CANCER-ASSOCIATED THROMBOSIS: PREDICTION, PREVENTION, AND MANAGEMENT
MIAMI CANCER MEETING APRIL 28, 2023

Ted Wun, M.D., F.A.C.P.
Professor of Medicine, Associate Dean for Research
Director/PI, UC Davis Clinical and Translational Science Center
MPI, California Cancer Reporting and Epidemiologic Surveillance (California Cancer Registry)
University of California, Davis School of Medicine

Objectives

Describe

- Describe the epidemiology, clinical relevance, and pathophysiology of cancer-associated thrombosis

Review

- Review recent developments in primary and secondary prophylaxis

Special Situations

- Upper Extremity DVT
- Isolated distal DVT
- Incidental thrombosis
- Brain tumors
- IVC Filters

Take

- Take questions


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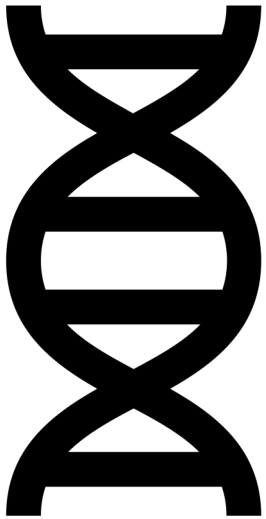
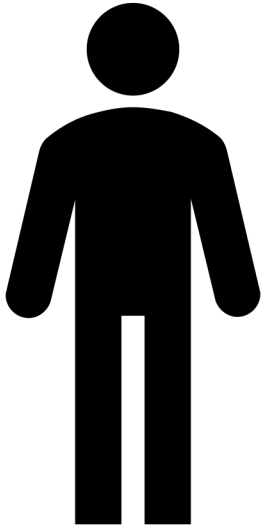
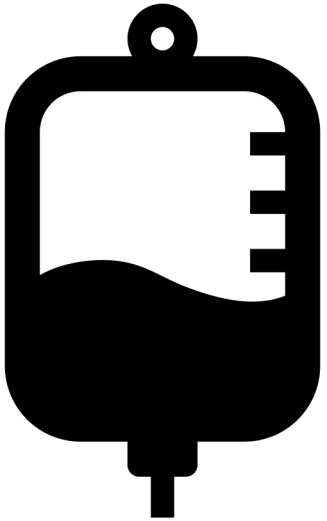
Clinical Relevance

Second leading cause of acute death in cancer patients

Morbidity and delays in therapy

Associated with increased cancer related mortality

Dinged by CMS

Pathophysiology

Therapy

Primary Prevention

Secondary Prevention

Primary Prevention

Identification of high-risk patients

Thromboprophylaxis

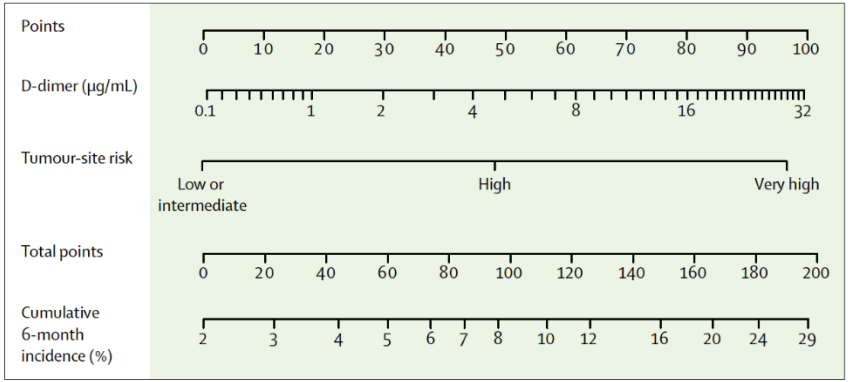
Khorana Score

Covariate	Points	Risk score (points)	VTE rate (%)
Cancer Type			
Stomach, pancreas	2	Low (0)	0.3–0.8
Lung, lymphoma, gynecologic, bladder, testicular	1	Intermediate (1–2)	1.8–2.0
Platelet count >350,000/μL	1	High (≥3)	6.7–7.1
White blood cell count >11,000/μL	1		
Hemoglobin <10 g/dL or erythropoietin therapy	1		
Body-mass index >35 kg/m²	1		

NEJM Journal Watch

Vienna CATS Prediction Model

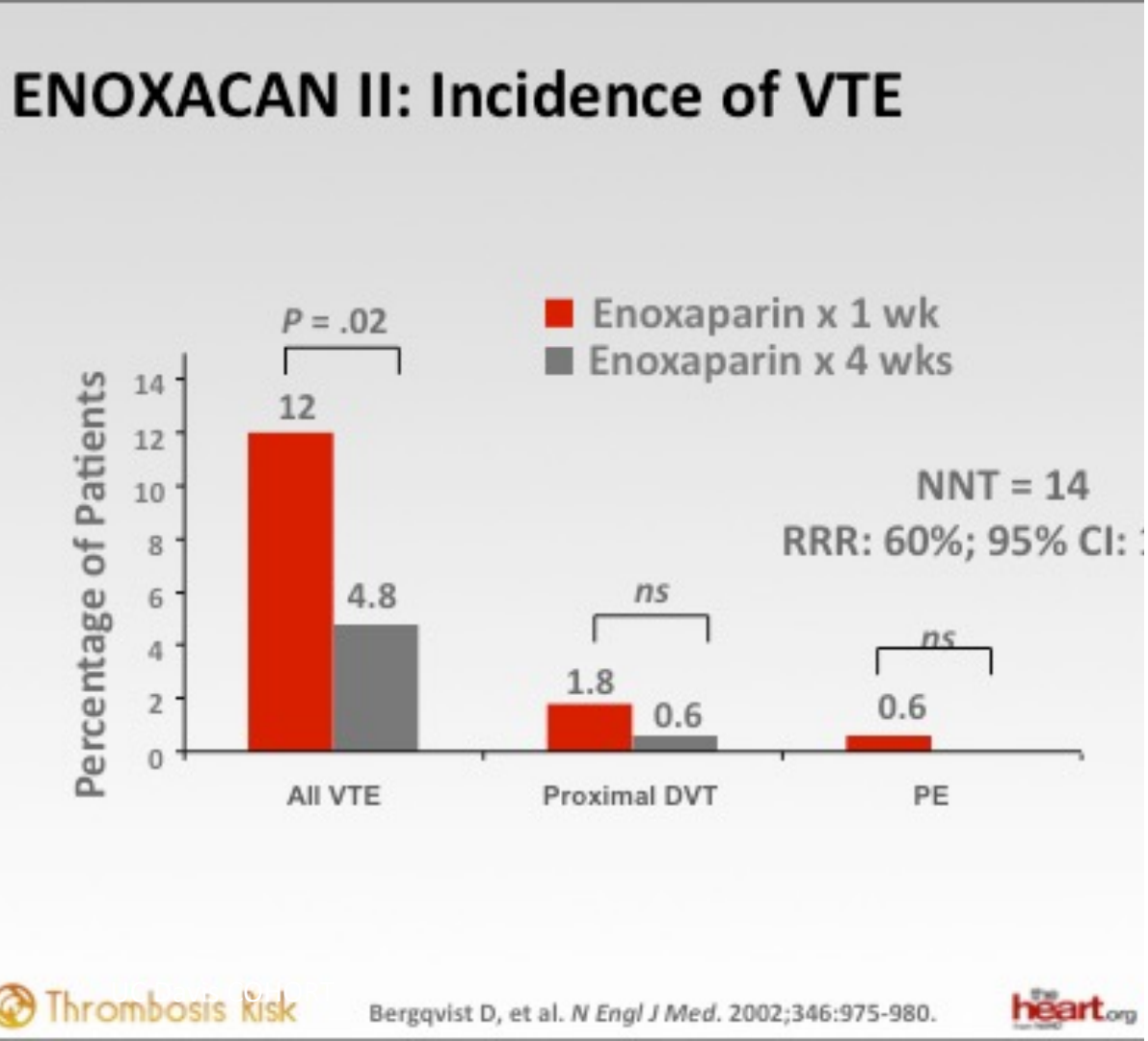
- D-dimer
- Type of tumor



Active cancer (metastases and/or chemoradiotherapy in the previous 6 months)	3
Previous VTE (with the exclusion of superficial vein thrombosis)	3
Bedrest for ≥3 days	3
Thrombophilia	3
Recent (≤1 month) trauma and/or surgery	2
Elderly age (≥70 years)	1
Heart and/or respiratory failure	1
Acute myocardial infarction or ischemic stroke	1
Acute infection and/or rheumatologic disorder	1
Obesity (BMI ≥30 kg/m^2)	1
Ongoing hormonal treatment	1

