment, although no reliable data is available about its long-term recurrence outcome.
    - Long-term treatment with a Vitamin K antagonist (Warfarin) with a target INR of 2.5 is recommended for a period of 3 to 6 months, or longer in the presence of permanent risk factors such as malignant disease.

- Initial and Long-term Treatment of Lower Extremity DVT:
    - Goal of anticoagulant therapy in the initial treatment of this disease are to prevent thrombus extension, early recurrences of DVT, and late occurrence of PE. Initial treatment should be with SC LMWH, IV UFH, or SC UFH for at least 5 days. Initial treatment with SC LMWH once or twice daily is recommended over UFH as an outpatient if possible, and as inpatient if necessary (unless patient has severe renal failure, in which IV UFH is recommended over SC LMWH. Because IV UFH has an unpredictable dose response and a narrow therapeutic range, it must be monitored using PTT. Must achieve and maintain a PTT prolongation corresponding to plasma Heparin levels from .3 to .7 IU/ml anti-Xa activity by the amidolytic assay.
    - In patients requiring large daily doses of IV UFH without achieving a therapeutic PTT, they recommend measuring the anti-Xa level for dose guidance.
    - Initiation of a Vitamin K antagonist together with LMWH or UFH on the 1st day of treatment and discontinuation of Heparin when the INR is stable and >2 (and ≤3).
    - In patients with DVT, they recommend against the routine use of IV/catheter-directed thrombolytic treatment, venous thrombectomy, or the routine use of an IVC filter in addition to anticoagulants.
    - In patients with contraindications to or complications from, anticoagulant therapy, as well as in those with recurrent thromboembolism despite adequate anticoagulation, IVC filter placement is suggested.
    - Long-term treatment with a Vitamin K antagonist with a target INR of 2.5 is recommended for a period of 3 to 6 months, or longer in the presence of permanent risk factors such as malignant disease.

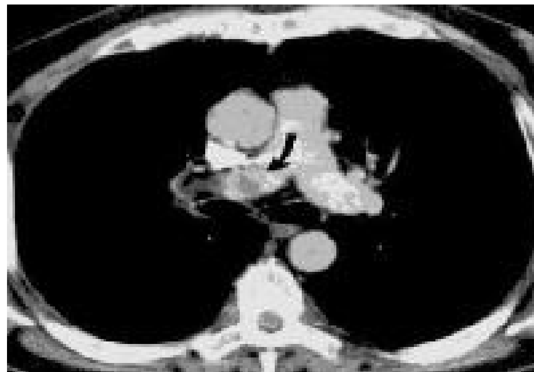
- Initial and Long-term Treatment of Acute PE:
    - IV UFH or SC LMWH for at least 5 days. In patients with acute nonmassive PE, LMWH is recommended over UFH.
    - If UFH chosen, administration by continuous infusion with dose adjustment to achieve and maintain PTT prolongation corresponding to plasma Heparin levels from .3 to .7 IU/ml anti-Xa activity by the amidolytic assay.
    - They also recommend initiation of a Vitamin K antagonist on the 1st day of treatment and discontinuation of Heparin when the INR is stable and >2 (and ≤3).
    - For patients with an episode of PE secondary to a transient/reversible risk factor, VKA therapy should be at least 3 months long, 6-12 months if patient has cancer

or hypercoagulable state, and indefinitely if patient has had $\geq$ 2 episodes of PE or in patient with first episode idiopathic PE.

- Absolute contraindications to antithrombotic or anticoagulant therapy include active bleeding, severe bleeding diathesis or platelet count less than 20,000/μL, or intracranial bleeding within the past 10 days.
- Relative contraindications include mild-to-moderate bleeding diathesis or platelet count 20,000-100,000/μL, brain metastases or recent major trauma, major abdominal surgery within past 2 days, gastrointestinal or genitourinary bleeding within past 14 days, infective endocarditis, or malignant HTN.



Ventilation-perfusion scan:
Left image: posterior view of normal findings on ventilation scan.
Right image: posterior view of a perfusion scan that reveals a perfusion defect in the LUQ. (The defect in the middle of the image is due to the position of the heart).



Helical CT scan of the Pulmonary Arteries. A filling defect in the right pulmonary artery is present, consistent with a PE.

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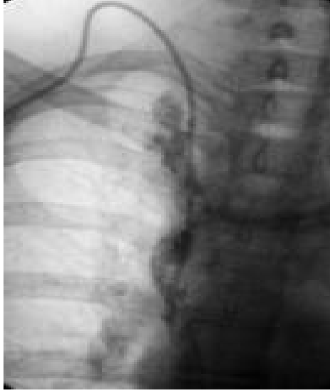
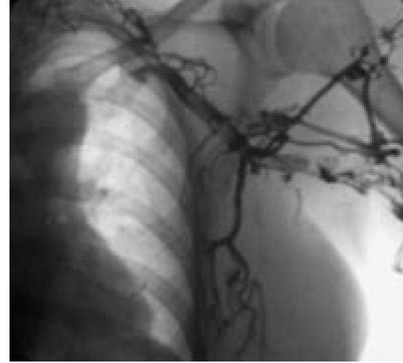
<td>
This contrast-enhanced study obtained thru Mediport placed thru chest wall thru IJV to facilitate chemotherapy. A thrombus has propagated peripherally from the tip of the catheter in SVC into both subclavian veins.</td>
<td>
The same patient as in previous image demonstrates thrombus in the left subclavian and axillary veins.</td>
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REFERENCES

- Bates SM, Ginsberg JS: Clinical practice. Treatment of deep-vein thrombosis. N Engl J Med 2004 Jul 15; 351(3): 268-77.

- Buller HR, et al: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. American College of Chest Physicians. Chest 2004 Sep;126(401 Suppl).

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