

# Deep vein thrombosis (DVT) as the first sign of an occult malignant disease – how often and what is the adequate diagnostic approach?

VEN3: Prevention and medical therapy of deep vein thrombosis (DVT)

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## Disclosure

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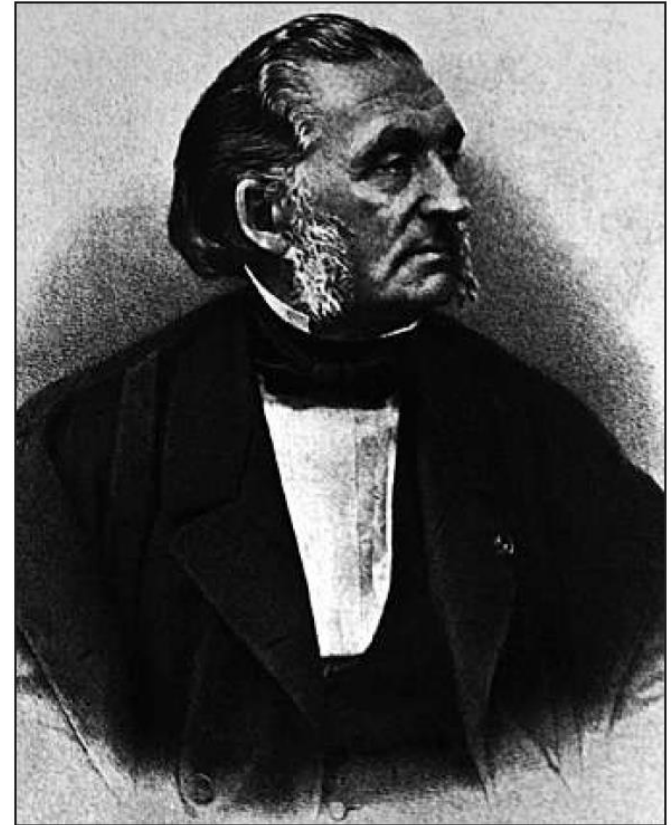
I have the following potential conflicts of interest to report:

- Consulting
- Employment in industry
- Stockholder of a healthcare company
- Owner of a healthcare company
- Other(s)
  
- I do not have any potential conflict of interest

## Trousseau`s Syndrome

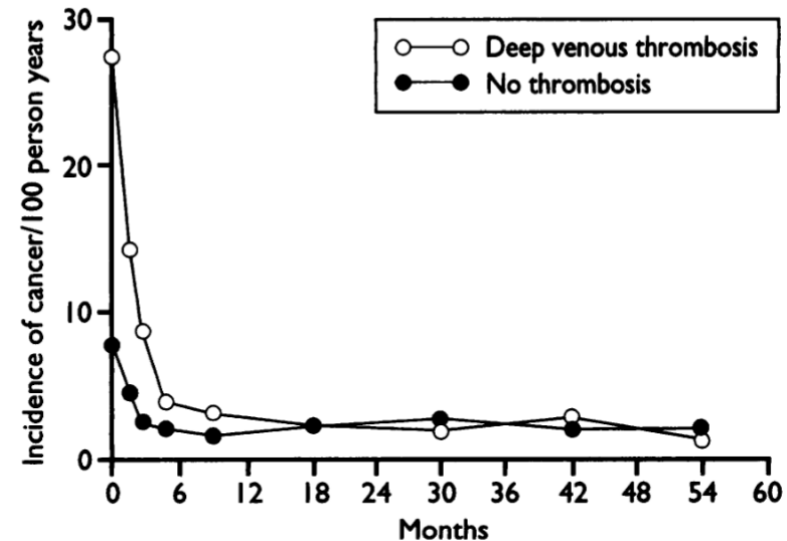
Armand Trousseau reported an association between thromboembolic disorders „*Phlegmasia alba*“ and malignant disease in his famous work „*Clinique médicale de l´Hôtel Dieu de Paris*“ first published in 1865.

When Trousseau himself later suffered from phlebitis of the left arm, he correctly diagnosed stomach cancer, from which he died six months later.