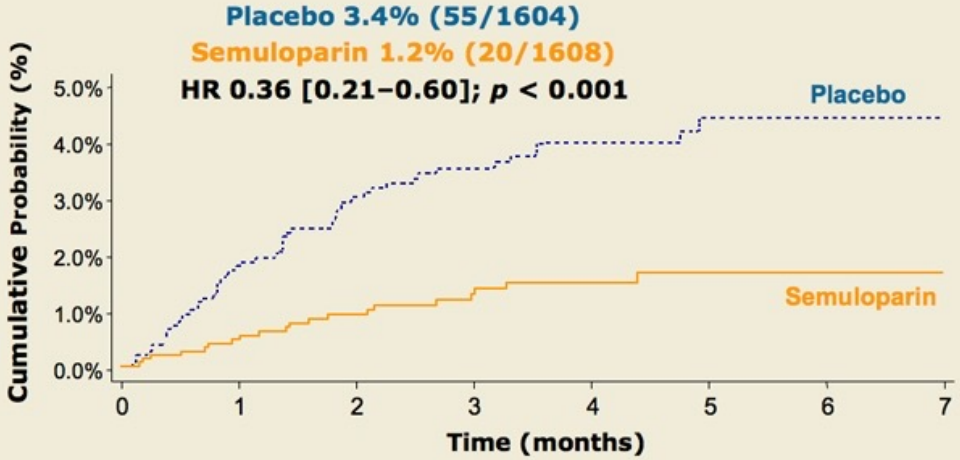
High risk of VTE: >4 points. VTE: Venous thromboembolism;

Padua Score Inpatient Risk



Postoperative prophylaxis

Primary Endpoint: Composite of VTE or VTE-Related Deaths



HR = hazard ratio
A 64% relative risk reduction was observed over median treatment duration of approximately 3.5 months.

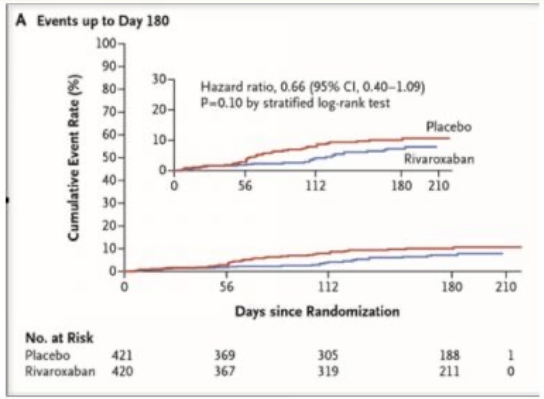
Agnelli G et al. *N Engl J Med* 2012;366(7):601-9. Copyright © 2012 Massachusetts

SAVE-ONCO

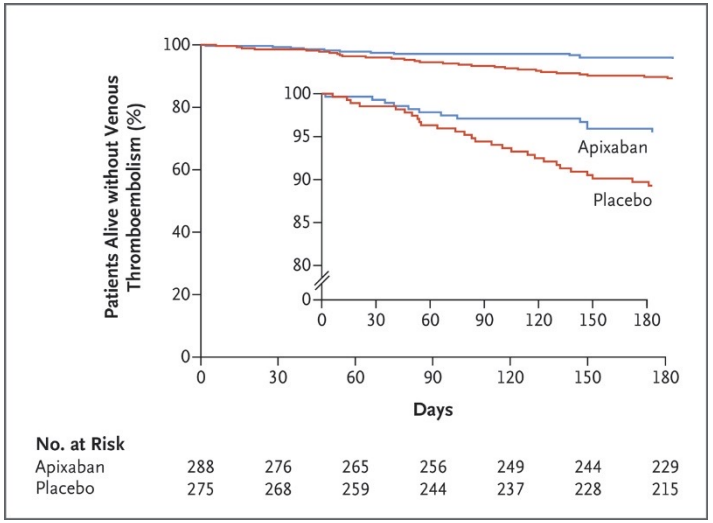
LMWH for Ambulatory Cancer Patients

Directed Oral Anticoagulants in Primary Prophylaxis Ambulatory Cancer Patients

Curve di Kaplan–Meier per Primary Efficacy End Point in the Intention-to-Treat period e Intervention period



Khorana et al. NEJM 2019;380:720-8.



Carrier et al. N Engl J Med 2019; 380:711-719

Secondary Prophylaxis

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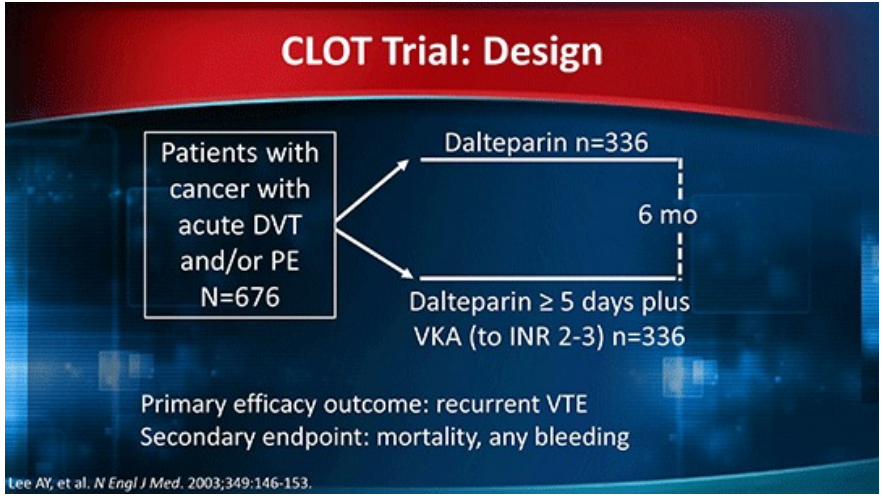
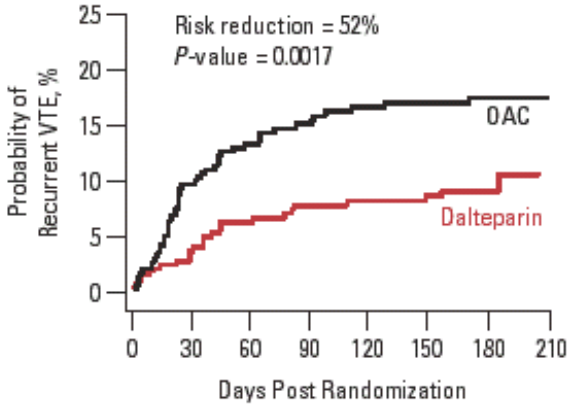


Figure 1.
CLOT Study: Recurrent VTE



Source: *N Engl J Med.* 2003;349:146-153.

