VTE Perioperative Prophylaxis in CRS

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Hospitalists are the frontline providers that diagnose and manage hospital-acquired VTEs in hospitalized patients.

Nearly half of all venous thromboembolism (VTE) events occur during or soon after hospitalizations

VTE: A Major Source of Mortality and Morbidity

Over **200,000** deaths per year due to PE annually in the U.S. alone.

More than HIV, MVAs & Breast Cancer combined

Over **600,000** patients diagnosed with DVT annually in the US alone

10% of Hospital Deaths most common preventable death

Huge Costs and Morbidity

Recurrence of DVT, post-thrombotic syndrome and chronic PE / PAH are long term sequelae

Some Causes of Death in the US	Annual Number of Deaths
PE	Up to 200,000
AIDS	16,371
Breast Cancer	40,580

DVT Development Risks

VTE prophylaxis has already made The Joint Commission's list of Patient Safety Goals, which call for anticoagulation to be managed by protocol. Using unfractionated heparin and even low-molecular-weight heparin, we're going to have to have a guideline to manage those patients.

Several studies, including last year's Million Women Study, have shown that patients who have surgery for abdominal and pelvic cancers face a clot risk for at least a month. In the @RISTOS trial, 40% of surgical cancer patients' VTEs occurred after discharge, and the risk factors were the same, whether the clot appeared early or late.

DVT: What we know

Venous thromboembolism (VTE) is manifested clinically by deep venous thrombosis (DVT) and pulmonary embolism (PE). DVT, usually of the lower extremity, nearly always precedes PE. The risk of VTE increases greatly after age 50.

Other Risk Factors

- Age
- Trauma
- Immobilization,
- Surgery
- Anti-estrogen tamoxifen also increases the risk of VTE
- Inherited conditions that increase risk (thrombophilia) usually present before age 40, although it is not unusual to see the first episode of VTE in a patient with factor V Leiden appear after total hip replacement at age 65

Occurrence

The disease most often occurs in hospitalized patients, particularly those with cancer or following surgical procedures, but also occurs sporadically in the community. In both settings, multiple risk factors are usually present.

