

Upper Extremity Deep Venous Thrombosis (UEDVT)



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Upper Extremity DVT (UEDVT): *something to discuss*

- Incidence has increased over the last few decades.
- Our understanding of UEDVT is evolving.
 - Recent registry data reporting incidence, risk factors, and outcomes
- Hopefully, understanding UEDVT will optimize patient care and decrease the incidence as it can affect the “bottom line”.
 - Centers for Medicare & Medicaid Services will not pay hospitals for hospital acquired thromboembolic events following certain orthopedic surgeries since 10/1/08.

Objectives

- Define UEDVT anatomically
- Differentiate between primary and secondary UEDVT
- Review the risk factors and clinical sequelae associated with UEDVT and compare these to lower extremity deep venous thrombosis (LEDVT).
- Describe an approach to treatment and prevention

Upper Extremity DVT

- Defined as a thrombus in any of the upper extremity deep veins.
 - Primary: axillary-subclavian vein thrombus which is related to unusual effort (Paget-Schroetter syndrome)
 - Secondary: related to a predisposing factor such as central catheters or other interventions. More than 80% of all upper extremity DVTs.

Vein Anatomy of the Upper Extremity

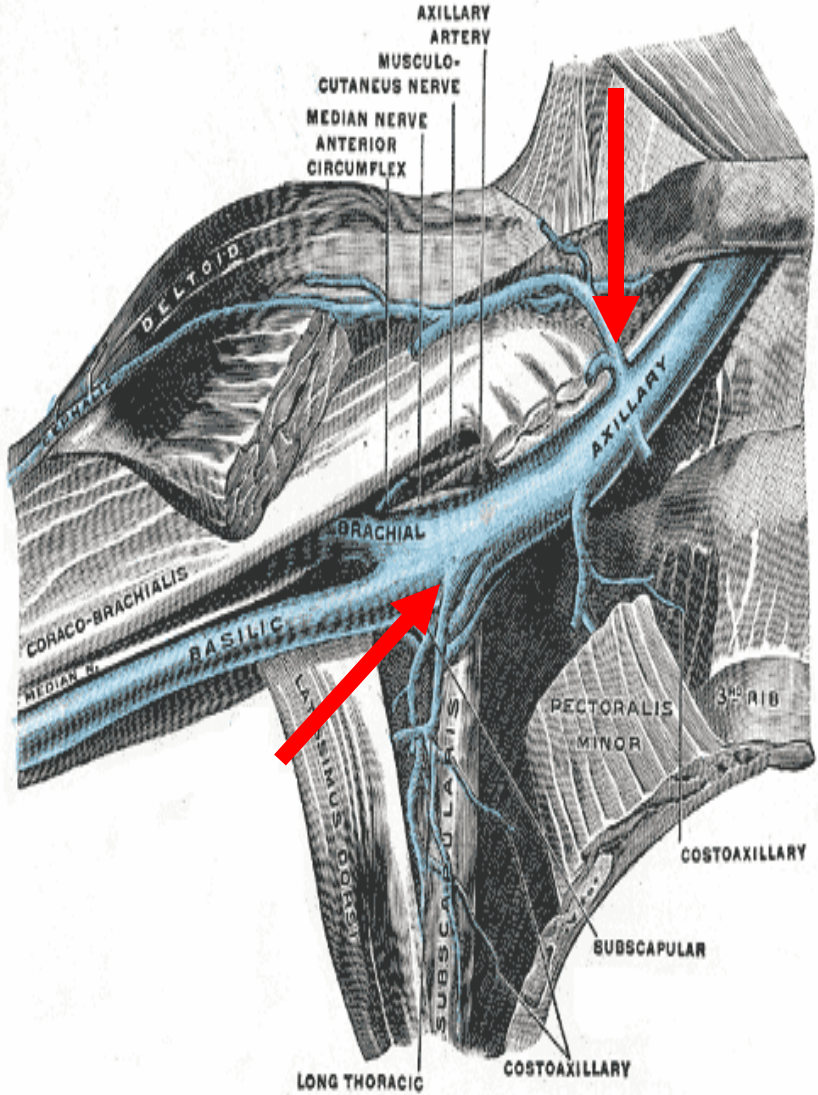
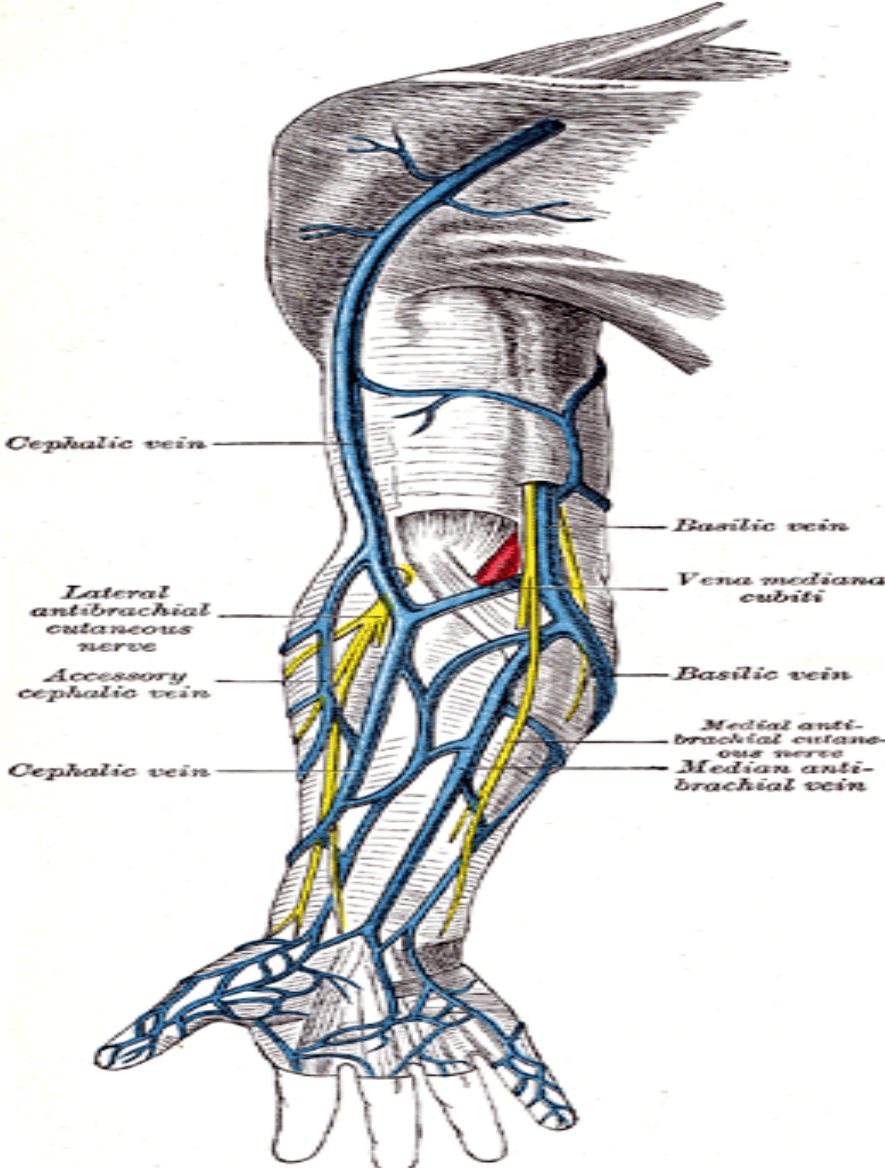
- **Deep Veins**