Treatment of Cancer-associated Thrombosis

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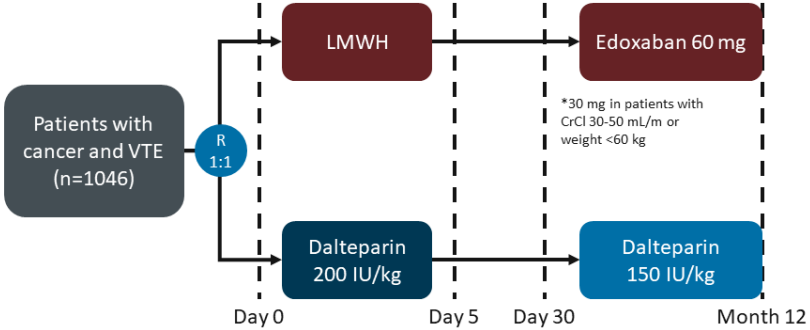
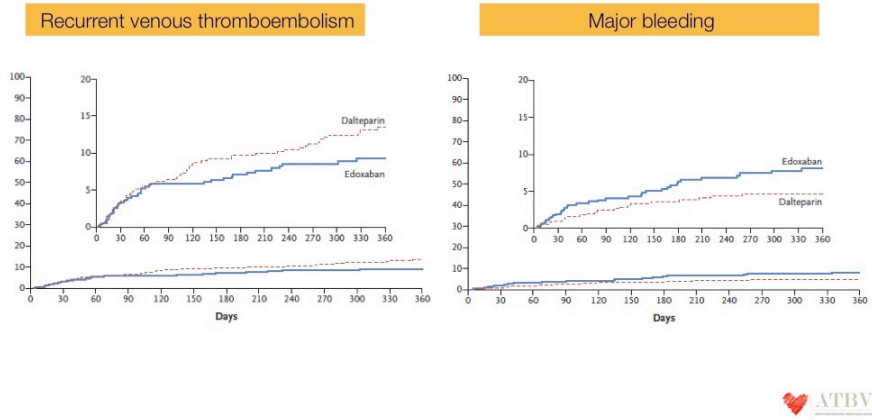
Hokusai VTE-Cancer Study: Design



- Primary outcomes: recurrent VTE, major bleeding

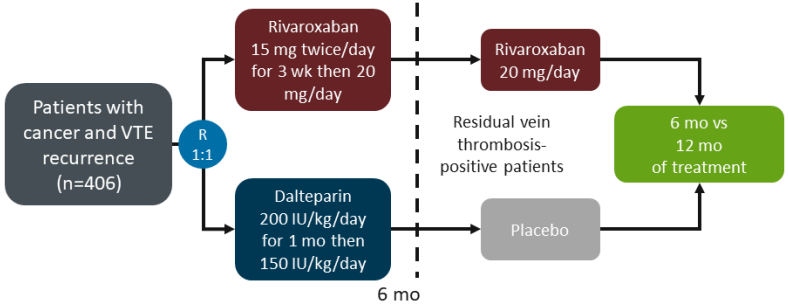
Hokusai VTE Cancer



Raskob G.E. et al. N Engl J Med, December 12, 2017

Edoxaban for Treatment of CAT

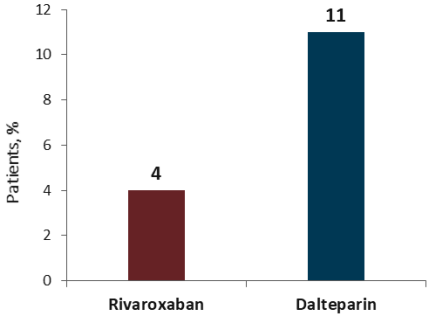
SELECT-D Trial: Design



- Primary outcome: recurrent VTE

Young A, et al. *Thromb Res.* 2016;140:S172-S173.

SELECT-D Trial: Primary Endpoint



54% of patients completed 6 months of trial treatment
- 52% on dalteparin
- 55% on rivaroxaban

- N=406
- Major bleeds were similar: 3% with dalteparin, 4% with rivaroxaban

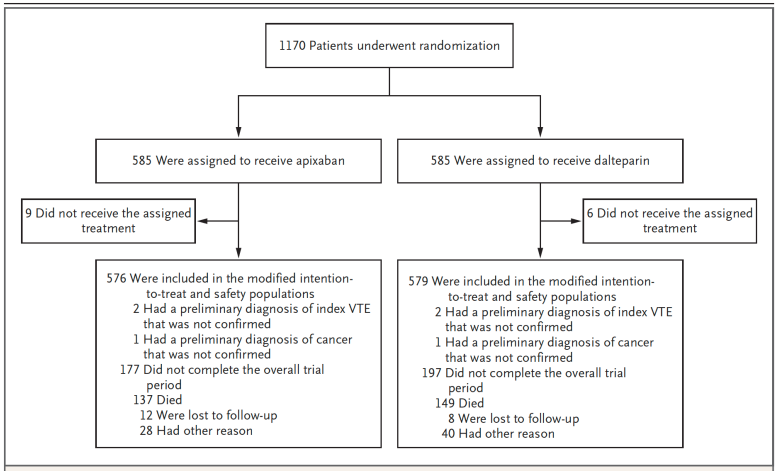
Young A, et al. Data presented at 59th ASH Annual Meeting, Atlanta, Georgia ,December 9-12, 2017. Abstract 625.

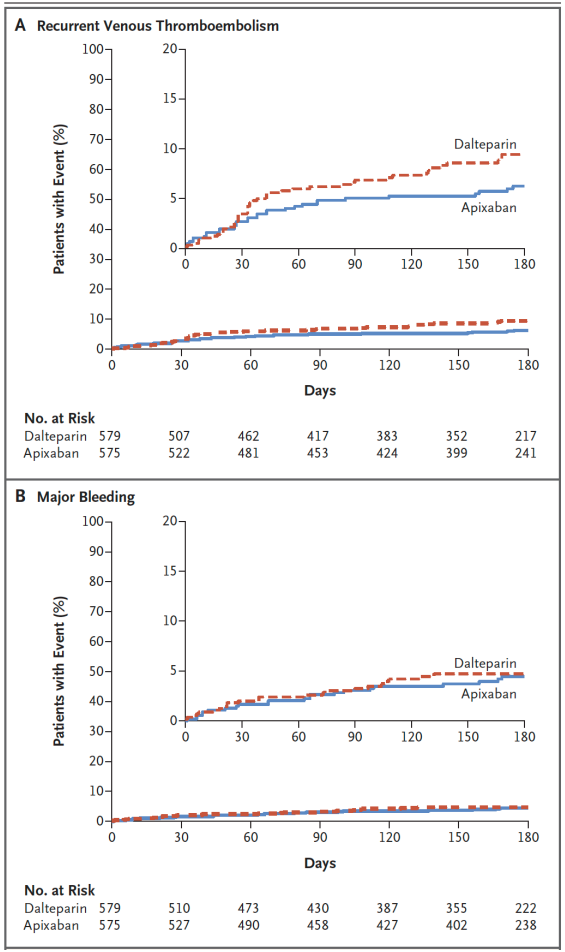
Rivaroxaban for CAT

ORIGINAL ARTICLE

Apixaban for the Treatment of Venous Thromboembolism Associated with Cancer

Giancarlo Agnelli, M.D., Cecilia Becattini, M.D., Guy Meyer, M.D., Andres Muñoz, M.D., Menno V. Huisman, M.D., Jean M. Connors, M.D., Alexander Cohen, M.D., Rupert Bauersachs, M.D., Benjamin Brenner, M.D., Adam Torbicki, M.D., Maria R. Sueiro, M.D., Catherine Lambert, M.D., Gualberto Gussoni, M.D., Mauro Campanini, M.D., Andrea Fontanella, M.D., Giorgio Vescovo, M.D., and Melina Verso, M.D., for the Caravaggio Investigators*