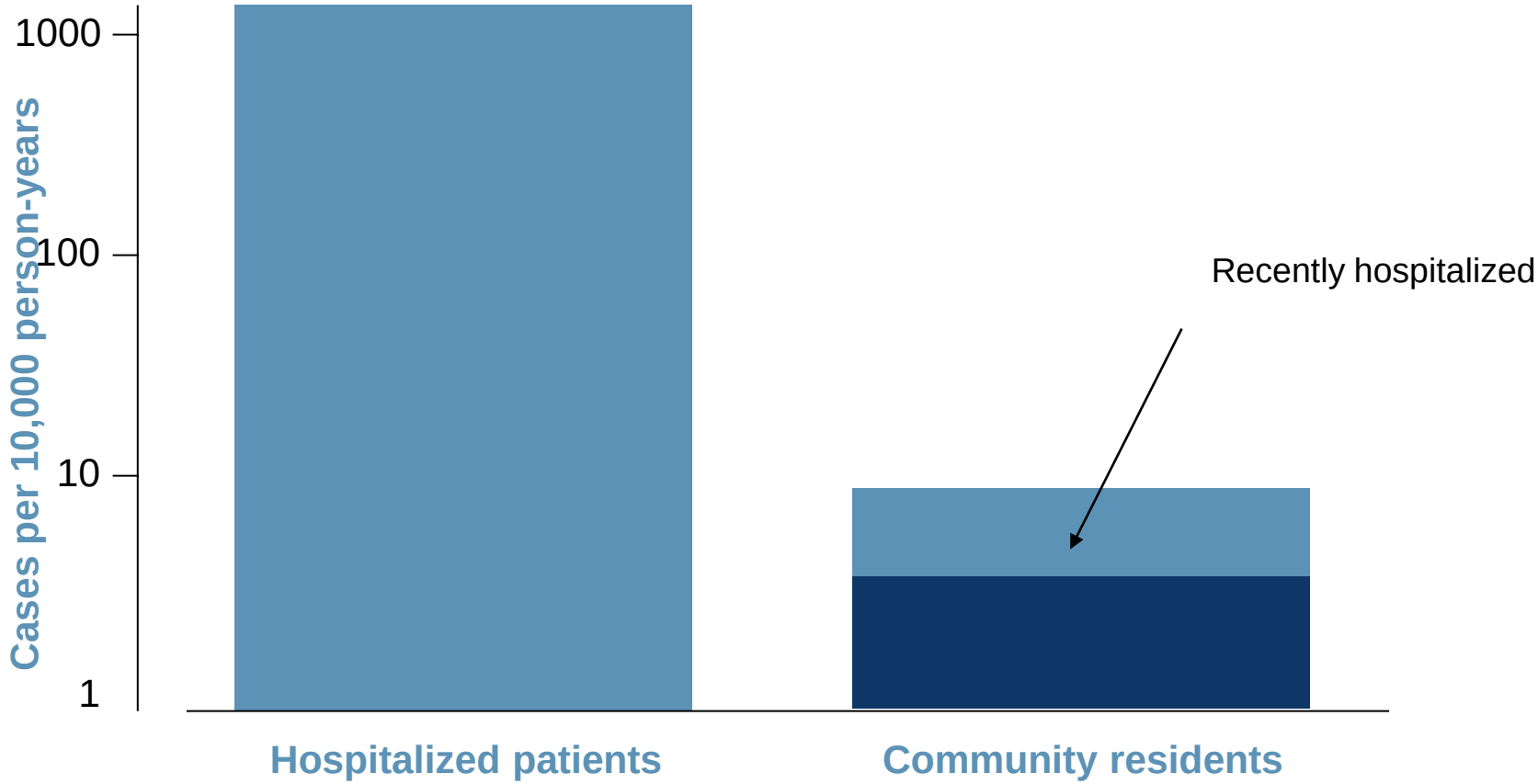
Risk of DVT in Hospitalized Patients

No prophylaxis + routine objective screening for DVT

Patient Group	DVT Incidence
Medical patients	10 - 26 %
Major gyne/urol/colorect surgery	15 - 40 %
Neurosurgery	15 - 40 %
Stroke	11 - 75 %
Hip/knee surgery	40 - 60 %
Major trauma	40 - 80 %
Spinal cord injury	60 - 80 %
Critical care patients	15 - 80 %