- Radial, Ulnar, Brachial, Axillary, Subclavian, Internal Jugular, Brachiocephalic (innominate)

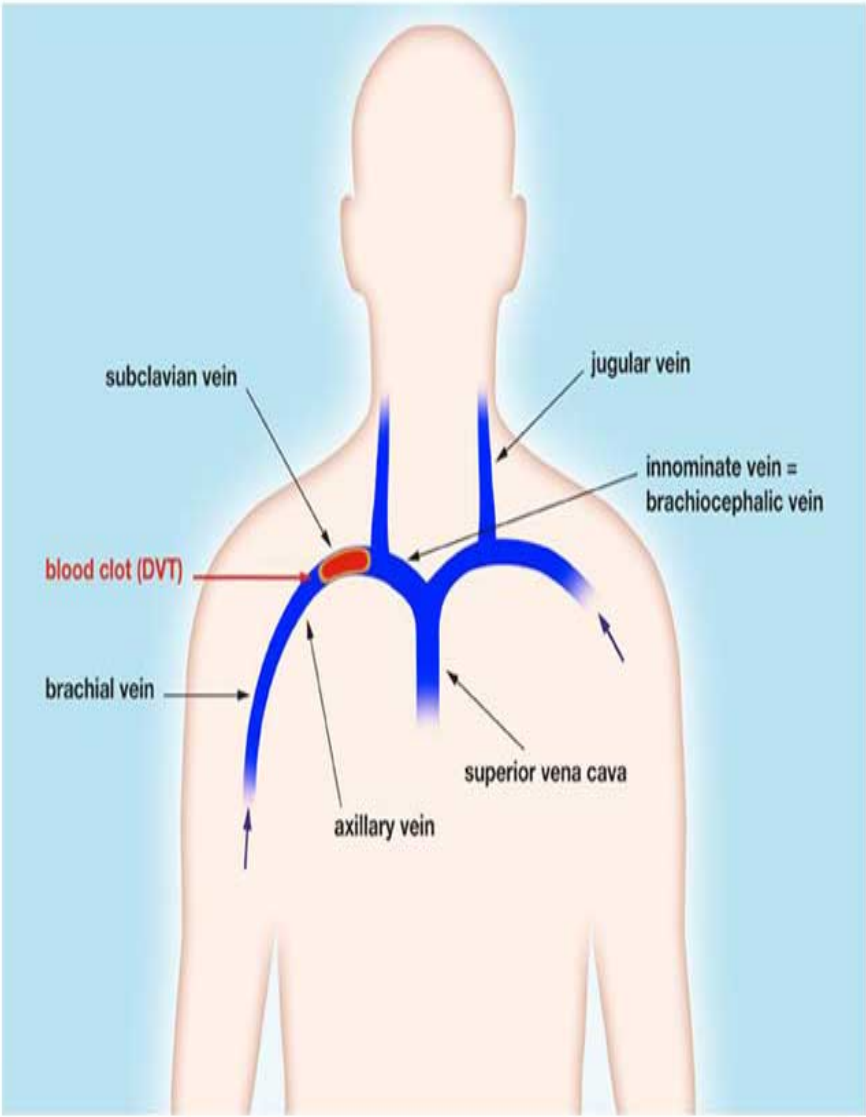
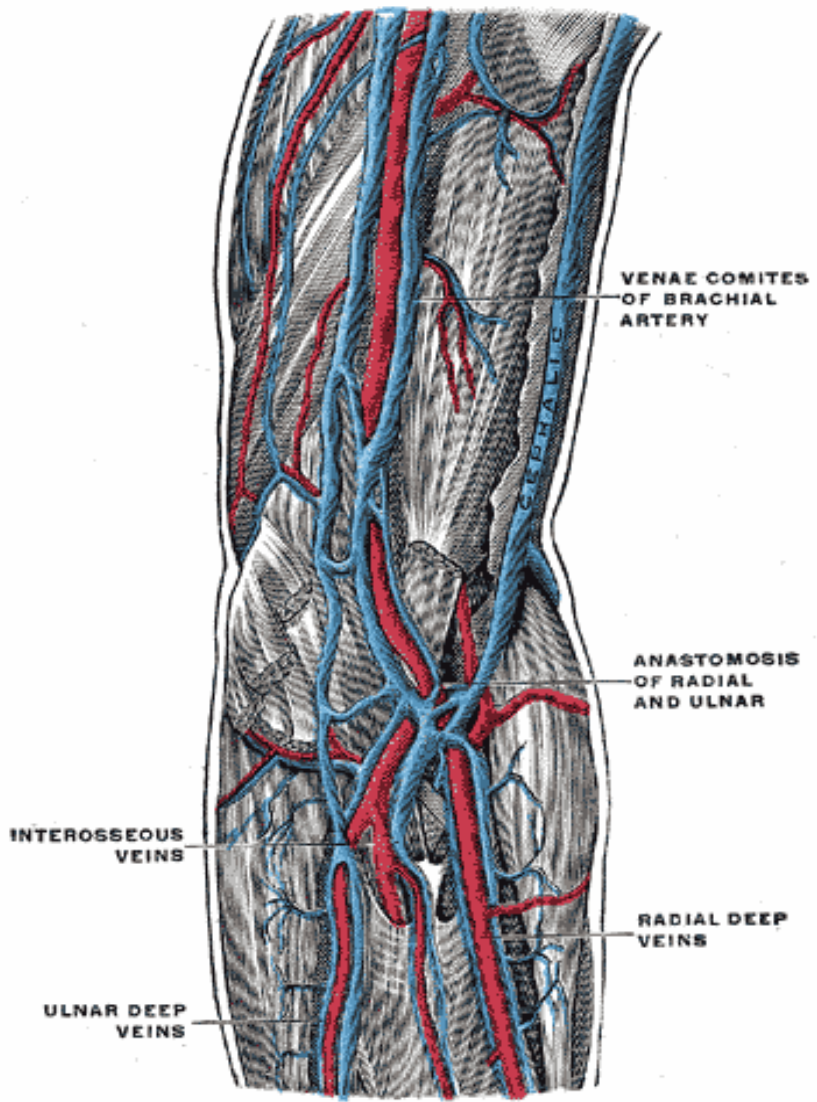
- **Superficial Veins**

- Digital, Metacarpal, Cephalic, Basilic, Median
- Cephalic and Basilic are veins usually canalized by peripherally inserted central catheters (PICC lines) and midlines and susceptible to clot formation. Both drain directly into the axillary vein.