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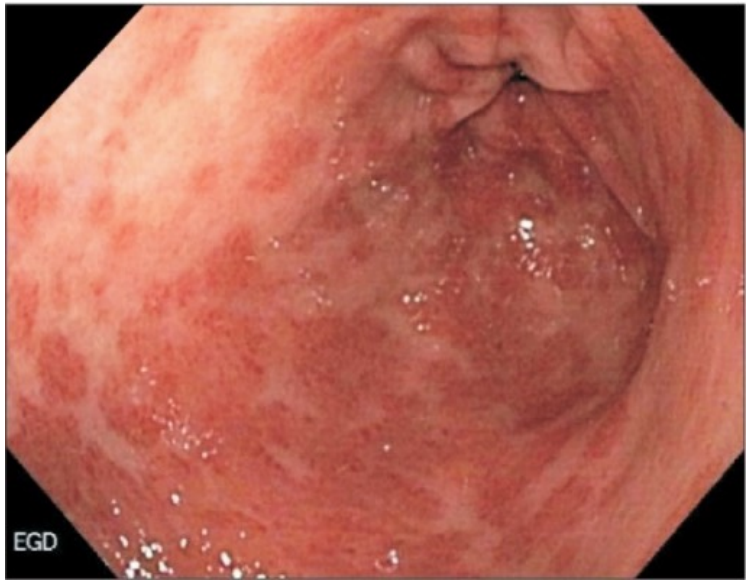
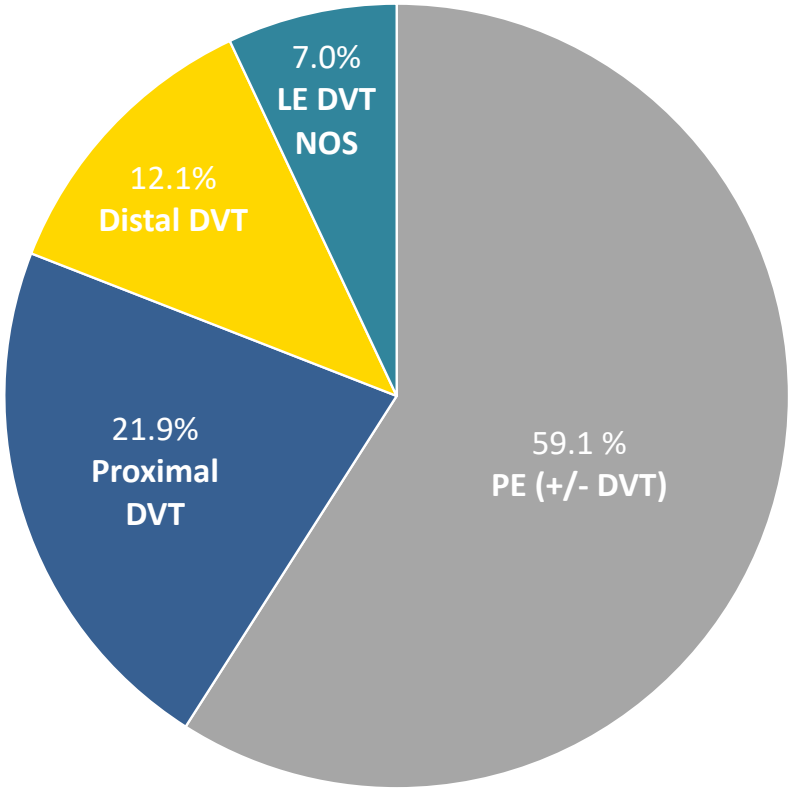
Overall Bleeding Higher with DOAC

Less CNS Bleeding with DOAC

More GI Bleeding with DOAC

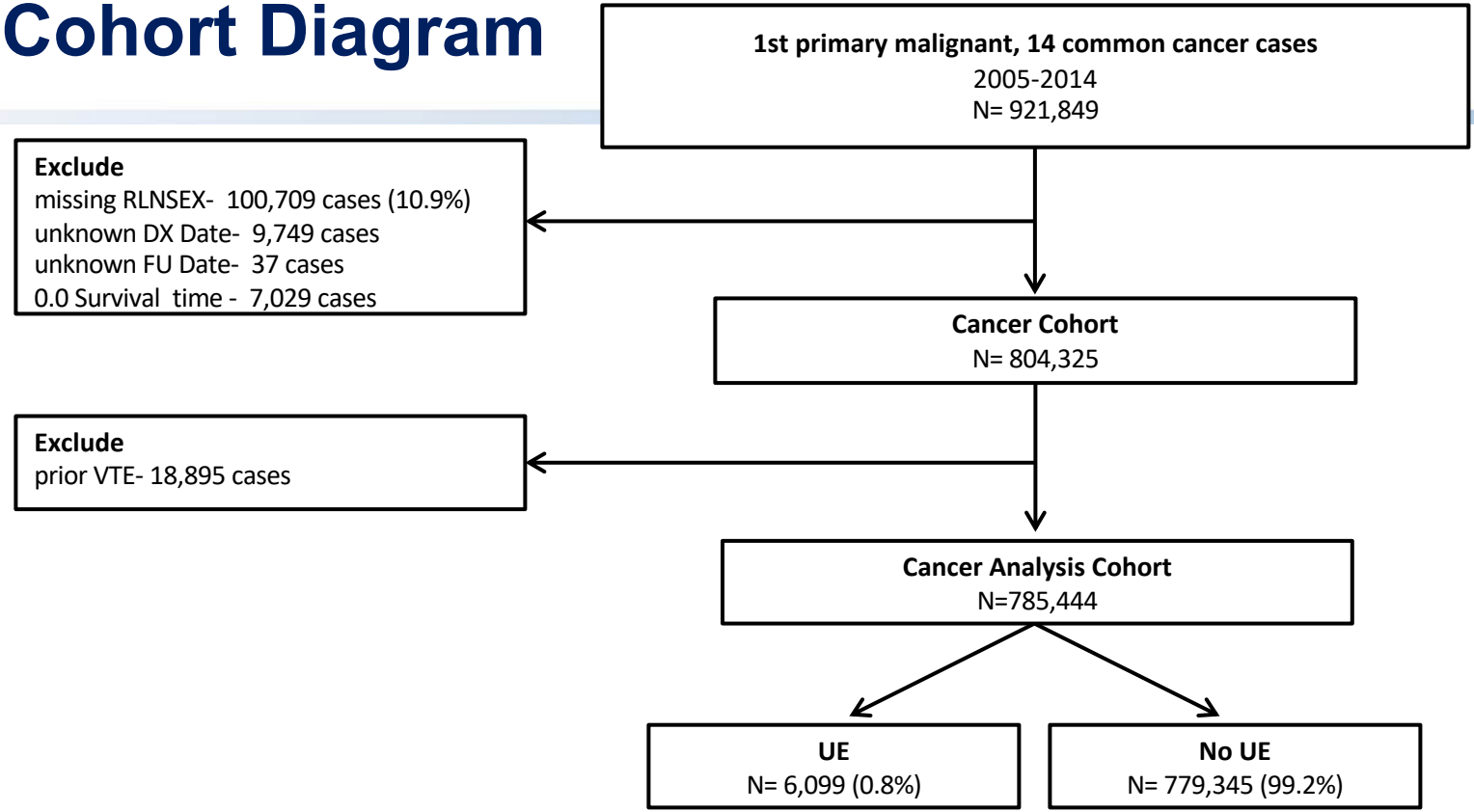


Distribution of Sites of Cancer-associated VTE (N=39,044)



