VTE Prophylaxis: Inpatient Management

Brenda Shinar

July 28, 2020

Learning Objectives

1. Define hospital acquired VTE and understand the burden of hospital acquired VTE in the US.
2. List as many risk factors for VTE in the hospital setting that you can and know their odds ratios.
3. Differentiate patients into LOW, MODERATE, and HIGHEST risk for hospital acquired VTE based on the VTE advisor order-set at BUMCP.
4. Describe the recommended dose and duration of VTE prophylaxis for hip and knee replacement and hip fracture surgery.
5. Understand the indications for extended (4 weeks -35 days) prophylaxis.

Hospital Acquired VTE: 50% of burden of VTE disease

- ***VTE occurring during or within 3 months of hospitalization***
  - 2/3 present as DVT
  - 1/3 presents as PE
  - 25% of PE presentation is sudden death
- ***Leading cause of preventable hospital death and increased length of stay***
- Annual cost estimates 7-10 billion dollars per year

- Agency for Healthcare Research and Quality (AHRQ) study group
- **Call to ACTION: Reduce hospital acquired VTE by 20% by 2030**

VTE Risks Defined:
40% of Hospital Patients have ≥ 3

1. Increased Age > 40
2. Obesity (BMI > 30)
3. Immobility (S)
4. Major Surgery (past 7 days) (S)
5. Central line (PICC)
6. History of VTE / Thrombophilia (S)(S)
7. Active Cancer (OR 7-28) (S)
8. Acute Stroke (OR 3.0)
9. Prior stroke with paresis
10. Myocardial Infarction
11. Heart failure
12. Acute Respiratory failure
13. Active Infection (S)
    - Intra-abdominal (OR 17.8)
    - Oral infection (OR 11.6)
    - Sepsis OR (10.7)
14. Estrogen (pregnant, post-partum(S)
15. Inflammatory bowel disease (S)
    (OR 1.5-3.5)
16. Autoimmune diseases (OR 3.0) (S)
    - Lupus (OR 15.2)
    - Systemic Sclerosis (OR 7.4)
17. Severe dehydration
18. Nephrotic syndrome

(S) = Strong Risk Factor

VTE Prevention: Ancient History to Modern Day…

- **2004-2012**
  - Everyone was started on pharmacologic VTE prevention unless they had an overt contraindication
- **2012**
  - American College of Chest Physicians (ACCP)Recommended Risk Stratification
  - **Caprini** score: Non-ortho surgery
  - **Padua** score: Medical patients
  - **IMPROVE** score: Medical patients
- **2018**
  - American Society of Hematology (ASH) Guidelines for Medical Patients

QUANTITATIVE RISK ASSESSMENT MODELS

Who is at risk for VTE in hospital?

- Risk Assessment Models (RAMs) can identify inpatients at high risk
- ***Examples:*** Padua, IMPROVE-VTE Scores

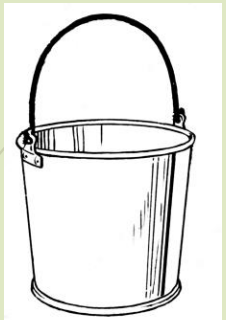
These RAMs are not extensively validated for guiding decisions about prophylaxis

Padua RAM: Factors
Previous VTE
Thrombophilia
Active cancer
Age > 70 years
Reduced mobility
Recent trauma/surgery
Heart or respiratory failure
Acute MI or stroke
Hormonal treatment
Obesity (BMI > 30)
Infection/rheumatologic

IMPROVE-VTE RAM: Factors
Previous VTE
Thrombophilia
Active cancer
Age > 60 years
Immobilization of ≥ 7 days
Lower limb paralysis
ICU/CCU stay

Spyropoulos Chest 2011
Leizorovicz Circulation 2004

Three Bucket Model



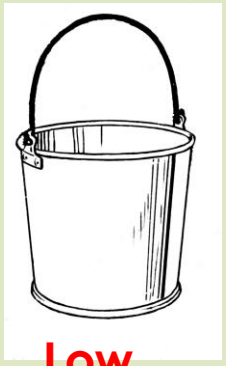
High

Pharmacologic Prophylaxis (plus IPC)