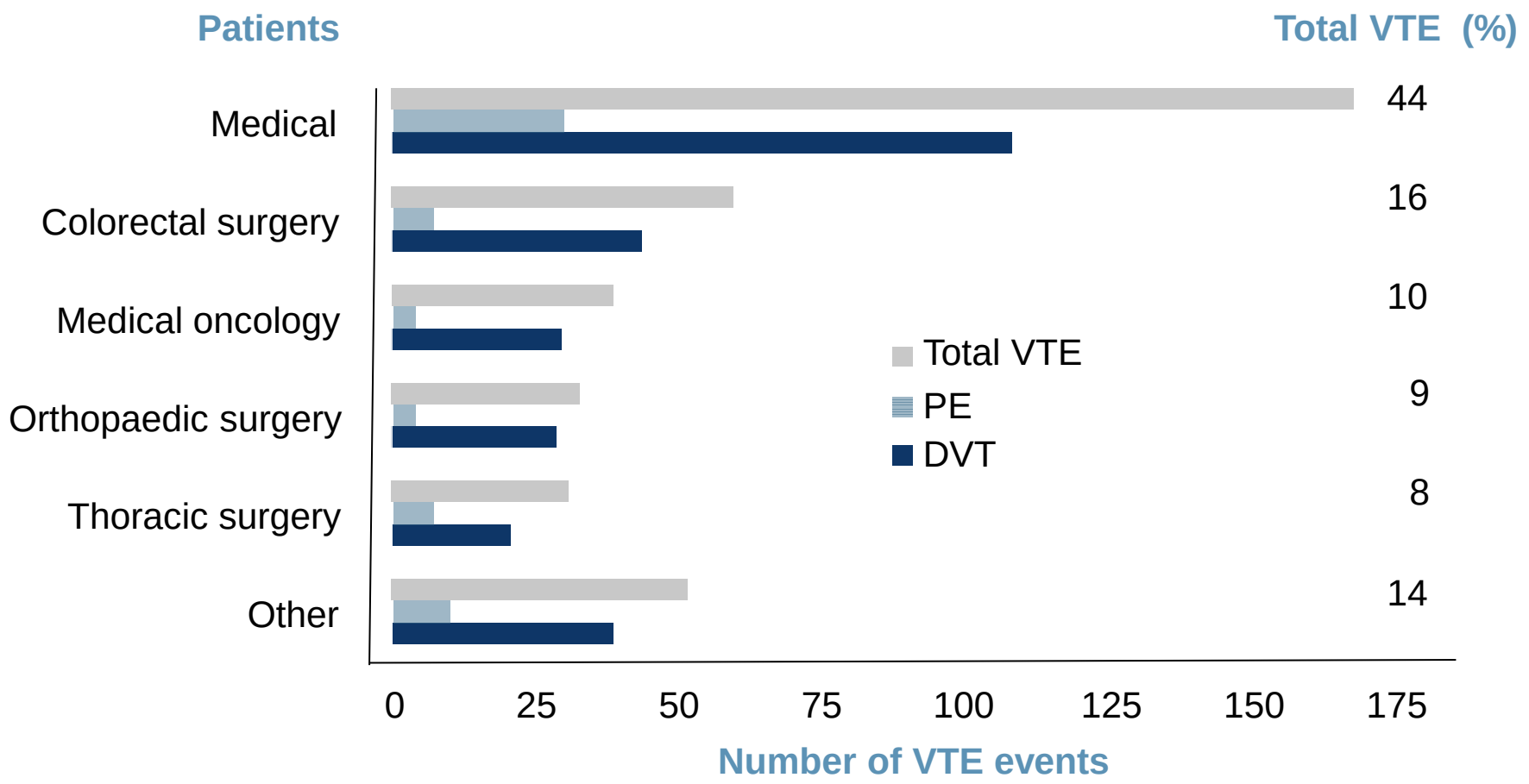
Heit – Mayo Clin Proc 2001;76:1102

VTE is a Disease of Hospitalized and Recently Hospitalized Patients



Heit – Mayo Clin Proc 2001;76:1102

VTE According to Service (N=384)



Goldhaber SZ et al. *Chest* 2000;118:1680-4.

DVT and the risk our patients face:

Stasis

Age > 40
Immobility
CHF
Stroke
Paralysis
Spinal Cord injury
Hyperviscosity
Polycythemia
Severe COPD
Anesthesia
Obesity
Varicose Veins

Hypercoagulability

Cancer
High estrogen states
Inflammatory Bowel
Nephrotic Syndrome
Sepsis
Smoking
Pregnancy
Thrombophilia

Endothelial Damage

Surgery
Prior VTE
Central lines
Trauma

Most hospitalized patients have at least one risk factor for DVT

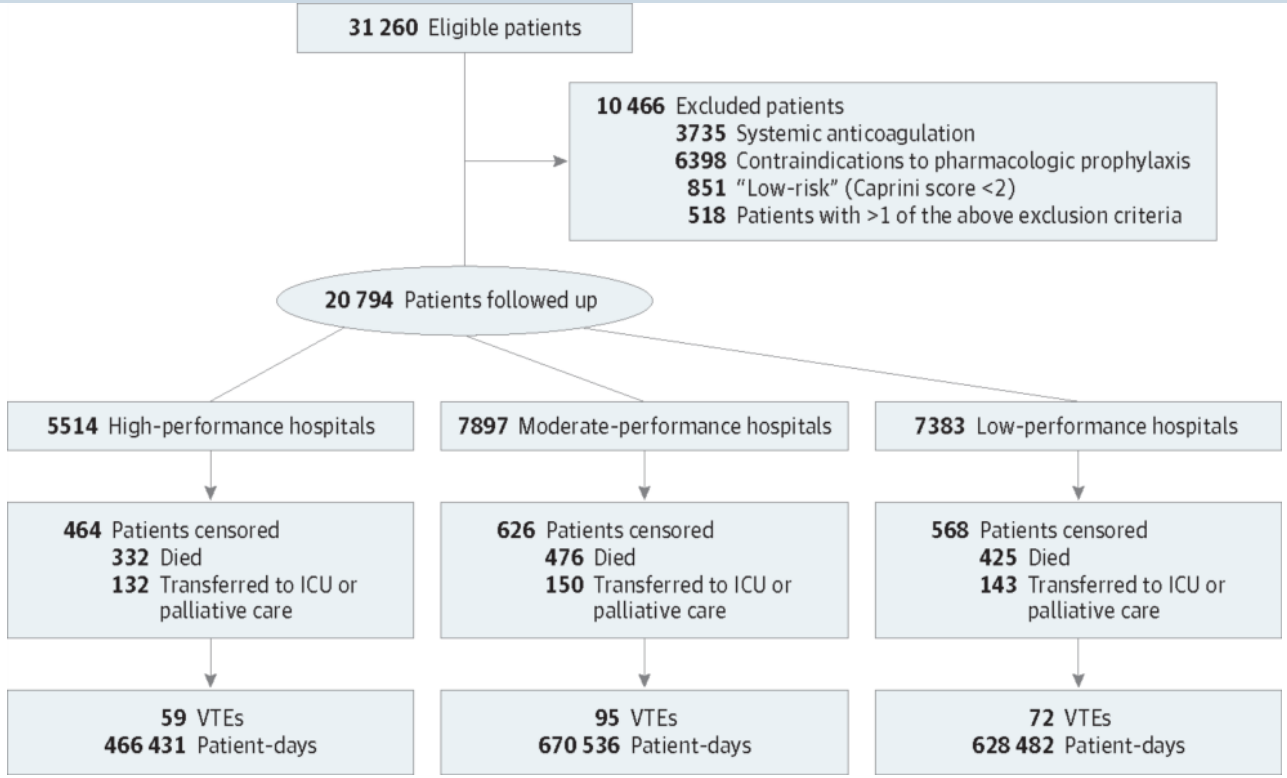
Hospital Performance for Pharmacologic Venous Thromboembolism Prophylaxis and Rate of Venous Thromboembolism: A Cohort

