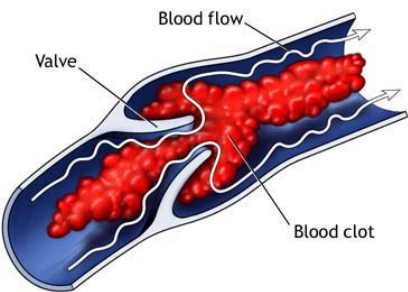


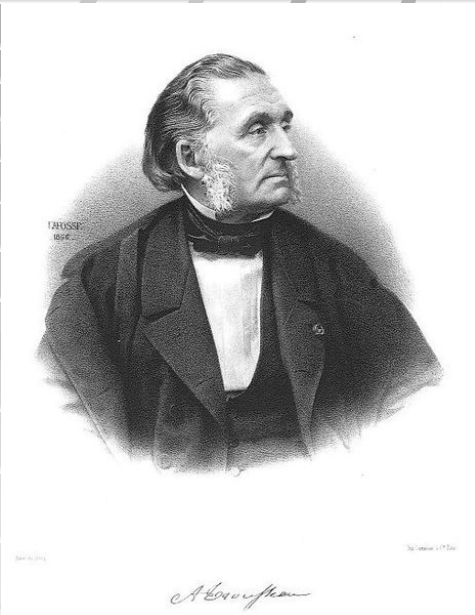
# ANTICOAGULATION THERAPY IN CANCER PATIENTS

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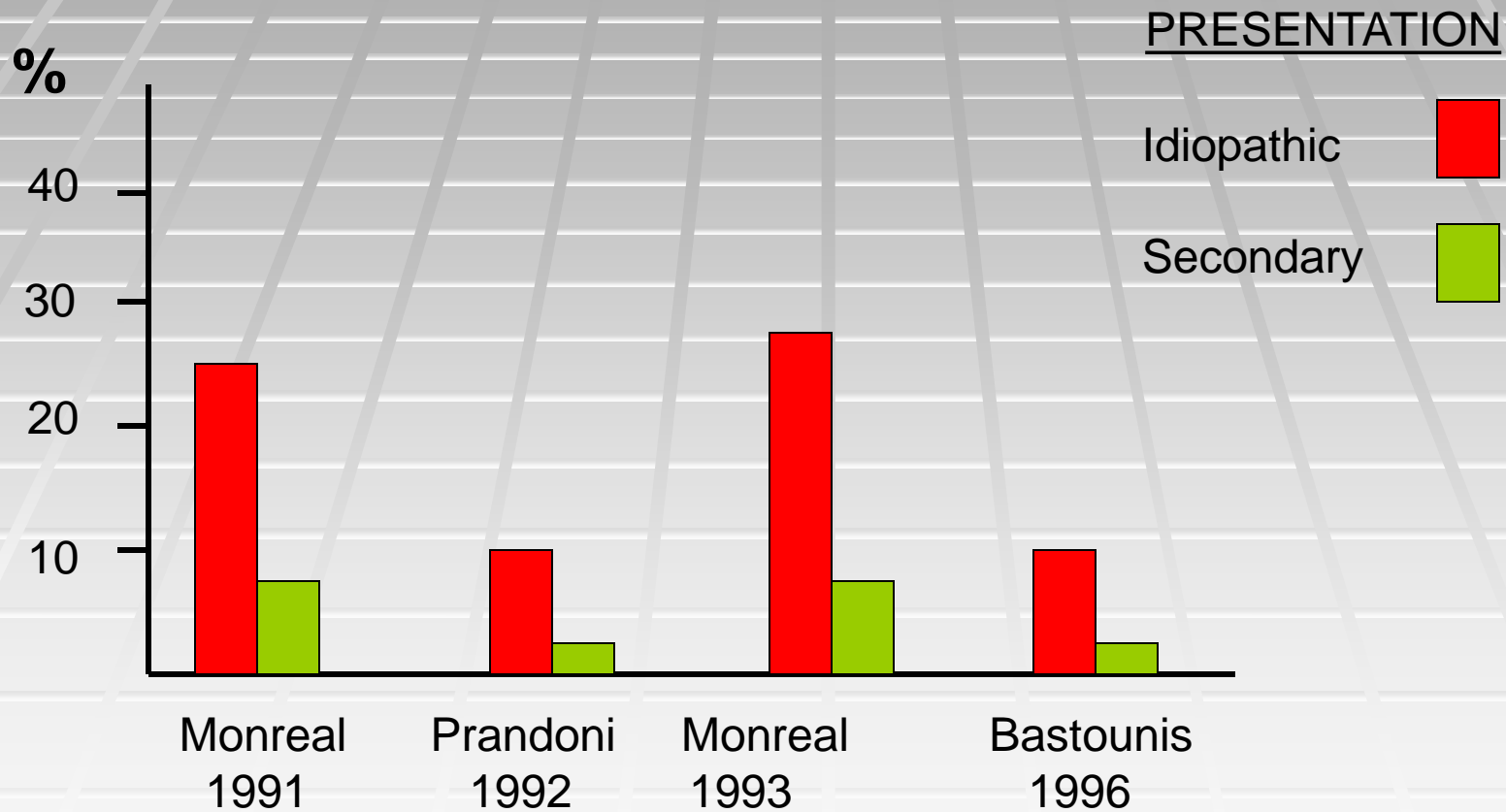