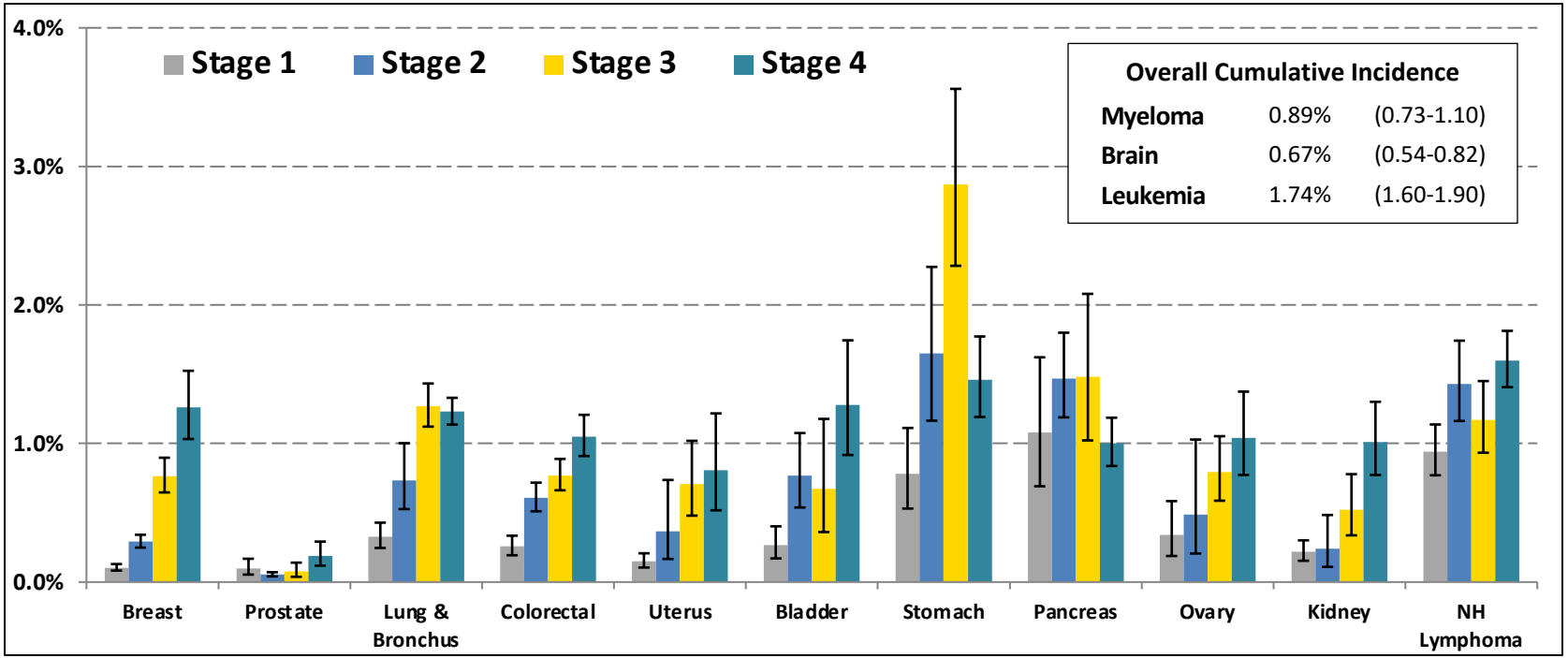
Upper Extremity Thrombosis

Cohort Diagram



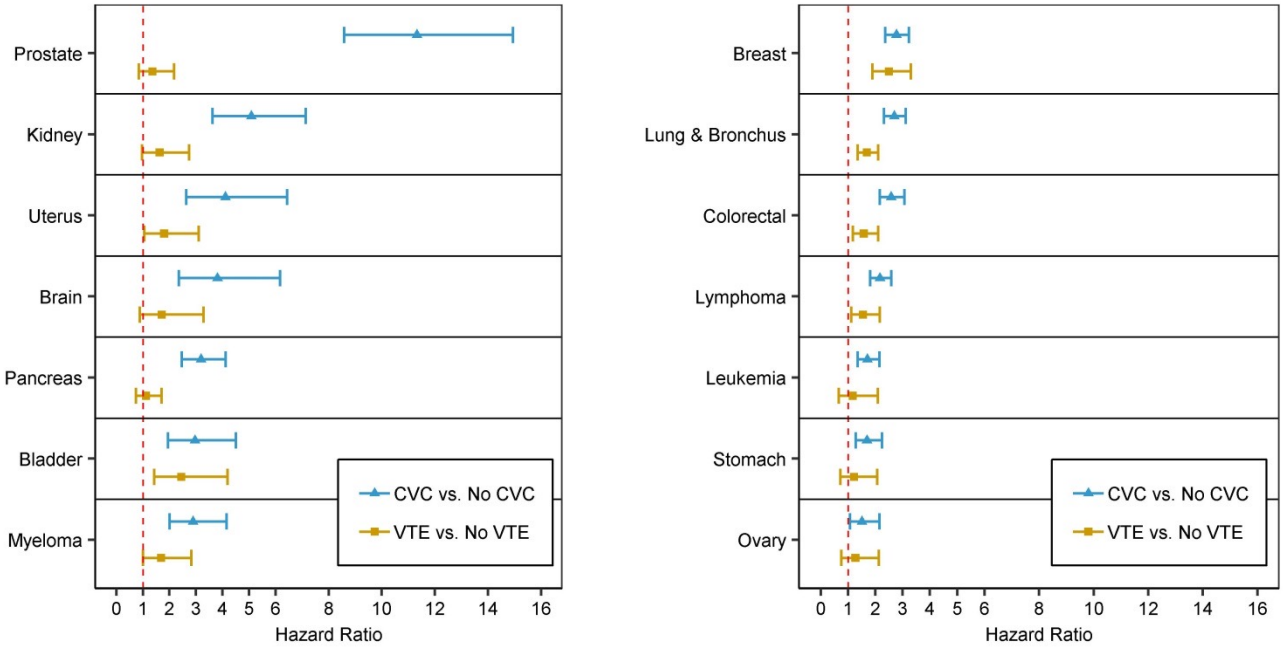
UCDAVIS COMPREHENSIVE CANCER CENTER

24-month cumulative incidence of incident UE-DVT by cancer type and stage at diagnosis