The JAMA Network

JAMA Intern Med. 2014;174(10):1577-1584. doi:10.1001/jamainternmed.2014.3384

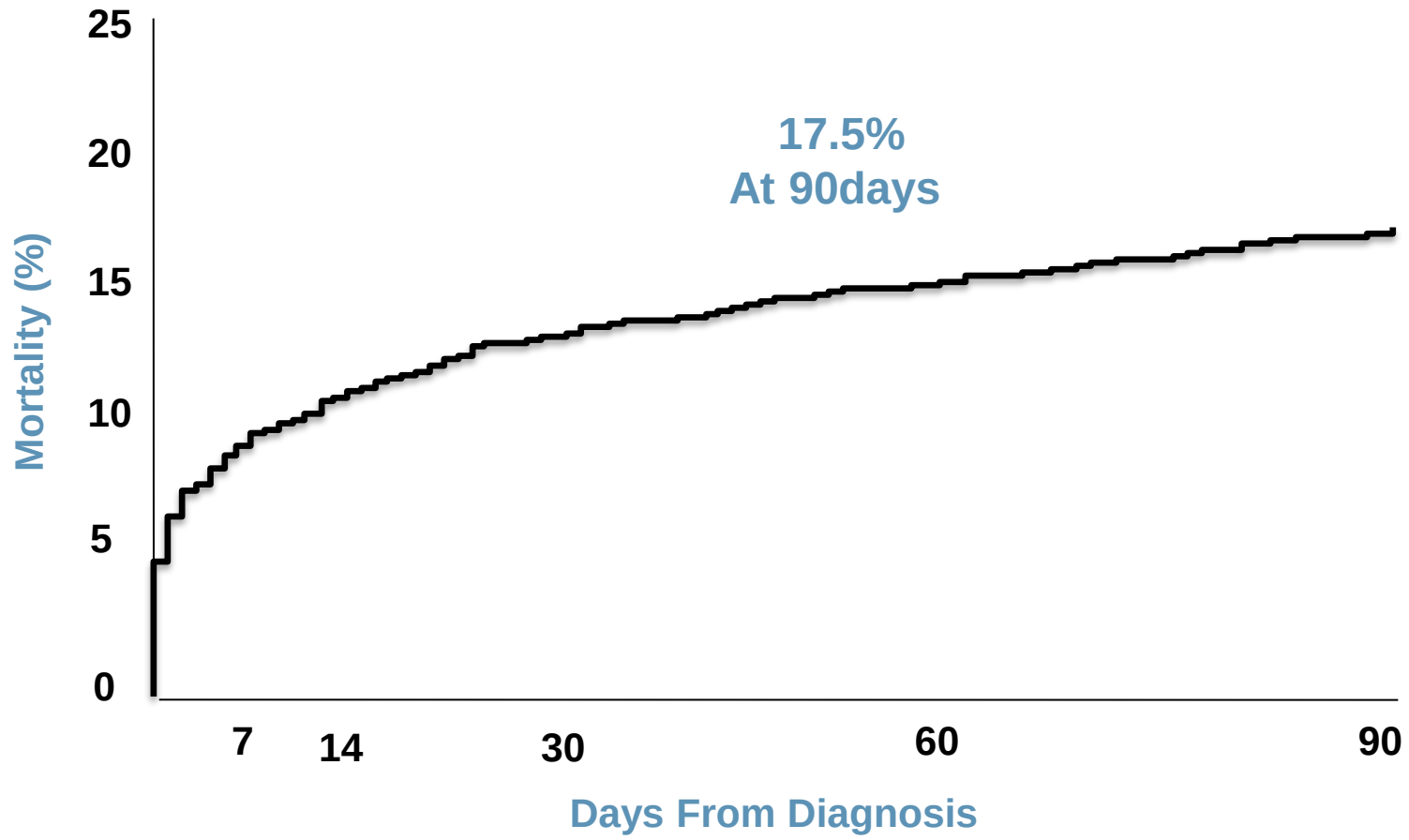
Figure Legend:

Flow Diagram of Patient Progress Through the 90-Day Observation Period -- *ICU indicates intensive care unit; VTE, venous thromboembolism.*



Studies continue to identify the risks showing the need for DVT awareness in the ICU

Icoper: Cumulative Mortality After Diagnosis of PE



Lancet. 1999;353:1386-1389.

Associated Illnesses that are a Consequence of VTE events

Chronic thromboembolic pulmonary hypertension

Mean pulmonary artery pressure greater than 25 mm Hg that persists 6 months after PE

2-4% of patients after PE

Post thrombotic Syndrome

Calf swelling and skin pigmentation; venous ulceration in severe cases

Up to 43% of patients develop PTS within 2 years

Goldhaber SZ, Bounameaux H. Lancet. 2012 May 12; 379:1835-46

Venous Thromboembolism (VTE) remains a major health problem

In addition to the risk of sudden death

30% of survivors develop recurrent VTE within 10 years

28% of survivors develop venous stasis syndrome within 20 years

DVT and the Risks

DVT risk and prophylaxis in the hospitalized patient

Low Risk	Moderate Risk	High Risk
Ambulatory patient *without* additional VTE Risk Factors	All other patients. Most patients (not LOW or HIGH category)	Elective major lower extremity arthroplasty
Ambulatory patient with expected LOS ≤ 2 days, or same day/minor surgery		Hip, pelvic, or sever lower extremity fractures
Only a few patients!		Acture spinal cord injury with paresis
		Multiple major trauma
		Abdominal or pelvic surgery for cancer
Ambulation and Education	*LMWH or UFH 5000 units SQ q8h*	*LMWH or Arixtra or Coumadin*

Physicians at UCSD use these checklists to assess all adult inpatients when they are admitted, transferred between units, or post-op

DVT and the Risks

DVT risk factors

Low	Moderate	High
Age > 50 years	Prior History of VTE	Acture or chronic lung disease
Myeloproliferative disorder	Impaired mobility	Obesity
Dehydration	Inflammatory bowel disease	Known thrombophilic state
CHF	Active rheumatic disease	Varicose veins/chronic stasis
Active malignancy	Sickel cell disease	Recent post-partum w/ immobility
Hormonal replacement	Estrogen-based contraceptives	Nephrotic syndrome
Moderate to Major surgery	Central venous catheter	Myocardial infarction

Physicians at UCSD use these checklists to assess all adult inpatients when they are admitted, transferred between units, or post-op