Superficial Veins of the Upper Extremity



Deep Veins of the Upper Extremity



Graphic assistance: Jeff Harrison, Wilmington, N.C.

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Case 1

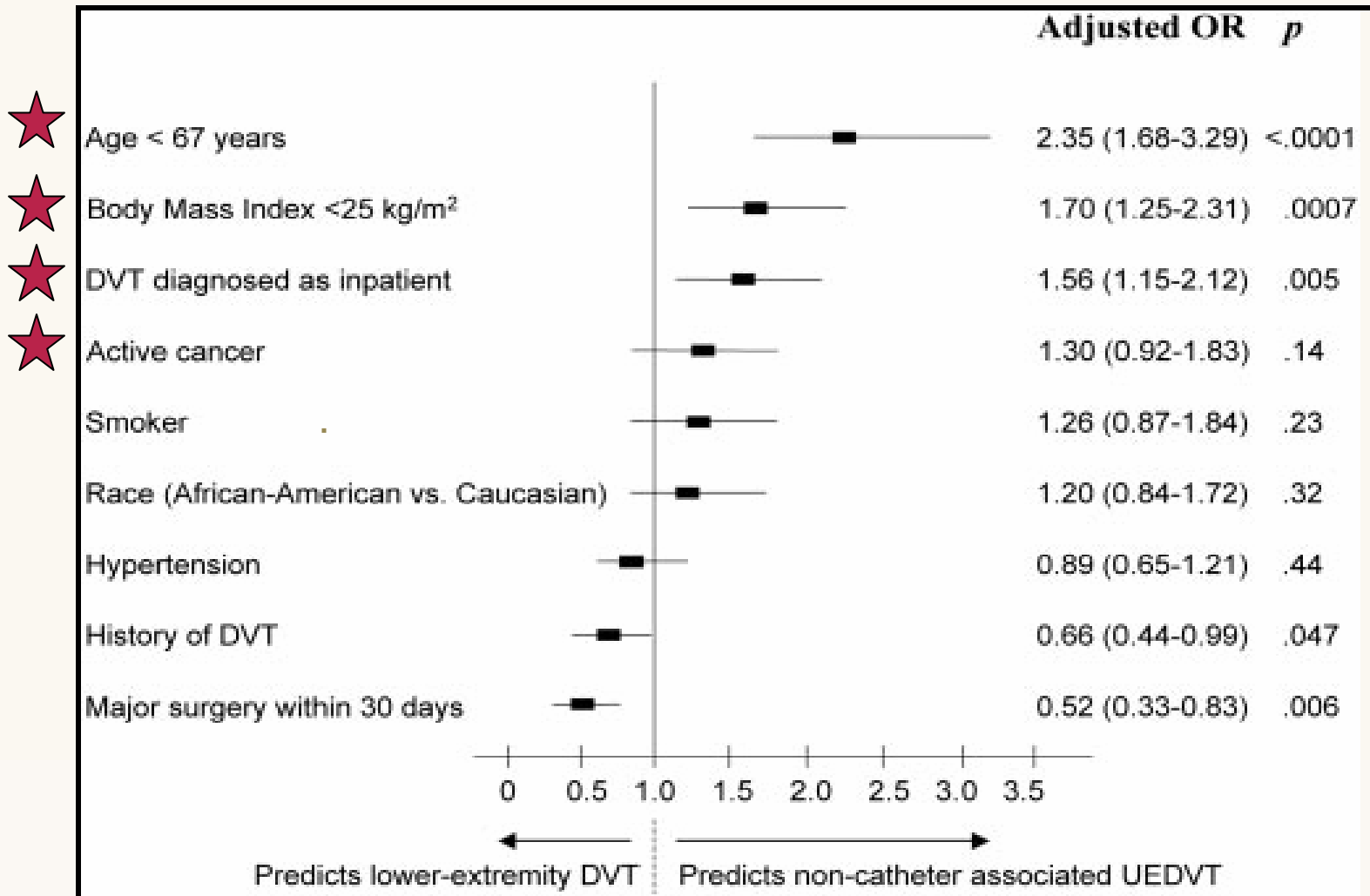
- 55 year old woman with history of CAD, DM, CKD admitted to the intensive care unit (ICU) with pneumonia and sepsis. Pt required intubation and pressor support. In the ICU, she had a right subclavian triple lumen catheter placed. After two weeks in the ICU, she is transferred out to the medicine floor under your care. You notice swelling in the right arm. You are concerned about the presence of a UEDVT.
 - What are the patient's risk factors for UEDVT?
 - How do you make the diagnosis?
 - What is the prognosis?
 - What is the treatment?
 - Could this have been prevented?