# Armand Trousseau (1801 – 1867)



- **Trousseau sign of malignancy** is a condition found in certain cancers that is associated with VTE and is characterized by successive tender nodules in affected veins. It is also referred to as **Trousseau syndrome**.
- First described in 1860s.
- Trousseau later developed pancreatic cancer and observed this condition in himself, dying soon thereafter.

# Incidence of Cancer in patients presenting with VTE



# Thrombosis in Cancer Patients

- Cancer patients have an approximately 6 fold increase risk of VTE compared to general population.
- The development of a DVT predicts for decreased overall survival in cancer patient population.

Chew, HK. et al. *Incidence of VTE and effects on survival among patients with common cancers. Arch Intern Med* 2006; 166(4): 458-464.

Sorensen, HT. et al. Prognosis of cancers associated with VTE. *NEJM* 2000; 343(25): 1846-1850.

# Thrombosis in Cancer Patients

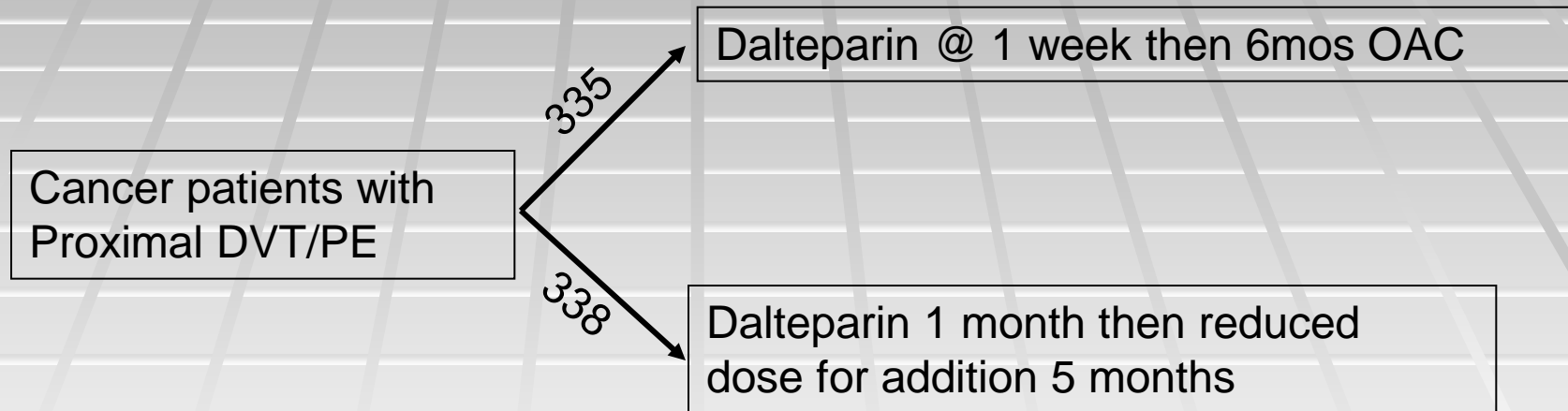
## ■ Cancers associated with highest risk of thromboembolism.