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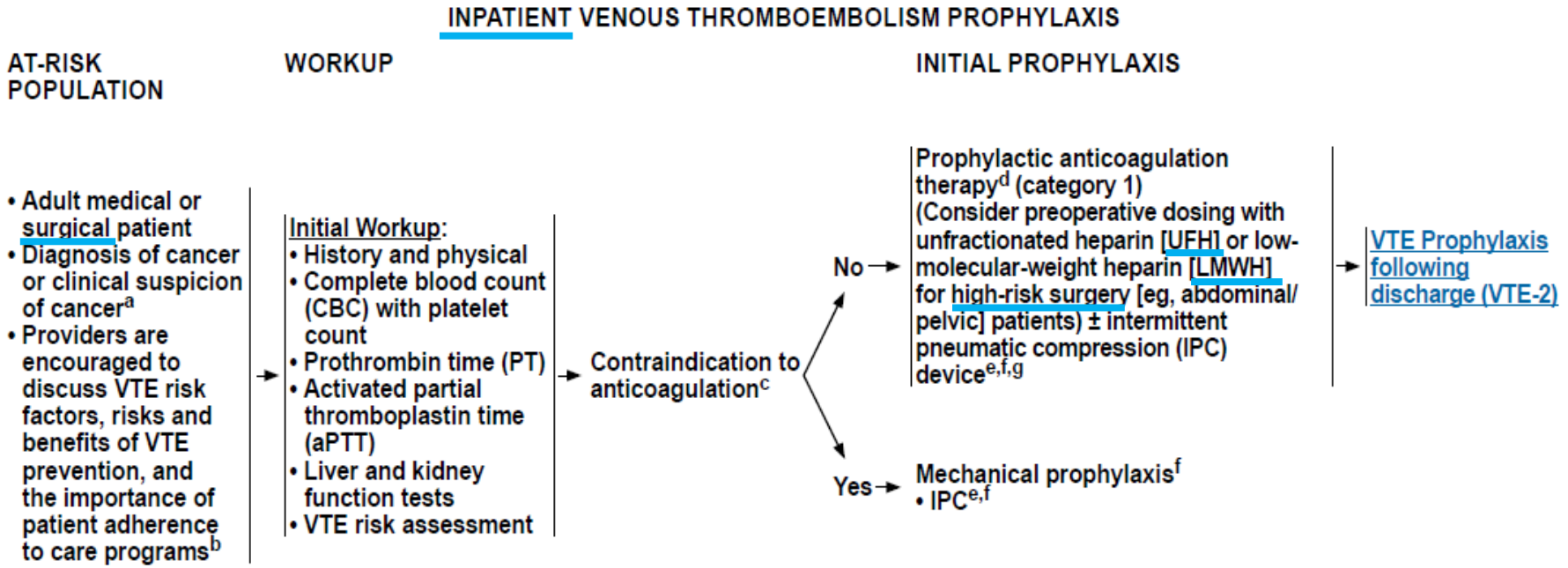
Inpatient VTE Prophylaxis



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VTE Prophylaxis following Discharge & for Ambulatory Cancer patients

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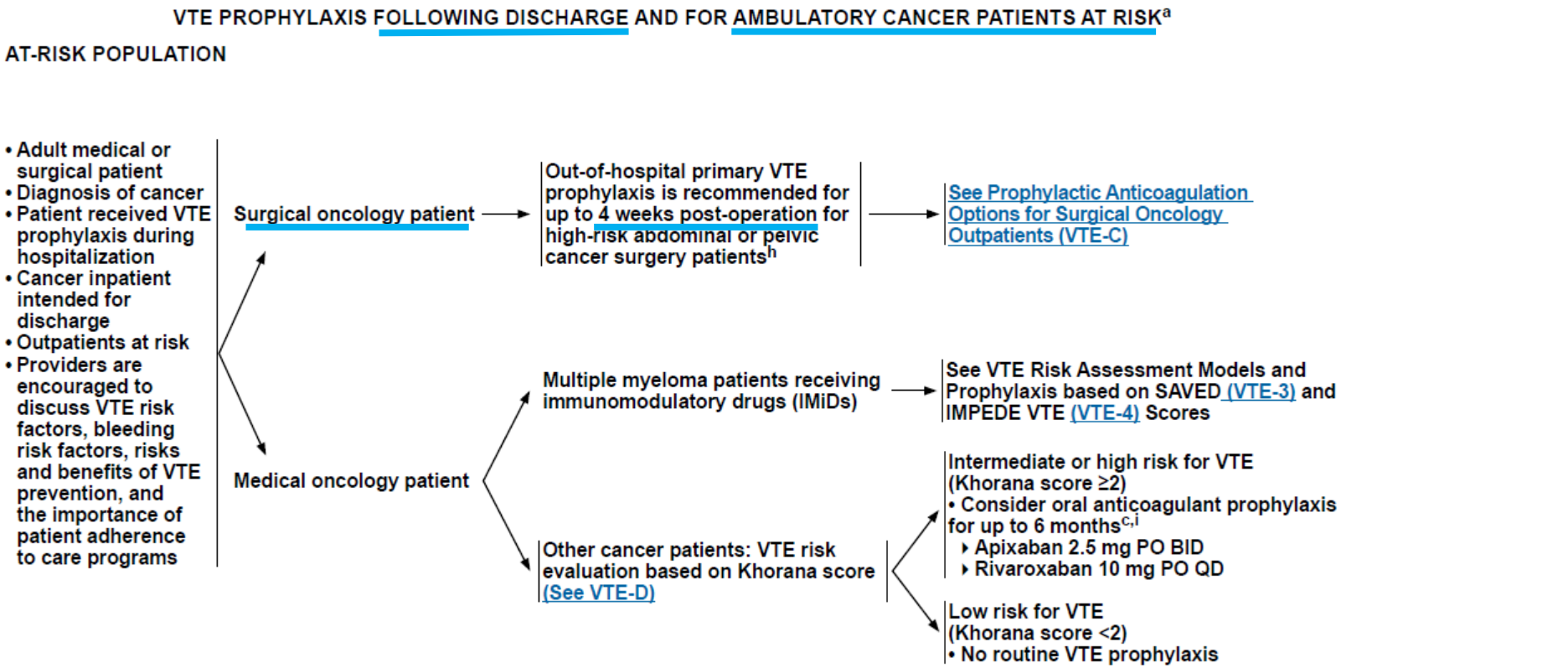