Moderate

Pharmacologic Prophylaxis or IPC if contraindication exits

NO Prophylaxis



Low

No prophylaxis; Ambulate & Reassess

Banner Health

Help

Patient Name:	ZZZCERNER, ROY	**Sex:** Male	**MRN:** 23959
Location:	58 EDH - EDH	**Age/DOB:** 57 Years / August 06, 1961	**FIN:** 42228619

	Risk Level	Risk Factors	
○	High Risk	• On ventilator • Hip or Knee arthroplasty (i.e. THA or TKA) • Hip Fracture surgery • Major Lower Extremity surgery • Acute CVA	• Multiple major trauma • Spinal Cord Injury • Major Neurosurgery • Spine Surgery • Abdominal-pelvic surgery for cancer (regardless of length of stay)

◉	Moderate Risk	• LOS >48 hours plus one **Strong** VTE risk factor
		  ○ Infection on IV antibiotics
		  ○ Major surgery last 7 days
		  ○ Active Cancer
		  ○ Prior DVT/PE
		  ○ Known thrombophilia (congenital or acquired)
		  ○ Rheumatic disease or Inflammatory Bowel Disorder (e.g UC, Crohns)
		  ○ Acutely bed or chair bound
		• LOS >48 hrs. with at least one **Intermediate** VTE Risk factor(s) plus decrease in ambulation from baseline
			• Most general, thoracic, gynecologic, urologic, and some orthopedic surgeries (not TKA or THA-see above) (> 24 hrs LOS)

○	Low Risk	• Observation status expected stay <48 hours • Minor Surgery • Ambulatory Cancer Patients admitted for short chemotherapy induction • Patients already on therapeutic anticoagulation or VTE Prophylaxis	

Intermediate Risk factors that need immobility to qualify for chemical prophylaxis:

1. CHF
2. MI
3. Active infection
4. Severe dehydration
5. Age greater than 65 y/o
6. Morbid Obesity (BMI > 30)
7. Nephrotic syndrome
8. Hormonal therapies
9. Central venous line
10. Previous CVA with paresis

(e.g. laparoscopic surgery <30 min, hernia repair, mastectomy, appendectomy, mastectomy, TURP)

Done

Case 1

- 35 y/o male rancher in northern Arizona with no PMHx got kicked by a horse. He presented to hospital with right pelvic fracture and underwent right hip fracture repair surgery.

  The Internal medicine team is consulted for pain management and discharge planning for acute rehab placement and VTE Prophylaxis recommendations.

  Your orders for VTE Prophylaxis are:

  A. UFH until discharge to rehab facility
  B. Enoxaparin in hospital and rehab facility until ambulatory
  C. Apixaban with extended prophylaxis for 35 days
  D. Enoxaparin with IPC and extended prophylaxis for 35 days

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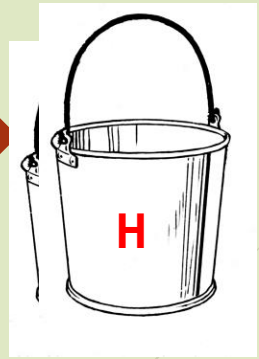

Highest Risk : MICU/SICU/NICU/Ortho

1. On Ventilator
2. Abdominal-pelvic surgery for Cancer

3. Acute stroke
4. Spine Surgery (not including elective spine surgery)

5. THA (Hip Replacement)
6. TKA (Knee Replacement)
7. Hip Fracture Surgery
8. Major Lower extremity Surgery
9. Multiple Major Trauma

Indication for extended VTE Prophylaxis

Extended Prophylaxis in **Surgical Cases**

ACP | MKSAP 18

	Cancer surgery		LMWH for 4 wk
Orthopedic	Hip or knee arthroplasty[d]		IPC + LMWH, LDUH, aspirin, NOAC, fondaparinux, warfarin, or IPC alone if high bleeding risk; continue for 10-35 d
	Hip fracture repair[d]		IPC + LMWH, LDUH, warfarin, fondaparinux, or IPC alone if high bleeding risk; continue for 10-35 d
	Isolated lower leg fracture repairs		None
	Knee arthroscopy with no previous VTE		Early ambulation

For patients **without increased bleeding** risk, extended duration of postoperative prophylaxis for **up to 35 days** is recommended over shorter-duration prophylaxis of 10 to 14 days, which is the minimum recommended duration of pharmacologic VTE prophylaxis in orthopedic surgery.