UEDVT: Epidemiology Overview

- Prevalence ranged from 4 to 14% of all DVT in recent registries.
- Risk Factors:
 - Prior Central Venous Catheter placement was the strongest risk factor for UEDVT
 - Malignancy and hospitalization was also common in patients with UEDVT
 - Conventional factors such as advancing age and obesity did not favor UEDVT unlike LEDVT
 - Thrombophilia is a common although less prevalent finding in noncatheter related UEDVT compared to LEDVT

UEDVT: Epidemiology

- **DVT FREE Steering Committee:**
 - Prospective Registry of 5451 patients with upper and lower extremity DVTs, confirmed by ultrasound.
 - 11% or 592 patients had UEDVT
 - 55% of UEDVT were related to a central venous catheter
 - 38% of patients with UEDVT had malignancy
- **RIETE Investigators:**
 - Prospective registry of 11,564 patients with DVT or PE confirmed by objective tests.
 - 4.4% of patients had UEDVT
 - 45% of patients with UEDVT had catheter related DVT
 - 38% of patients with UEDVT had malignancy



Joffe et al (DVT FREE Steering Committee). Upper Extremity DVT: A Prospective Registry of 592 Patients. Circulation. 2004; 110: 1605-1611. Figure 3.

UEDVT: Epidemiology

- **MAISTHRO (Main-ISar-THROmbosis) registry:**
 - 150 patients with UEDVTs were compared to 300 age and gender matched patients with LEDVTs
 - Screening for factor V Leiden, prothrombin G20210A mutation, antiphospholipid antibodies and factor VIII, protein C, protein S, and antithrombin activities were performed and compared between the two groups.
 - At least one thrombophilic condition was present in 39.2% of patients with noncatheter related UEDVT compared to 55.3% of patients with LEDVT ($p < 0.001$)

UEDVT: Epidemiology

- Catheter Related Thrombosis & Risk Factors
 - Lack of reliable data on catheter characteristics which may influence risk for UEDVT
 - Timsit et al. found that age >65 years old, internal jugular route, and the absence of heparinization were independently associated with catheter related central vein thrombosis
 - Lee et al. found that two or more insertion attempts and a second central venous catheter increased risk of UEDVT, with OR 5.5 and 3.8 respectively

LIVE LIFE LAUGHING



UEDVT: Symptoms & Signs Overview

- Over 80% of patients had swelling.
- Pulmonary embolus was found less frequently in UEDVT group compared to LEDVT AT THE TIME OF DIAGNOSIS.
- Patients with UEDVT had less extremity discomfort, dyspnea, and chest pain compared to LEDVT.

UEDVT: Symptoms & Signs

- **DVT FREE Steering Committee**
 - PE in noncatheter related UEDVT group 2% vs. LEDVT group 16% at diagnosis; $P < 0.0001$
- **RIETE Investigators**
 - Symptomatic PE in UEDVT group 46/512 (9%) vs. LEDVT group 3186/11052 (29%) at diagnosis; $P < 0.001$



"The tests are back and they show what caused those bruises on your stomach."

Upper Extremity DVT: Diagnosis

- Contrast Venography: considered the gold standard, need to tolerate contrast, and have adequate distal veins
- Duplex Ultrasound: sensitivity ranges from 78 to 100% and specificity ranges from 82 to 100% compared to contrast venography. More difficult to view and assess compressibility of proximal subclavian and brachiocephalic veins.
- CT and MR venography: no robust data on sensitivity in UEDVTs; literature supports role for diagnosis of proximal UEDVT and in patients who have contraindications to contrast venography for MR venography

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He was different from the other doctors.
For one thing, he refused to play God.

UEDVT: Prognosis Overview

- Outcomes of mortality and recurrent thromboembolism are statistically equivalent between UEDVT and LEDVT.
- Postthrombotic syndrome is common.
- Catheter associated UEDVT may be associated with increased risk of infection.