- Malignant brain tumors
- Adenocarcinomas of lung
- Ovary
- Pancreas
- Colon
- Stomach
- Prostate
- Kidney
- Hematologic Malignancies
- Breast on Tamoxifen (2-5x)

Falanga, A et al. Pathogenesis of thrombosis in patients with malignancy. *Int J Hematol* 2001; 73(2):137-144.

# Thrombosis in Malignancy

- **CLOT Trial** (Multicenter randomized, open-label study)

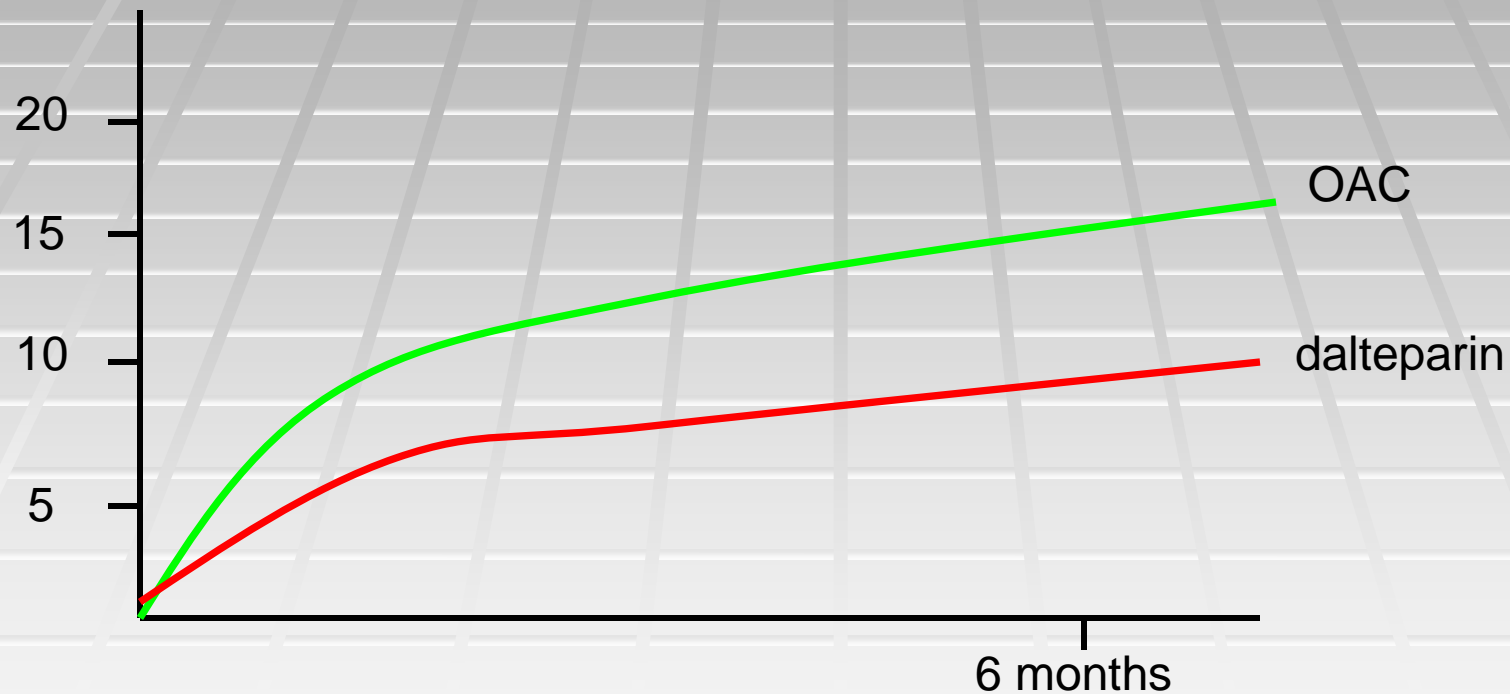


Lee, A. NEJM 2003

# CLOT trial

- Comparing LMWH versus a coumarin in the prevention of recurrent VTE in cancer patients.
  - 676 cancer patients with new VTE.
  - LMWH bridge 5-7 days then Oral Anticoagulation (OAC) therapy for 6 months.
  - LMWH for 6 months.
- OAC rate of recurrent VTE at 6 months was 17% versus 9% for LMWH.

# CLOT Trial – Recurrent VTE





# CLOT Trial – Bleeding Events

- LMWH – 5.6% Major Bleed (13.6 Any bleed)
- OAC – 3.6% Major Bleed (18.5% Any bleed)
- Neither were statistically significant

# Prophylactic OAC in Malignancy

- 5 Randomized Control Trials
  - 1656 patients
  - OAC vs none
- No reduction in mortality at 6 months, 1 year, 2 years, and 5 years.

# Prophylactic LMWH in Malignancy

- 9 Randomized Control Trials.

- 2857 metastatic or locally advanced cancer.  
(1 UFH and 8 LMWH)

No difference in overall survival at 12 months, but Relative Risk was 0.92 (95% CI 0.88-0.97) in favor of LMWH in OS at 24 months.

Development of Symptomatic VTE had RR of 0.55 (95% CI 0.37-0.82) in favor of LMWH.

Major and minor bleeding was not statistically significant between treatment and control groups.

# Central Venous Catheters and Malignancies

## INCREASED RISK OF THROMBOSIS

- Peripherally inserted > IJ or Subclavian