UC DAVIS COMPREHENSIVE CANCER CENTER

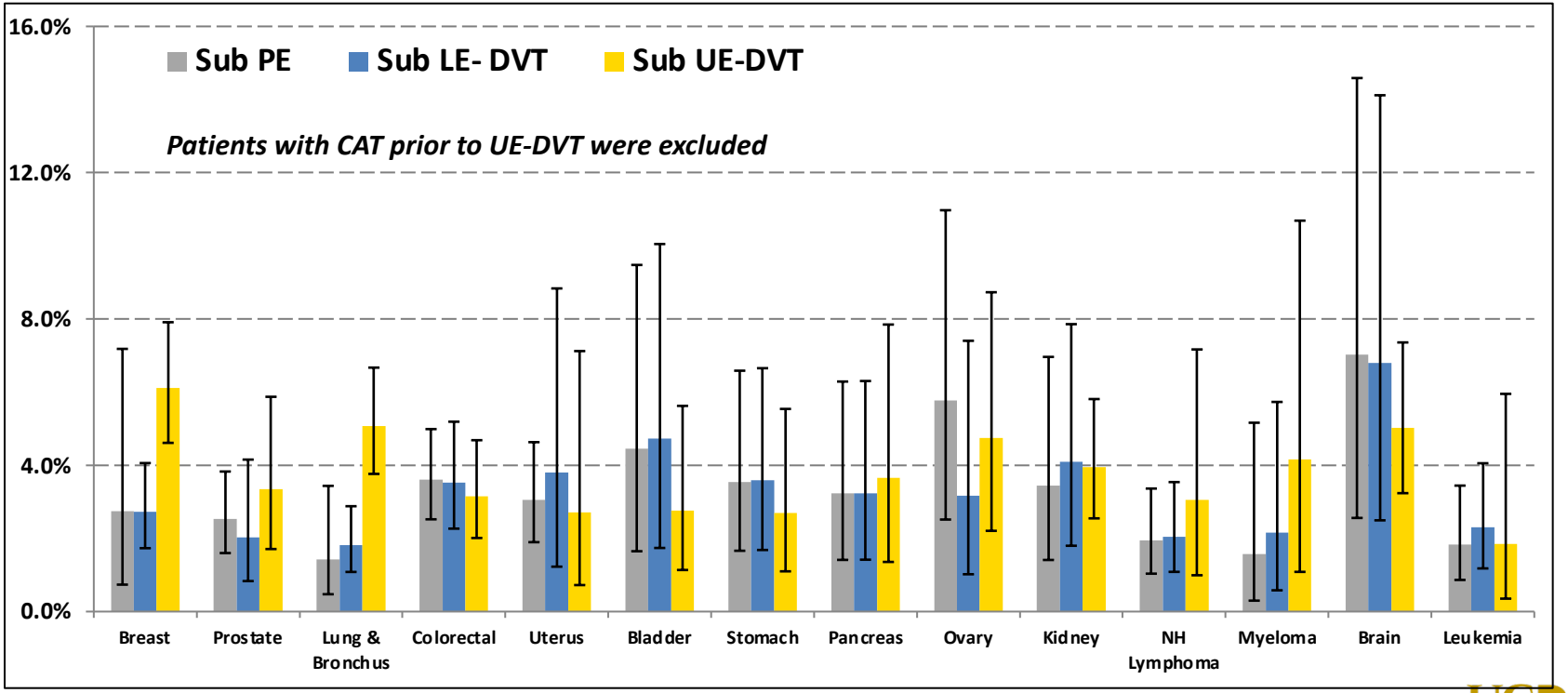
Association of CVC and VTE (cancer-associated) with UE-DVT by Cancer



Multivariable models were stratified by cancer type and adjusted for baseline characteristics. CVC and VTE were included as time-dependent covariates.

UCDAVIS COMPREHENSIVE CANCER CENTER

12-month cumulative incidence of subsequent thrombosis event after incident UE-DVT



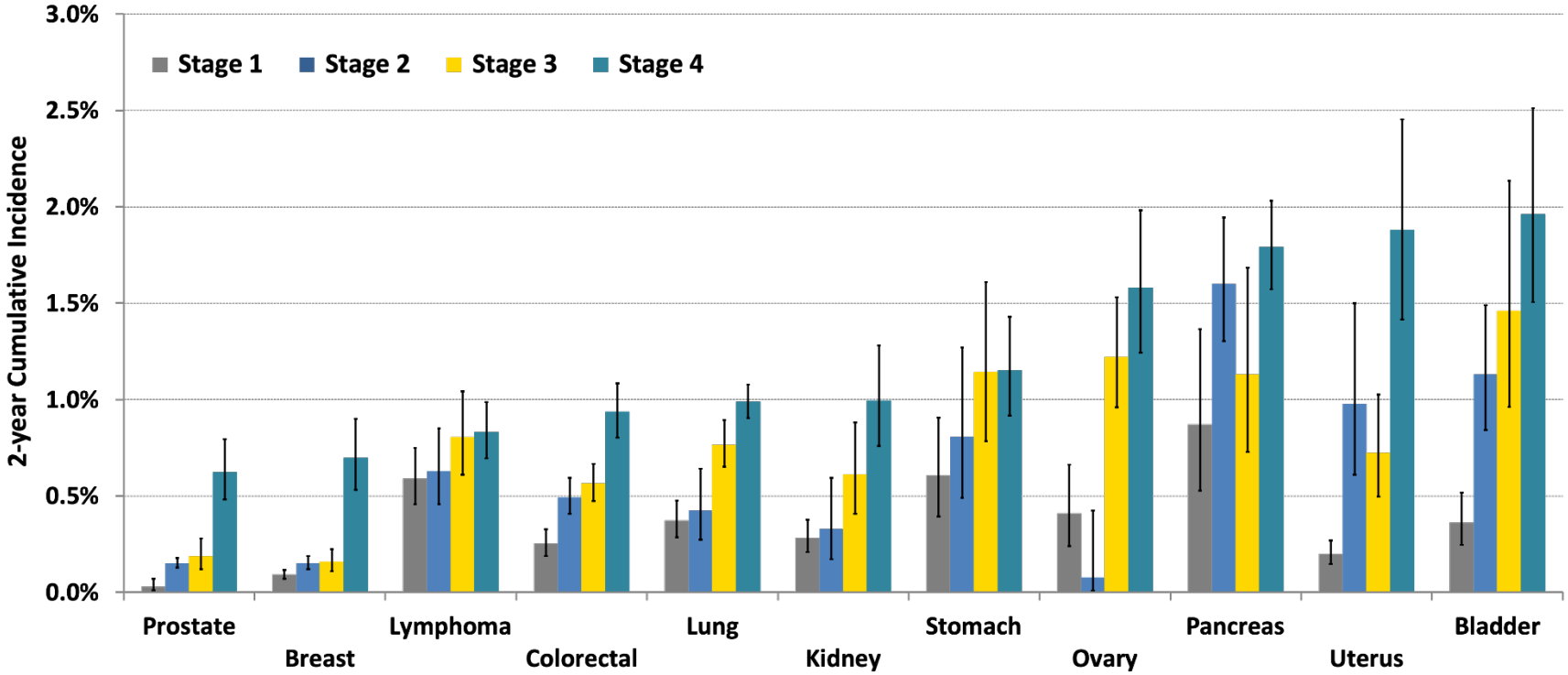
UCDAVIS COMPREHENSIVE CANCER CENTER

Upper Extremity DVT Summary

- The highest incidence of subsequent VTE were in patients with brain and ovarian and these tumors were also associated with the highest risk of subsequent PE
- The median time from index UE-DVT to subsequent VTE was 52 days (quartile range: 12-209 days)
- The lowest risks of subsequent VTE were in patients with prostate cancer and myeloma