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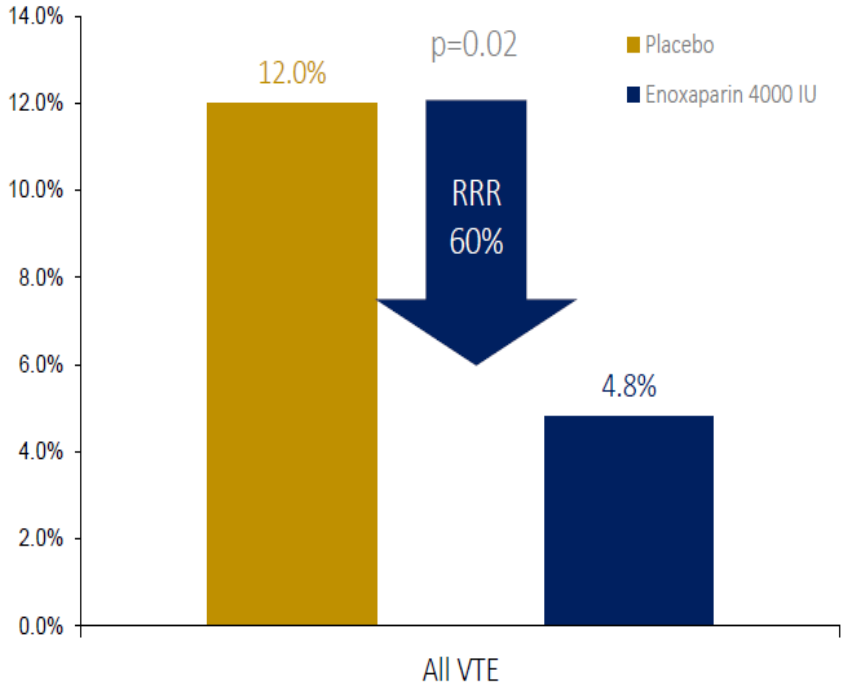
ENOXACAN II

RESULTS

- Four weeks extended prophylaxis with enoxaparin 4000 IU reduced the risk of all VTE by 60% compared with in hospital only (short-term) prophylaxis.
- No significant difference in the incidence of major bleeding 1.2% in the enoxaparin group and 0.4% in the placebo group (p=0.62).



REFERENCES

Bergqvist et al. for the ENOXACAN II Investigators. Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. N Engl J Med. 2002;346:975-

- In the setting of surgery performed specifically in cancer patients:
  - Short duration Clexane/Lovenox 4000 IU (40mg) once-daily is at least as effective as UFH 5000 IU bid or tid at preventing VTE without significant increase in major bleeding.
  - Overall bleeding rate is higher with Clexane/Lovenox 4000 IU (40mg) versus UFH, possibly due to the initiation of a full "high-risk dose" close to the surgery (2 hours preoperatively).
  - Extended-prophylaxis with Clexane/Lovenox 4000 IU (40mg) significantly decreases by 60% the incidence of VTE without significant increase in bleeding versus short term regimen.