- Catheter tip too shallow.
- Left sided catheter.
- Prior Radiation Therapy to the Chest.
- Previous CVC.

# Central Venous Catheters and Malignancies

- 12 Randomized Control Trials
  - 3611 cancer patients with CVC.
  - Treatment (LMWH,LDUH,LD-VKA) vs none.

Could not confirm or exclude benefit or detrimental effects to prophylactic therapy in cancer patients with CVCs.

# Questions

- When to prophylactic anti-coagulate a cancer patients ?
- Should cancer patients with CVCs be prophylactically anti-coagulated?
- How to treat a cancer patient with an acute VTE?
- How to treat a cancer patient with an acute catheter associated VTE?
- What about prophylaxis in the travelling cancer patient?

# **American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (9<sup>th</sup> Edition)**

Holbrook, Anne et al. *Chest* 2012:  
141(2-supplement): e1525-e1845.

# GRADE SYSTEM

- Grade 1 = Strong recommendation
  - Grade 2 = Less certainty, weaker recommendation.
- 
- A = High-quality evidence
  - B = Moderate-quality evidence
  - C = low-quality evidence



# Prevention of VTE in Nonsurgical Patients

- 4.2.1 In outpatients with cancer and without additional risk factors\* recommend against prophylaxis with LMWH or LDUH [2B] and against VTA [1B].
- 4.2.2 Outpatients with solid tumors and risk factors\* then recommend LMWH or LDUH prophylaxis [2B].
- Prior VTE, immobilization, Hormonal therapy, Angiogenesis inhibitors, thalidomide or lenolidomide use.

# Cancer Patients with CVCs

- Outpatients with cancer and indwelling CVCs, recommendation against prophylaxis with LMWH or LDUH [2B] or VKA [2C].