CAVEAT #1:
What about Pharmacologic + Mechanical Prophylaxis: Is it indicated?

- Yes by **Chest 2012 Guidelines for Surgical patients**
- Yes in surgical cases (**2019 Draft ASH S**urgical Guidelines)

Question 3: Should pharmacological combined with mechanical prophylaxis vs. pharmacological prophylaxis alone be used for patients undergoing surgery?

The ASH guideline panel suggests using combined prophylaxis with mechanical and pharmacological methods over prophylaxis with pharmacological agents alone in surgical patients (conditional recommendation based on very low certainty of the evidence about effects).

- No in Medical patients in ICU per **ASH Guidelines 2018** (next slide)

Recommendation

In **acutely and critically ill medical patients**, the panel **suggests pharmacological VTE prophylaxis alone** over mechanical combined with pharmacological VTE prophylaxis *(conditional recommendation, very low certainty)*

Mechanical combined with pharmacologic compared with **pharmacologic alone**:

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with pharmacologic prophylaxis alone	*Risk difference with combined prophylaxis*
Mortality	**0.50** (0.05 to 5.30)	8 per 1,000	**4 fewer deaths per 1,000** (8 fewer to 34 more)
PE	**0.35** (0.05 to 2.22)	1 per 1,000	**1 fewer PE per 1,000** (1 fewer to 1 more)
Symptomatic proximal DVT	**0.13** (0.04 to 0.40)	2 per 1,000	**2 fewer DVT per 1,000** (2 fewer to 1 fewer)
Major bleeding	**2.83** (0.30 to 26.70)	28 per 1,000	**51 more bleeds per 1,000** (20 fewer to 720 more)

Quality of Evidence (GRADE): Low Moderate Strong

CAVEAT #2: What about total knee arthroplasty?

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- For patients undergoing THA, TKA, or HFS, we recommend that pharmacologic prophylaxis is administered for a minimum of 10 to 14 days (**Grade 1B**). (See 'Duration' above.)
  - For those undergoing THA, we suggest that pharmacologic prophylaxis is continued for up to 35 days after surgery (**Grade 2B**).
  - For those undergoing TKA, shorter courses at the 10 to 14 day end of the spectrum may be preferred.

CAVEAT #3 What about Aspirin?....

June 2013

ORIGINAL RESEARCH | Annals of Internal Medicine

Aspirin Versus Low-Molecular-Weight Heparin for Extended Venous Thromboembolism Prophylaxis After Total Hip Arthroplasty

A Randomized Trial

David R. Anderson, MD; Michael J. Dunbar, MD; Eric R. Bohm, MD; Etienne Belzile, MD; Susan R. Kahn, MD; David Zukor, MD; William Fisher, MD; Wade Gofton, MD; Peter Gross, MD; Stephane Pelet, MD; Mark Crowther, MD; Steven MacDonald, MD; Paul Kim, MD; Susan Pleasance, BScN; Nicki Davis, BSc; Pantelis Andreou, PhD; Philip Wells, MD; Michael Kovacs, MD; Marc A. Rodger, MD; Tim Ramsay, PhD; Marc Carrier, MD; and Pascal-Andre Vendittoli, MD

EPCAT II TRIAL Feb 2018

ORIGINAL ARTICLE

Aspirin or Rivaroxaban for VTE Prophylaxis after Hip or Knee Arthroplasty

David R. Anderson, M.D., Michael Dunbar, M.D., John Murnaghan, M.D., Susan R. Kahn, M.D., Peter Gross, M.D., Michael Forsythe, M.D., Stephane Pelet, M.D., William Fisher, M.D., Etienne Belzile, M.D., Sean Dolan, M.D., Mark Crowther, M.D., Eric Bohm, M.D., et al.