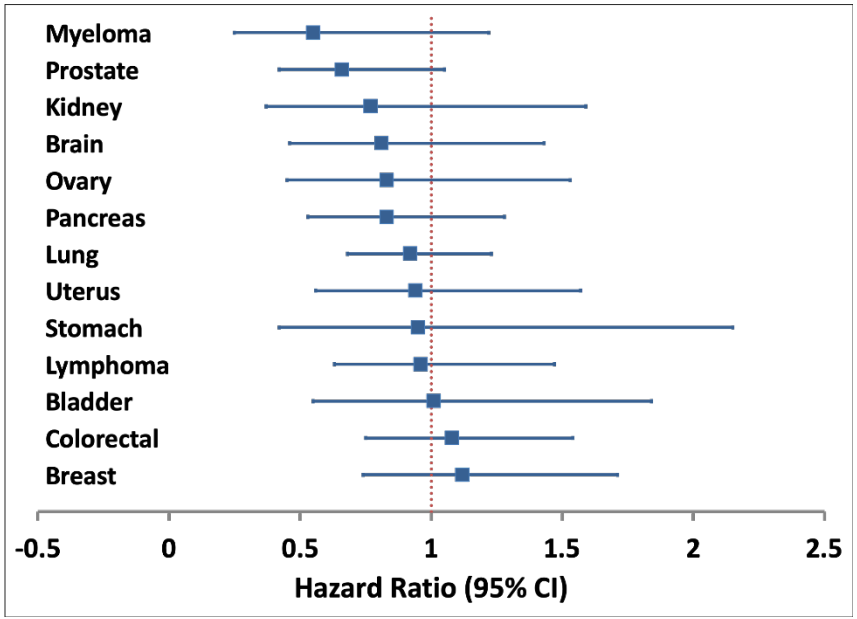
Isolated Distal DVT

Isolated Distal DVT

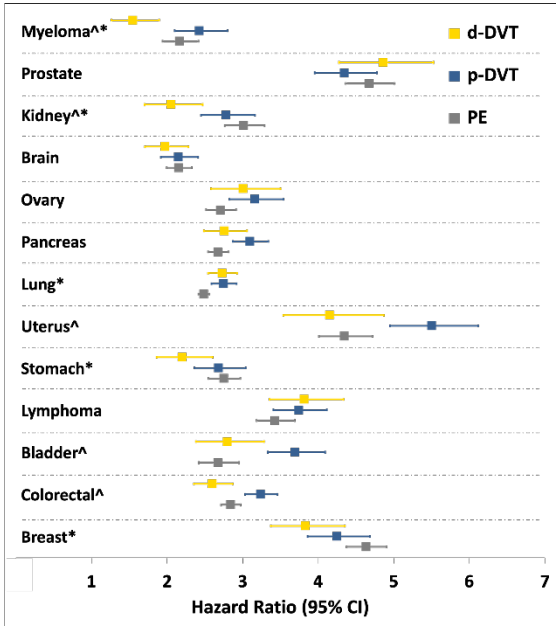


Clinical Relevance of iDDVT

Subsequent VTE not different than pDVT



Similar association with death

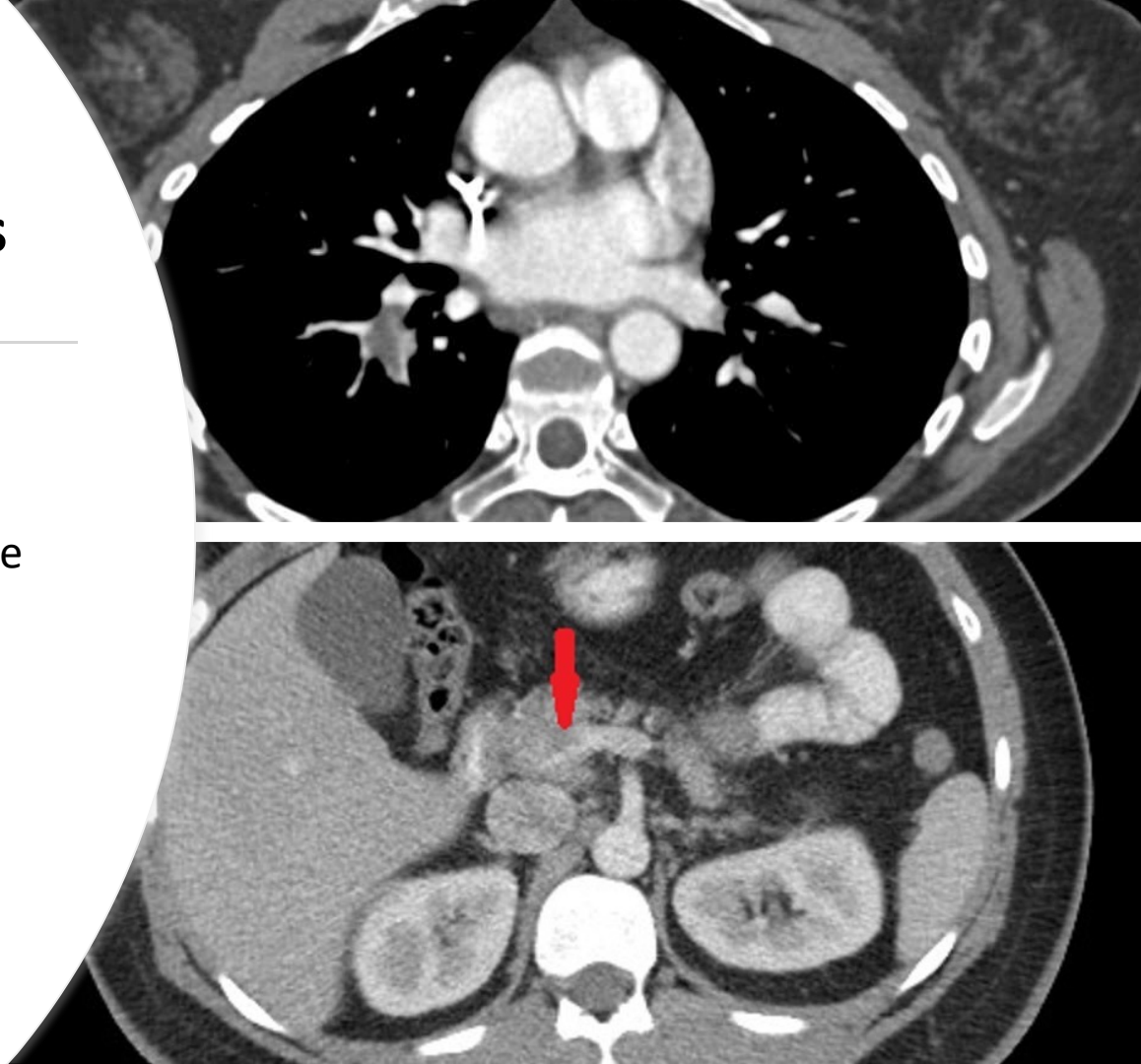


Recurrent Events After iDDVT

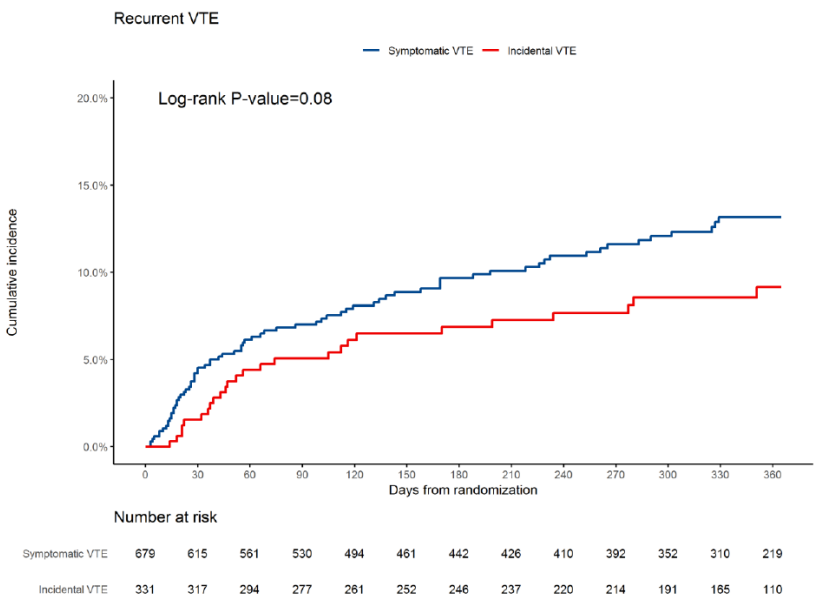
Index Site/Site of Recurrence	**PE**	**Proximal DVT**	**iDDVT**	**LE NOS**	**Total**
iDDVT					
4731	162	90	62	32	**346**
Percent	47%	26%	18%	9%	**7.3%**