# Travelling Cancer Patient

- For prolonged travel in patients with active malignancy...
  - 6.1.1 Frequent ambulation, calf muscle exercises, sitting in aisle seat [2C].
  - 6.1.2 Use of below the knee graduated Compression stockings [2C].
  - 6.1.3 Against use of ASA or anticoagulants [2C].

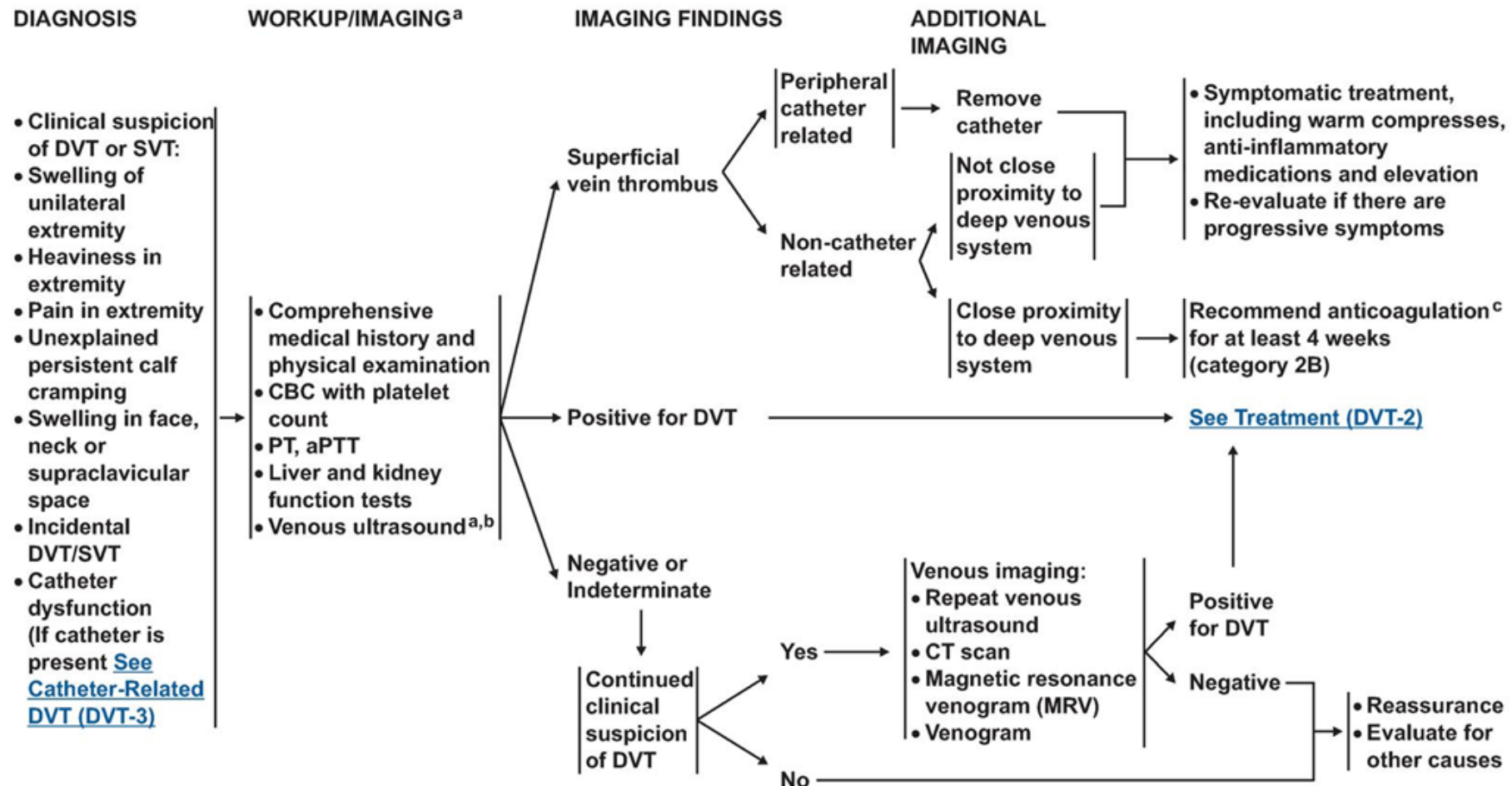
# Acute LE-DVT in Cancer Patient

- 3.1.5 If no high risk for bleeding, then anticoagulation to extend beyond 3 months [1B]. Reassess annually
- 3.2.2 Recommend LMWH over VKA [2B].  
VKAs over Dabigatran / Rivaroxaban [2B].
- 4.1 Recommend Compression stockings for 2 years [2B].

# Administration of LMWH

- **2.5.2. In patients with acute DVT of the leg treated with LMWH, we suggest once- over twice-daily administration (Grade 2C) .**
- *Remarks: This recommendation only applies when the approved once-daily regimen uses the same daily dose as the twice-daily regimen (ie, the once-daily injection contains double the dose of each twicedaily injection). It also places value on avoiding an extra injection per day.*