UEDVT: Prognosis

■ Mortality

- RIETE Investigators reported 3 month mortality
 - Overall mortality 11% for UEDVT vs. 7% for LEDVT (p 0.002)
- Worcester Venous Thromboembolism Study Group reported 3, 6, 12 month mortality
 - 3 month 4.4% for UEDVT vs. 5.8% for LEDVT
 - 6 month 14.5% for UEDVT vs. 12.1% for LEDVT
 - 12 month 20.3% for UEDVT vs. 14.7% for LEDVT
- Hingorani et al.
 - 2 month mortality rates did not differ based on proximity of UEDVT. Subclavian/axillary vein DVT 29%; IJ DVT 25%; Brachial vein DVT 21%

UEDVT: Prognosis

- Risk of recurrent DVT and recurrent PE were statistically equivalent for UEDVT and LEDVT.
 - RIETE Investigators reported 3 month outcomes
 - Recurrent DVT 2.3 % for UEDVT vs 1.7% for LEDVT
 - Recurrent PE 1.8 % for UEDVT vs. 1.2% for LEDVT
 - Worcester Venous Thromboembolism Study Group reported 3, 6, and 12 month outcomes
 - All recurrent venous thromboembolism occurred during the first 6 months for patients with UEDVT
 - At 12 months cumulatively
 - Recurrent DVT 14.5% for UEDVT vs. 11.4% for LEDVT
 - Recurrent PE 1.5% for UEDVT vs. 2.9% for LEDVT

UEDVT: Prognosis

- Discrepancy between mortality rate and rate of recurrent thromboembolism suggests UEDVT is not cause of death.
 - RIETE Investigators reported 3 month outcomes
 - Recurrent DVT 2.3 % for UEDVT vs 1.7% for LEDVT
 - Recurrent PE 1.8 % for UEDVT vs. 1.2% for LEDVT
 - RIETE Investigators reported 3 month mortality
 - Overall mortality 11% for UEDVT vs. 7% for LEDVT (p 0.002)

UEDVT: Prognosis

- Post thrombotic syndrome develops in one-fifth of patients with UEDVT
 - Prandoni et al.
 - Post thrombotic syndrome developed in 20.8% of patients at one year and 27.3% of patients at two years.

UEDVT: Prognosis

- Infection: Relationship between catheter related thrombosis and infection has been documented. Data from Timsit et al. found
 - Significant catheter colonization
 - 32% of Thrombosis vs. 19% of No Thrombosis (LLR 1.6)
 - Catheter related sepsis
 - 19% of Thrombosis vs. 7% of No Thrombosis (LLR 2.6)
 - Catheter related septicemia
 - 11.6% of Thrombosis vs. 3.6 % of No Thrombosis (LLR 3.2)

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"Laughter is the best medicine, but your insurance only covers chuckles, snickers and giggles."

UEDVT: Treatment Overview

- No trial data available about efficacy or optimal duration of anticoagulation treatment.
- Treatment guidelines are based on LEDVT data.
- Data from registries show lack of consensus regarding treatment w/ anticoagulation
 - Worcester Venous Thromboembolism Study
 - 56.5% of UEDVT vs. 73.7% of LEDVT discharged on warfarin

UEDVT: Treatment Overview

- American College of Chest Physicians (ACCP) 8th edition guidelines (2008)
 - Initial Treatment with LMWH, UFH, or fondaparinux (Grade 1C)
 - Treatment with Vitamin K Antagonist for at least 3 months (Grade 1C)

UEDVT: Treatment and Other Considerations

- Scenarios:
 - What do you do about the catheter?
 - What if the patient develops a contraindication to anticoagulation?

UEDVT: Treatment--What about the catheter?

- American College of Chest Physicians (ACCP) 8th edition guidelines (2008)
 - For most patients with UEDVT in association with an indwelling catheter, catheter does not need to be removed if it is functional and there is ongoing need for the catheter (Grade 2C).

UEDVT: Treatment--What about the catheter?

- Sajid et al. and Baarslag et al recommend line removal if patient has any of the following
 - With Infection/Line Sepsis
 - Greater than 1 week old thrombus
 - Greater than 2 cm thrombus

UEDVT: Treatment--What about the catheter?