Contraindications to VTE Prophylaxis

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CONTRAINDICATIONS TO VTE PROPHYLAXIS[1]

Contraindications to Prophylactic Anticoagulation

- Active bleeding
- Thrombocytopenia (platelets <30,000–50,000/mcL or clinical judgment)[2]
- Underlying hemorrhagic coagulopathy (eg, abnormal PT or aPTT excluding a lupus inhibitor/anticoagulant) or known bleeding disorder in the absence of replacement therapy (eg, hemophilia, von Willebrand disease)
- Indwelling neuraxial catheters (contraindication for apixaban, dabigatran, edoxaban, fondaparinux, rivaroxaban, or enoxaparin dose exceeding 40 mg daily)
- Neuraxial anesthesia/lumbar puncture[3,4]
- Interventional spine and pain procedures[5]

Contraindications to Mechanical Prophylaxis

- Absolute
  - Acute DVT
  - Severe arterial insufficiency (pertains to graduated compression stockings [GCS] only)
- Relative
  - Large hematoma
  - Skin ulcerations or wounds[6]
  - Thrombocytopenia (platelets <20,000/mcL)
  - Mild arterial insufficiency (pertains to GCS only)
  - Peripheral neuropathy (pertains to GCS only)

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BLEEDING RISK !!

Predictive variables for major bleeding events in patients presenting with documented acute venous thromboembolism Findings from the RIETE Registry

Table 3: Multivariate analysis for major bleeding in the derivation sample.

	β	Odds ratio (95% CI)	P-value	Points
Recent major bleeding	0.996	2.7 (1.6–4.6)	<0.001	2
Creatinine levels >1.2 mg/dl	0.761	2.1 (1.7–2.8)	<0.001	1.5
Anemia	0.739	2.1 (1.7–2.7)	<0.001	1.5
Cancer	0.553	1.7 (1.4–2.2)	<0.001	1
Clinically overt PE	0.545	1.7 (1.4–2.2)	<0.001	1
Age >75 years	0.504	1.7 (1.3–2.1)	<0.001	1

PE, pulmonary embolism; CI, confidence intervals.

Low risk (0)
Intermediate risk (1–4)
High risk (>4)

http://williams.medicine.wisc.edu/bleeding_risk_after_vte.pdf

Bleeding Risk Assessment

BLEEDING RISK ASSESSMENT TABLES

Estimated Bleeding Risk of Various Surgical Procedures

Bleeding Risk Category	Type of Surgery or Procedure	
Very high	• Neurosurgical procedure (intracranial or spinal) • Urologic surgery • Cardiac surgery	
High	• Major cancer surgery • Major vascular surgery (abdominal aortic aneurysm [AAA] repair, peripheral artery bypass) • Reconstructive plastic surgery • Renal or hepatic biopsy	• Bowel polypectomy (if part of a colonoscopy) • Major orthopedic surgery • Head and neck surgery • Major intra-abdominal surgery • Major intra-thoracic surgery
Low	• Pacemaker or automatic implantable cardioverter defibrillator (AICD) placement • Laparoscopic cholecystectomy or hernia repair • Coronary angiography • Arthroscopy • Biopsy (prostate, bladder, thyroid, lymph node)	• Bronchoscopy ± biopsy • Central venous catheter placement and removal • GI endoscopy with biopsy
Very low	• Minor dermatologic procedures (excisions of basal and squamous cell carcinomas, actinic keratoses, and malignant or premalignant nevi) • Cataract removal • Electroconvulsive therapy (ECT)	• Arthrocentesis • Joint or soft tissue injections • GI endoscopy without biopsy

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Dosing Regimen

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PROPHYLACTIC ANTICOAGULATION OPTIONS FOR INPATIENTS AND SURGICAL ONCOLOGY OUTPATIENTS[1,2,3,4]

Options for Inpatients (VTE-1) or Surgical Oncology Outpatients (VTE-2)

Agent	Standard Dosing	Obesity Dosing (BMI ≥40 kg/m^2)[5]
LMWH: Dalteparin	5,000 units SC daily (category 1 for inpatient)	Consider 7,500 units SC daily (limited data)
LMWH: Enoxaparin	40 mg SC daily (category 1 for inpatient)	Consider 40 mg SC every 12 hours
Fondaparinux	2.5 mg SC daily (category 1 for inpatient)	Consider 5 mg SC daily (limited data)
UFH	5,000 units SC every 8–12 hours (category 1 for inpatient)	Consider 7,500 units SC every 8 hours

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Thank You