### DVT/SVT: DIAGNOSIS

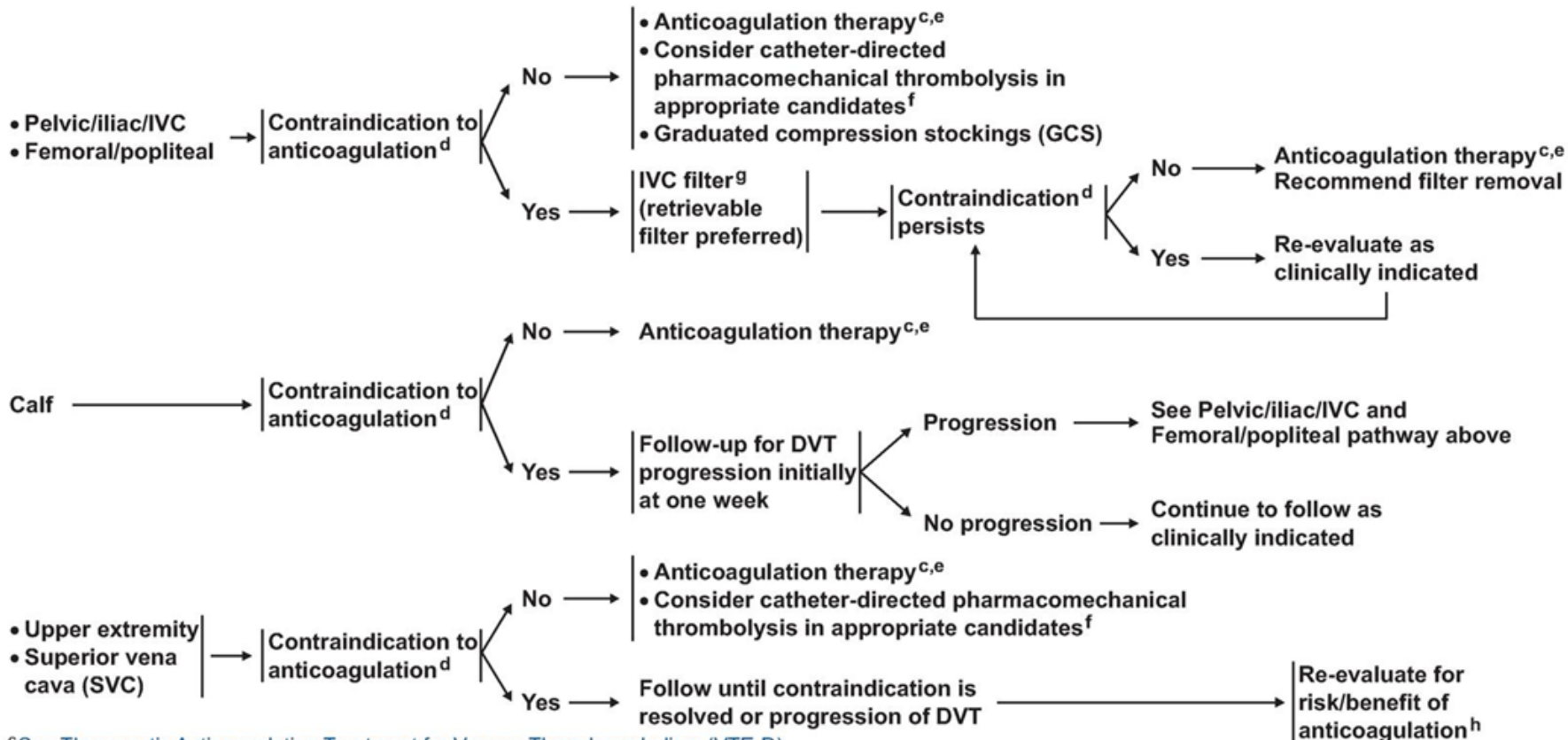


<sup>a</sup>Imaging recommendations reflect initial diagnostic workup of an individual who has not previously been diagnosed with DVT.  
<sup>b</sup>In cases with high suspicion of DVT and no contraindications, consider initiating early anticoagulation while waiting for imaging results.  
<sup>c</sup>[See Therapeutic Anticoagulation Treatment for Venous Thromboembolism \(VTE-D\)](#).

**Note:** All recommendations are category 2A unless otherwise indicated.  
**Clinical Trials:** NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

DVT LOCATION

DVT: TREATMENT



<sup>c</sup>See [Therapeutic Anticoagulation Treatment for Venous Thromboembolism \(VTE-D\)](#).

<sup>d</sup>See [Contraindications to Prophylactic or Therapeutic Anticoagulation Treatment \(VTE-B\)](#).

<sup>e</sup>See [Anticoagulation Failure \(VTE-H\)](#), if extension of VTE or new VTE while on recommended anticoagulation therapy.

<sup>f</sup>Choice of regimen should be made based upon institutional expertise/preferences in conjunction with interventional radiology or vascular surgery colleagues. (Vedantham S, Thorpe, PE, Cardella, JF, et al. Quality improvement guidelines for the treatment of lower extremity deep vein thrombosis with use of endovascular thrombus removal. J Vasc Interv Radiol 2009; 20(7suppl):S227–S239.)

<sup>g</sup>Consider permanent filters only for rare patients with permanent contraindications to anticoagulation or with chronic comorbidities.

<sup>h</sup>See [Elements for Consideration in Decision Not To Treat \(VTE-F\)](#).

Note: All recommendations are category 2A unless otherwise indicated.

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# Acute Pulmonary Embolism in Cancer Patient

- 6.4 If no high risk for bleeding, then anticoagulation to extend beyond 3 months [1B]. Reassess annually.

If high risk for bleeding, then anticoagulation to extend beyond 3 months [2B]. Reassess annually.