Recommendation

In **critically ill medical patients**, the panel suggests using **LMWH over UFH** *(conditional recommendation, moderate certainty)*

LMWH compared with **UFH** in critically ill patients:

Outcomes	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)	
		Risk with UFH	*Risk difference with LMWH*
● Mortality	**0.90** (0.75 to 1.08)	243 per 1,000	**24 fewer deaths per 1,000** (61 fewer to 19 more)
● PE	**0.80** (0.44 to 1.46)	11 per 1,000	**2 fewer PE per 1,000** (6 fewer to 5 more)
● Symptomatic proximal DVT	**0.87** (0.60 to 1.25)	25 per 1,000	**3 fewer DVT per 1,000** (10 fewer to 6 more)
● Major bleeding	**0.98** (0.76 to 1.27)	53 per 1,000	**1 fewer bleeds per 1,000** (13 fewer to 14 more)
● Heparin-induced thrombocytopenia	**0.42** (0.15 to 1.18)	6 per 1,000	**4 fewer episodes per 1,000** (5 fewer to 1 more)

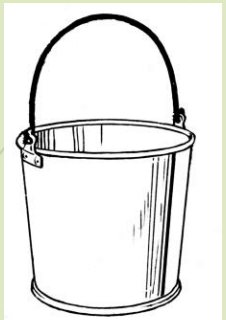
Critically ill patients may require other prophylaxis options due to **hepatic or renal dysfunction.**

Quality of Evidence (GRADE): Low ● Moderate ● Strong ●

Preferred Pharmacologic Prophylaxis Dosing Strategy

Orders for Moderate Risk Patients		
Prophylaxis for Moderate Risk Patient: Choose one pharmacologic option.		
Current Pharmacologic Order:		
◉ enoxaparin	40 mg, 0.4 mL, SubCutaneous, Daily	07/16/2020 00:09
Pharmacologic:		
○ enoxaparin	40 mg SubCutaneous, Soln-Inj, Daily	CrCl > 30 mL/min, weight ≤ 150 Kg
○ enoxaparin	40 mg SubCutaneous, Soln-Inj, BID	CrCl > 30 mL/min, weight > 150 Kg
○ enoxaparin	30 mg SubCutaneous, Soln-Inj, Daily	CrCl 15 to 30 mL/min
○ heparin	5,000 units SubCutaneous, Soln-Inj, Q8h-interval	CrCl < 15 mL/min
○ Currently therapeutic on anticoagulation and will continue during hospitalization		
○ Reason Pharmacologic Prophylaxis Not Given		

Three Bucket Model



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Pharmacologic Prophylaxis or IPC if contraindication exits

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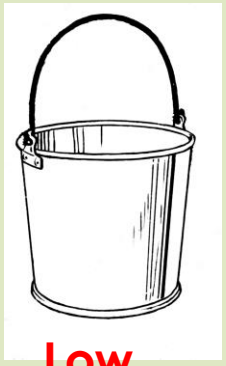
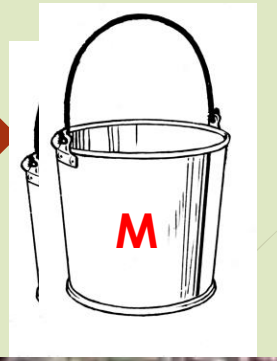


Low

No prophylaxis; Ambulate & Reassess



Moderate Risk : Majority Med/Sx Patients!

Moderate Risk Category

- >48-hour stay + Strong risk factor

  Or

- > 48-hour stay + Intermediate risk factor + **Decreased ambulation**

- **Pharmacologic Prophylaxis (or Mechanical if Pharmacologic is contraindicated)**

◉	Moderate Risk	• LOS >48 hours plus one **Strong** VTE risk factor
		  ○ Infection on IV antibiotics
		  ○ Major surgery last 7 days
		  ○ Active Cancer
		  ○ Prior DVT/PE
		  ○ Known thrombophilia (congenital or acquired)
		  ○ Rheumatic disease or Inflammatory Bowel Disorder (e.g UC, Crohns)
		  ○ Acutely bed or chair bound
		  ○ Postpartum
		• LOS >48 hrs. with at least one **Intermediate** VTE Risk factor(s) plus decrease in ambulation from baseline
			• Most general, thoracic, gynecologic, urologic, and some orthopedic surgeries (not TKA or THA-see above) (> 24 hrs LOS)

Intermediate Risk factors that need immobility to qualify for chemical prophylaxis:

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2. MI
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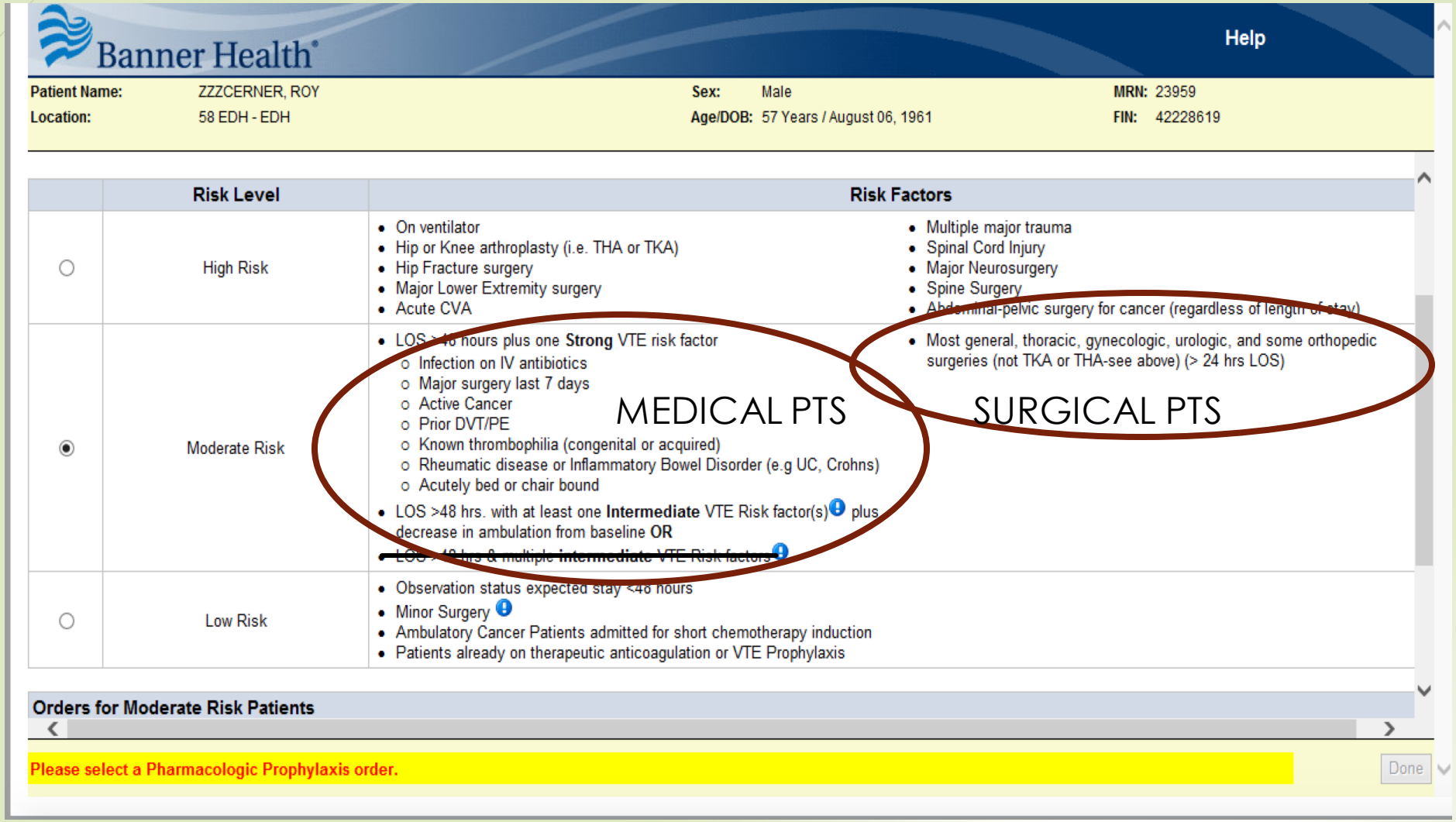
VTE Prophylaxis: Three bucket Model



CASE 2

65 y/o male with PMHx CAD with CABG and chronic grade I diastolic CHF is transferred from outside hospital after 3 days on IV Zosyn for cholecystitis being evaluated for laparoscopic cholecystectomy.