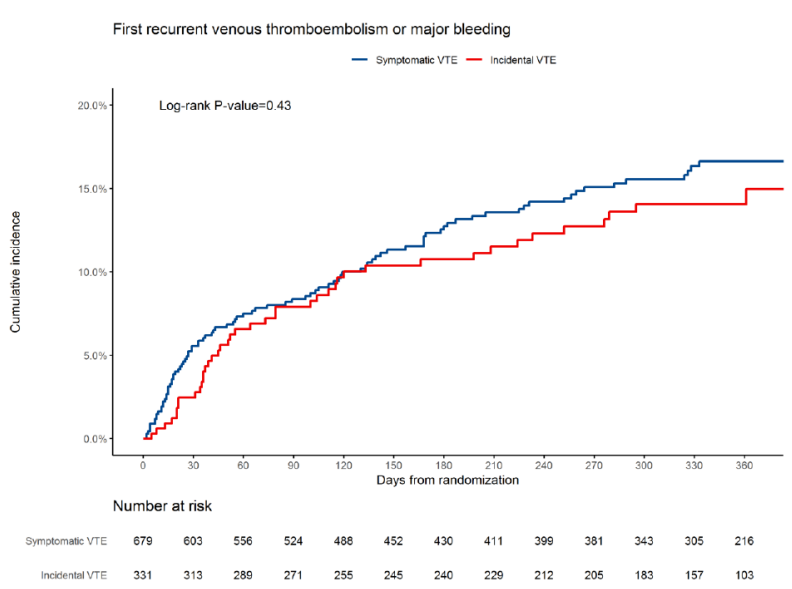
Incidental Thrombosis

- Found on routine scans
- Retrospective studies suggest that recurrence rates are same as for symptomatic events
  - Many have symptoms when queried
- Current recommendations are to treat as for symptomatic disease



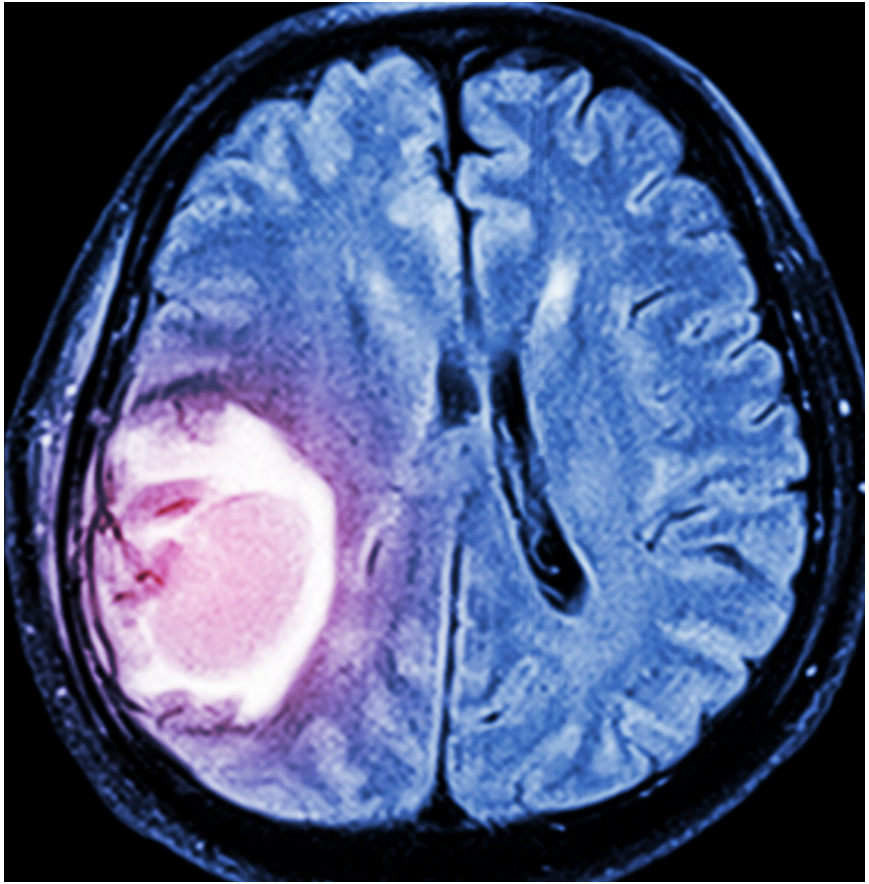
Incidental Versus Symptomatic VTE
Hokusai VTE Cancer





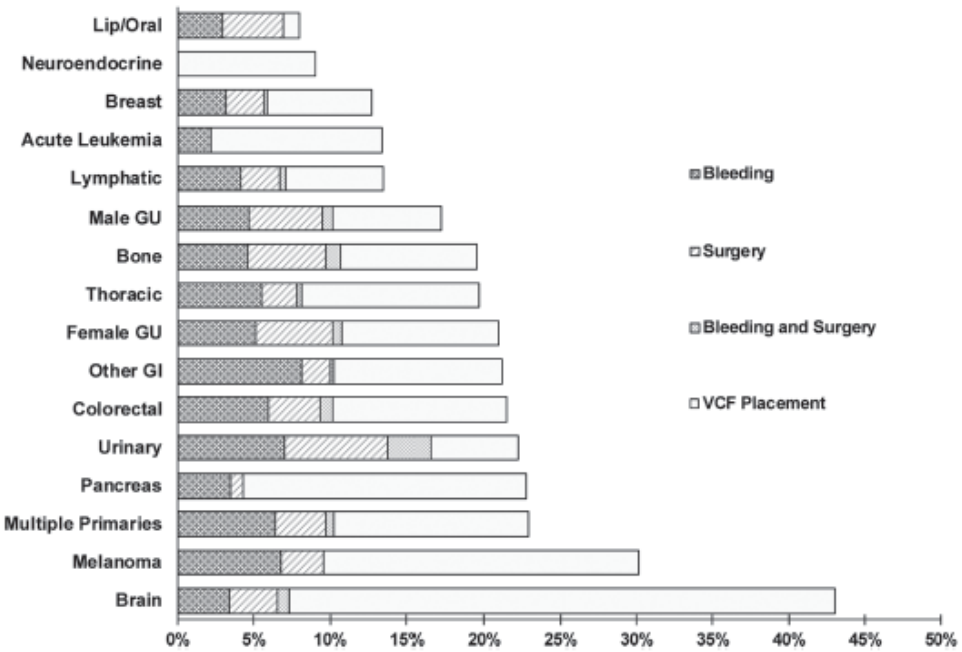
Brain Tumors and Therapeutic Anticoagulation

- Metastatic disease: no increased risk of intracranial hemorrhage (ICH)
- Glioma: 3X increased incidence of ICH
- Risk may be lower with DOAC than LMWH



Inferior Vena Cava Filters

- 14,000 cancer patients with acute VTE
- No decrease in
  - Bleeding
  - PE
  - Mortality
- Increase in recurrent DVT
- Recent observational study showed increased PE free survival with IVCF for patients with DVT only



Effect on mortality?

Recent studies do not demonstrate improvement in survival with anticoagulation

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Oncology COHORT

Conclusions

- Venous thromboembolism is a common complication of cancer
- Recent prospective RCT demonstrated the role of DOAC in treatment (secondary prophylaxis) of cancer-associated thrombosis
- There may be a role for primary prophylaxis in high-risk ambulatory patients
- The management of incidental and less common sites of cancer-associated thrombosis is predominantly informed by retrospective studies
- Research is needed to make improve risk prediction and tailor therapy for specific situations

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