- **Kovacs et al. with The Catheter Study**
 - Prospective cohort study of cancer patients with central venous catheter associated thrombus treated with anticoagulation without catheter removal. Study followed 74 patients for 3 months. Primary outcome was central line failure. Secondary outcome was recurrent venous thromboembolism, major bleeding, and death.
 - No patients had central line failure, extension or recurrence of thrombus. Only 57% of patients had catheter at end of 3 months.
- **Lee et al**
 - Prospective study of patients with cancer with long term catheter evaluating for symptomatic catheter related thrombosis.
 - No statistically significant difference in catheter life span between cases of patients with thrombosis treated with anticoagulation only (n=9) and those without thrombosis.

UEDVT: Treatment

Superior Vena Cava Filters

- American College of Chest Physicians (ACCP) 8th edition guidelines (2008)
 - Consider in selected patients with acute upper extremity DVT where anticoagulation is contraindicated and there is clear evidence of DVT progression or clinically significant PE. (Grade 2C)

UEDVT: Treatment Considerations

Superior Vena Cava Filters

- Technically, placement is more difficult due to short length of SVC (7 cm)
- Contraindications: presence of catheter, vena cava > 28 mm, venous stenosis, concomitant mass
- Complications: SVC perforation, cardiac tamponade, malplacement, dislodgement, erosion, thrombosis, occlusion, hemorrhage, pneumothorax

UEDVT: Treatment

Superior Vena Cava Filters

■ Ascher et al.

- Case control study with 72 patients followed for 22 months. Greenfield filter placed due to contraindication to anticoagulation or extension of thrombus despite anticoagulation
- 1.3% complication rate, no new PE documented, 47% mortality due to underlying disease.

■ Spence et al.

- Case series of 41 patients undergoing SVC filter placement for UEDVT due to contraindication to anticoagulation or failure of anticoagulation. Median followup was 15 months. No new PE documented and no complications noted. Mortality rate 51% at 1 year.

UEDVT: Treatment Considerations

ACCP Guidelines for Other Interventional Modalities

- For most patients with acute UEDVT, systemic or catheter directed thrombolytic therapy is not recommended (Grade 1C).
- For patients with acute UEDVT who have low bleeding risk and severe symptoms, a short course of catheter directed thrombolytic therapy may be used in appropriate expertise and resources are available (Grade 2C).
- For patients with acute UEDVT who have severe persistent symptoms despite anticoagulation or thrombolysis, catheter extraction, surgical thrombectomy, angioplasty, or a stage approach of lysis can be used if appropriate expertise and resources are available (Grade 2C).

UEDVT: Treatment

Other Interventional Modalities

- **Primary UEDVT (Paget-Schroetter)**
 - Anecdotal case series in the medical literature advocates consideration for earlier aggressive (thrombolysis/thrombectomy) management in addition to anticoagulation due to risk of longer term morbidity in young patients and possible structural abnormalities in these patients.

Pandemic Flu Emergency Response Plan

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"What you have, Ms. Bates, sounds highly contagious. You'd better see another doctor!"

UEDVT: Prevention Overview

- Low number of patients with UEDVTs were on prophylaxis in the prospective registries.
 - Only 20% of patients without obvious contraindications to anticoagulation received prophylaxis at the time of diagnosis in DVT Free Steering Committee registry.
 - No data about benefit of thromboprophylaxis for UEDVT
- The balance between benefits and risk of longer term thromboprophylaxis in cancer patients with central venous access is uncertain, but mainly shows no benefit. Studies are small and patient population is ambulatory.
- Guidelines for thromboprophylaxis based on LEDVT data.

UEDVT: Prevention

- American College of Chest Physicians (ACCP) 8th edition guidelines (2008)
 - For acutely ill medical patients admitted to the hospital with congestive heart failure or severe respiratory disease, or who are confined to bed and have one or more additional risk factors, including sepsis, acute neurologic disease, or inflammatory bowe disease, we recommend thromboprophylaxis with low molecular weight heparin, low dose unfractionated heparin, or fondaparinux (grade 1A)

Kirkpatrick et al. Prevention of Central Venous Catheter-Associated Thrombosis: A Meta analysis. The American Journal of Medicine. 2007; 120: 901-910.

- Meta analysis of 15 randomized controlled trials which included only upper extremity central venous catheters.
- 10 included only cancer patients and 5 included patients receiving TPN.
- Duration of prophylaxis and follow-up period was highly variable among studies.