Admission orders for VTE prophylaxis should include the following:

A) SCDS
B) Enoxaparin
C) Combination of SCDS + LMWH
D) Ambulate when tolerated

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Approach to Surgical Patients

- **First Consider Procedure**
  1. Duration (greater than 45 minutes)
  2. Position
  3. Area
  4. Cancer
  5. ? emergency
- **Second consider Other Risk factors surrounding patients**
  1. Strong VTE Risk Factors
  2. Intermediate Risk Factor

VTE Risk Factors

9 **Strong** Risk Factors

1. Major Surgery in last 7 days
2. Previous history of VTE
3. Active infection on IV abx
4. Thrombophilia (congenital or acquired)
5. Rheumatic disease
6. IBD
7. Acute total immobility i.e. bedbound
8. Active malignancy
9. Postpartum

11 **Intermediate** Risk Factors

1. MI
2. CHF
3. Active infection
4. COPD /Acute respiratory failure
5. Severe dehydration
6. Age greater than 65 y/o
7. BMI>30
8. Nephrotic syndrome
9. Hormonal therapies
10. Central line
11. Previous CVA with paresis

Equation #1

Strong VTE RISK FACTOR + >48 hrs. = VTE Prophylaxis.

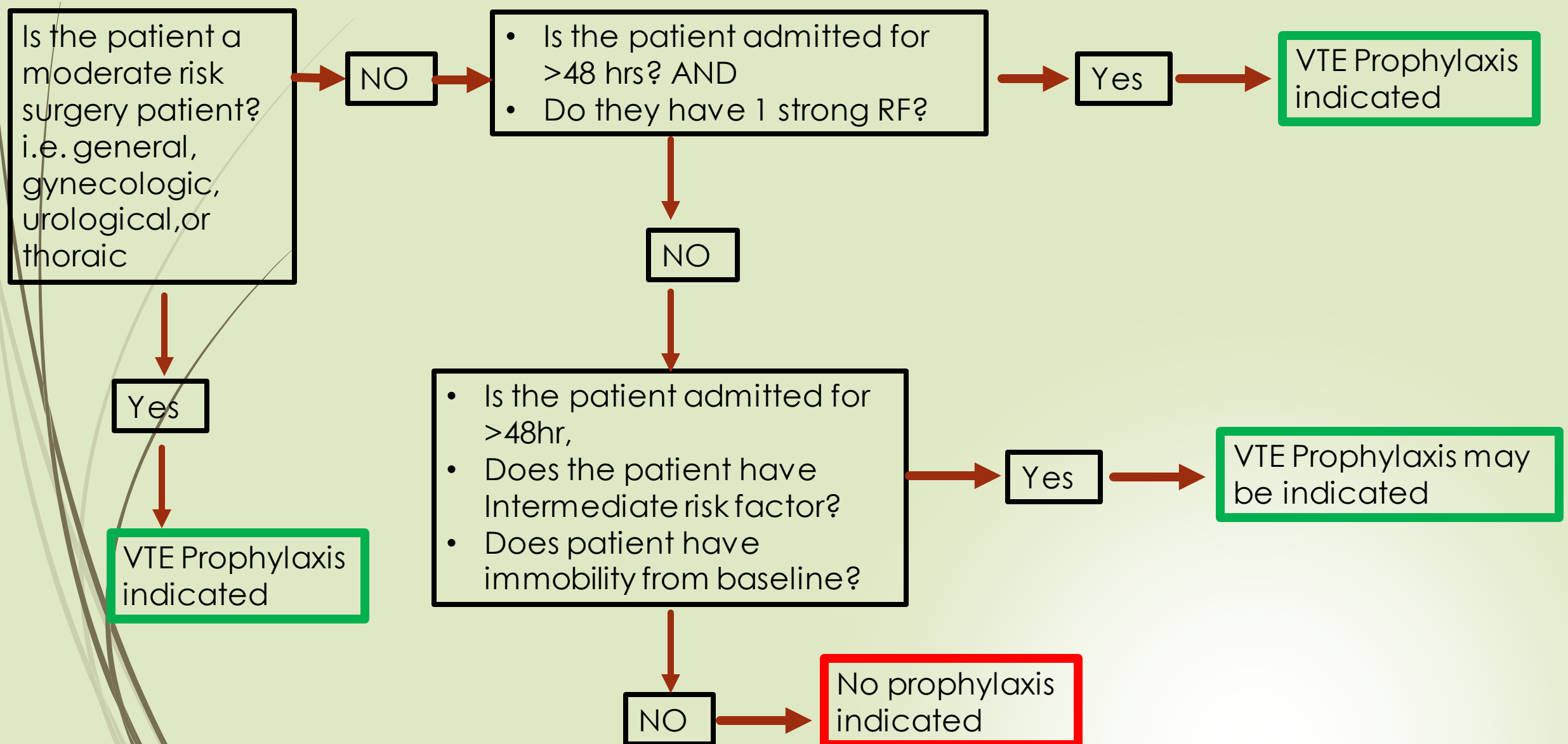
- Major Surgery in last 7 days
- Previous history of VTE
- Active infection on IV abx
- Thrombophilia (congenital or acquired)
- Rheumatic disease
- IBD
- Acute total immobility i.e. bedbound
- Active malignancy
- Postpartum