## Incidence of Occult Malignancy in Patients with DVT

- Reported incidence of a subsequent diagnosis of malignancy in unselected patients presenting with DVT:  $\leq 10\%$
- Highest risk during the first six months following the initial diagnosis of DVT
  - $>60\%$  of occult cancers are shortly diagnosed after DVT
  - thereafter incidence declines and returns to the rate in general population after one year
- Most common malignancies found
  - hematologic malignancies
  - cancer of the ovary, pancreas, liver, kidney, lung



Deep venous thrombosis and occult malignancy: an epidemiological study. Nordström et al. BMJ. 1994;308(6933) 891.

# Screening for Occult Cancer in Patients with Unprovoked DVT

## Pros

Screening often is considered with the aim of

- detecting underlying cancer at an early curable stage
- reducing cancer-related morbidity and mortality

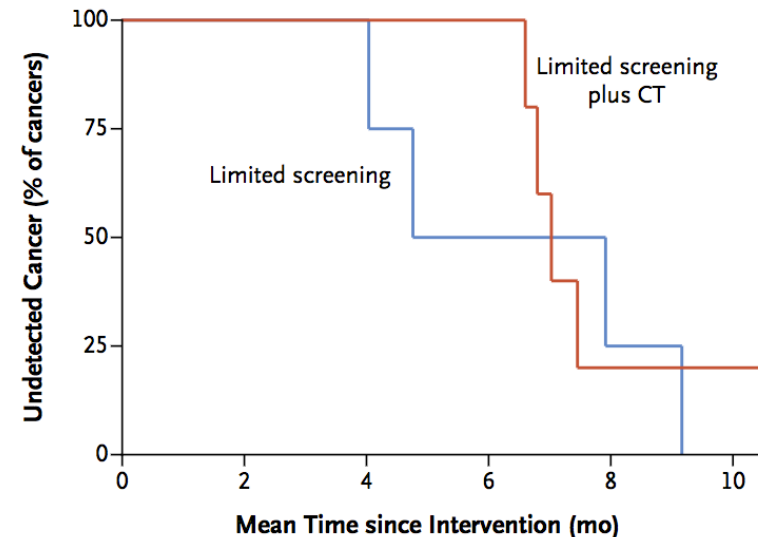
## Cons

Extensive screening strategies may

- yield false-positive findings
  - require additional, sometimes invasive testing
  - increase health care costs
  - lead to patient anxiety
- Extent to which screening for occult cancer should be done in patients with unprovoked DVT is controversial

# SOME-Trial


- multicenter, open-label, randomized controlled clinical trial
- Patients (n=854)  
first unprovoked venous thromboembolism
- Limited occult cancer screening ↔ more extensive screening including CT scan of abd/pelvis
- Primary outcome measure  
confirmed cancer missed by respective screening and detected by the end of the 1-year follow-up
- Results  
no significant difference between the two study groups regarding
  - time to cancer diagnosis
  - cancer-related mortality



No. at Risk	0	2	4	6	8	10
Limited screening	4	4	4	2	1	0
Limited screening plus CT	5	5	5	5	1	1

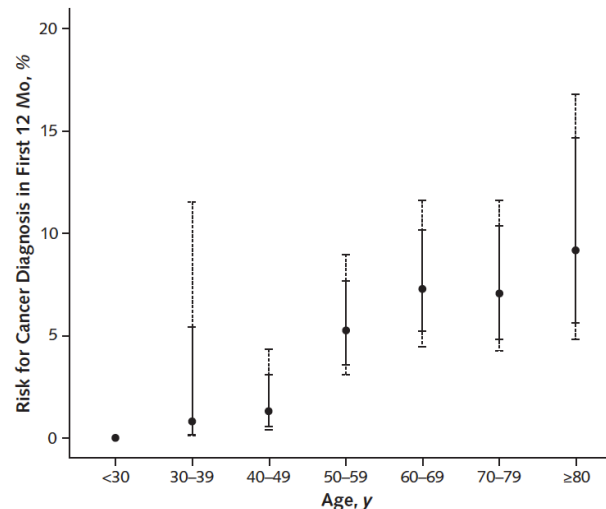
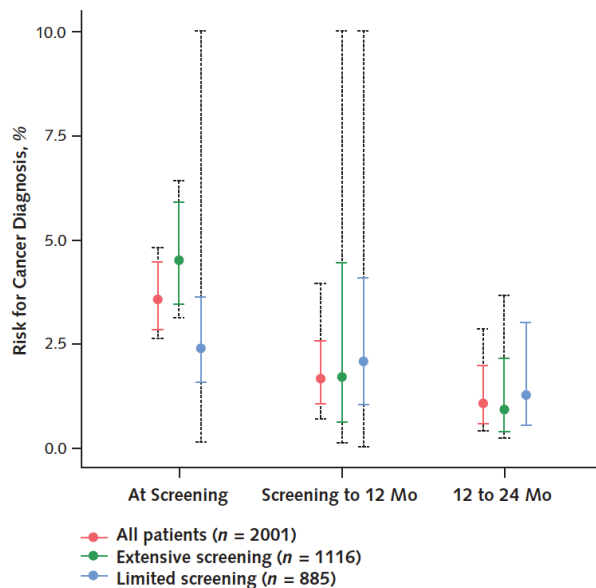
Screening for Occult Cancer in Unprovoked Venous Thromboembolism.  
Carrier et al. N Engl J Med 2015;373:697-704.