Citation	Prophylaxis n/n (%)	No Prophylaxis n/n (%)
Fixed Low-dose Heparin		
Abdelkefi et al., 2004 ⁷⁷	1/65 (1.5)	5/68 (7.4)
Fabri et al., 1984 ⁷³	0/20 (0)	0/20 (0)
Fixed	1/85 (1.2)	5/88 (5.7)
Random	1/85 (1.2)	5/88 (5.7)
Low Molecular Weight Heparin		
Karthaus et al., 2006 ⁸¹	10/293 (3.4)	5/145 (3.4)
Monreal et al., 1996 ⁷⁵	0/16 (0)	0/13 (0)
Verso et al., 2005 ⁸³	2/191 (1.0)	6/194 (3.1)
Fixed	12/500 (2.4)	11/352 (3.1)
Random	12/500 (2.4)	11/352 (3.1)
Low-dose Vitamin-K Antagonist		
Bern et al., 1990 ⁷⁴	4/42 (9.5)	13/40 (3.3)
Couban et al., 2005 ⁸²	6/130 (4.6)	5/125 (4.0)
Heaton et al., 2002 ⁷⁸	2/45 (4.4)	1/43 (2.3)
Fixed	12/217 (5.5)	19/208 (9.1)
Random	12/217 (5.5)	19/208 (9.1)
Fixed Combined (8)	25/802 (3.1)	35/648 (5.4)
Random Combined (8)	25/802 (3.1)	35/648 (5.4)

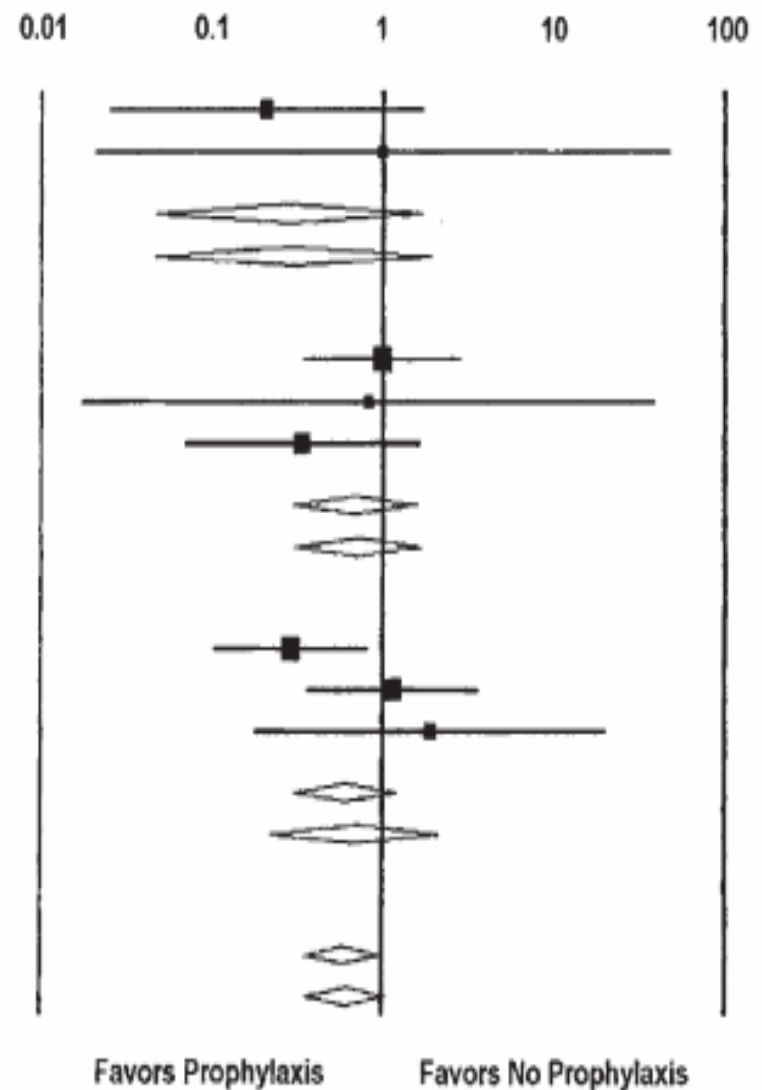


Figure 3 Relative risk of symptomatic catheter-associated deep vein thrombosis with anticoagulant prophylaxis.

Conclusions

- UEDVTs account for 4 to 14% of all DVTs.
- Strongest risk factor for secondary UEDVTs is central venous catheterization. Other risk factors are hospitalization and malignancy.
- Although UEDVTs have lower risk of PE at presentation, outcomes of recurrent thromboembolism and mortality are similar to LEDVTs.
- Treatment recommendations are 3 months of anticoagulation for patients without contraindications at minimum. Data regarding benefit of SVC filters is not clear.
- Recommendations for short term thromboprophylaxis is similar to LEDVT. Long term thromboprophylaxis is not recommended for cancer patients with long term central access.

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