# UE Catheter Associated DVT

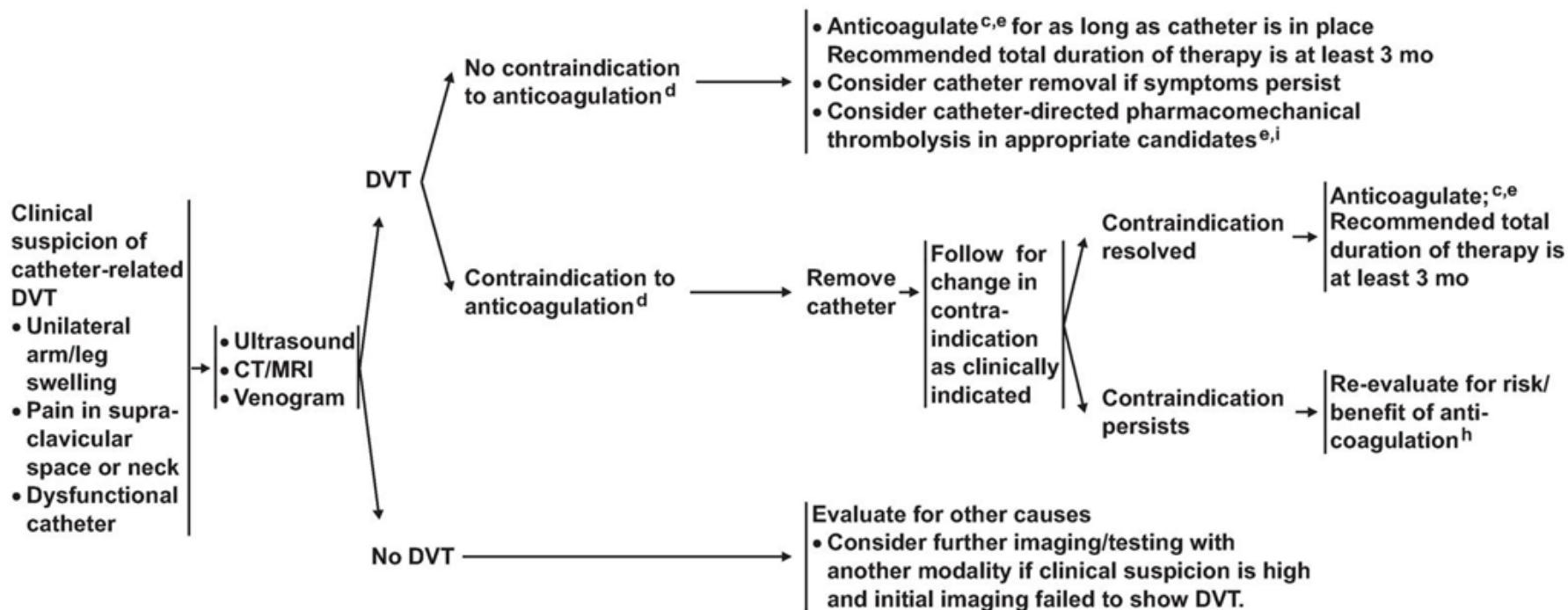
- 9.3.3 UE DVT with properly functioning CVC that has an ongoing need for use, then recommend not to remove catheter [2C].
- 9.3.2 Recommend anticoagulation therapy for at least 3 months [2B].
- 9.3.3. In patients who have UEDVT that is associated with a central venous catheter that is removed, we recommend 3 months of anticoagulation over a longer duration of therapy in patients with no cancer (Grade 1B) , and we suggest this in patients with cancer (Grade 2C) .
- 9.3.4 UEDVT that is associated with a central venous catheter that is not removed, we recommend that anticoagulation is continued as long as the central venous catheter remains over stopping after 3 months of treatment in patients with cancer (Grade 1C)

CATHETER-RELATED DVT: DIAGNOSIS AND TREATMENT

DIAGNOSIS

WORKUP/IMAGING

TREATMENT



<sup>c</sup>See Therapeutic Anticoagulation Treatment for Venous Thromboembolism (VTE-D).

<sup>d</sup>See Contraindications to Prophylactic or Therapeutic Anticoagulation Treatment (VTE-B).

<sup>e</sup>See Anticoagulation Failure (VTE-H), if extension of VTE or new VTE while on recommended anticoagulation therapy.

<sup>f</sup>Choice of regimen should be made based upon institutional expertise/preferences in conjunction with interventional radiology or vascular surgery colleagues (See Thrombolytic Agents [VTE-I]).

<sup>h</sup>See Elements for Consideration in Decision Not To Treat (VTE-F).

<sup>i</sup>See Contraindications to Thrombolysis (VTE-J).

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**THE END**