## $^{18}\text{F}$ FDG-PET/CT in Screening for Occult Malignancy

- multicenter, open-label, randomized controlled clinical trial
- Patients (n=399)  
unprovoked venous thromboembolism
- Limited occult cancer screening  more extensive screening  
including  $^{18}\text{F}$ FDG-PET/CT scan
- Primary outcome  
proportion of patients receiving a cancer diagnosis after completing  
the initially allocated screening assessment
- Results
  - screening strategy including  $^{18}\text{F}$ FDG-PET/CT was not  
associated with a significantly higher rate of cancer diagnosis
  - risk of subsequent cancer was lower in patients with  
negative results on initial screening including  $^{18}\text{F}$ FDG-PET/CT

# Systematic Review and Meta-Analysis

- Purpose  
estimating prevalence of occult cancer in patients with unprovoked VTE stratified for type of screening and patients age
- Study selection  
10 prospective studies evaluating screening strategies in adults with unprovoked VTE  
n=2316



Screening for Occult Cancer in Patients with Unprovoked Venous Thromboembolism. A Systematic Review and Meta-analysis of Individual Patient Data. van Es et al. Ann Intern Med.2017;167:410-417.



## Feasible Diagnostic Approach

- **Limited testing**  
all patients with a first episode of unprovoked DVT
- **Extensive testing**  
restricted to patients considered at high risk for malignancy
  - symptoms/signs suggestive of an underlying malignancy
  - recurrent DVT
  - venous thromboembolism at rather unusual sites, e.g.
    - \* hepatic and portal vein thrombosis
    - \* arterial thromboembolism suggestive of nonbacterial thrombotic endocarditis
    - \* splanchnic vein thrombosis or cerebral vein thrombosis

## Limited Testing

- Complete medical history
- Physical examination including
  - digital rectal examination
  - testing for fecal occult blood
  - pelvic examination in women
- Basic laboratory testing including
  - complete blood count and smear
  - erythrocyte sedimentation rate (ESR)
  - urinalysis
  - electrolytes, calcium, creatinine and liver function tests
- Chest radiograph
- Routine age- and sex-specific cancer screening

## Extensive Testing

- panel of essential investigations -beyond the components of limited testing- still not defined
- testing is frequently symptom-directed, e.g.
  - CT scan of chest, abdomen and pelvis
  - Tumormarkers, e.g. CEA, CA19-9, AFP, CA125, PSA
  - Mammography and Papanicolaou smear in women
  - Upper and lower gastrointestinal tract evaluation

## Summary and Conclusion

- For patients with unprovoked DVT limited screening for occult malignancy is currently suggested appropriate
  - medical history, physical examination, basic blood work, chest radiograph and age-/sex-specific cancer screening
- Additional testing is solely recommended for patients who are thought to be at high risk of having a malignancy
- Testing should be done preferably at the time of admission or shortly thereafter as incidence of cancer diagnosis is greatest in the first six months following DVT
- Although testing leads to an increased detection of cancer no convincing survival advantage due to any testing strategy could have been shown so far

Thank you very much for your attention!