Equation #2

Intermediate Risk Factors + > 48 hrs.
+ immobility from baseline= VTE Prophylaxis

- MI
- Acute COPD/Acute respiratory Failure
- CHF
- Active infection
- Severe dehydration
- Age greater than 65 y/o
- BMI>30
- Nephrotic syndrome
- Hormonal therapies
- CVL
- Previous CVA with paresis

Moderate Risk Bucket Algorithm



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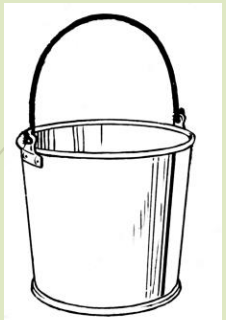

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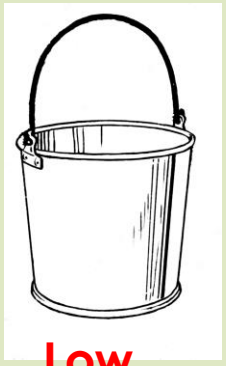

Low

No prophylaxis; Ambulate & Reassess

Low Risk Category

- Ambulate and Reassess

○	Low Risk	• Observation status expected stay <48 hours • Minor Surgery • Ambulatory Cancer Patients admitted for short chemotherapy induction • Patients already on therapeutic anticoagulation or VTE Prophylaxis

(e.g. laparoscopic surgery <30 min, hernia repair, mastectomy, appendectomy, mastectomy, TURP)

- Dynamic Process
- Consider how likely they will stay in observation
- Consider their VTE strong risk Factors

LOW RISK Nonorthopedic Surgery VTE RISK =1.5%

- Low Risk (Caprini=1-2; Plastic/Reconstruction Caprini 3-4)

1. Minor elective abdominal-pelvic Surgery
   - Appendectomy
   - Laparoscopic cholecystectomy
   - Minor thoracic surgery (diagnostic thorascopy)
   - Vein ablation
   - Elective spine surgery (e.g. spinal fusion)

CASE 3

65 y/o male with PMHx CAD with CABG and chronic grade I diastolic CHF presents for laparoscopic cholecystectomy

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Guidelines on Low Risk Surgery

- **ACCP** 2012 for Low Risk Nonorthopedic surgery VTE Prevention is mechanical prophylaxis
- **SAGES** (Society of American Gastrointestinal and Endoscopic Surgeons) 2018 Recommendations:

  "A meta-analysis on laparoscopic cholecystectomy indicated that routine use of VTE chemoprophylaxis was likely to be unnecessary and suggested considering its use only in higher risk patients based on risk stratification "

  Rondelli F, Manina G, Agnelli G, Becattini C. Venous thromboembolism after laparoscopic cholecystectomy: clinical burden and prevention. Surg Endosc. 2013;27(6):1860-4.

- **ASH** "Draft" Surgical VTE Prophylaxis Guidelines

ASH Draft Recommendations for VTE Prevention in Surgical Hospitalized Patients

Question 19: Should pharmacological prophylaxis vs. no pharmacological prophylaxis be used for patients undergoing laparoscopic cholecystectomy?

The ASH guideline panel suggests against pharmacological prophylaxis over no prophylaxis in patients undergoing laparoscopic cholecystectomy (conditional recommendation based on low certainty of the evidence about effects)

Case 4

You are consulted on 45 y/o female with BMI 30 no PMhx other than diabetes with severe abdominal pain with abdominal mass anticipating laparoscopic hysterectomy .

Intraoperatively pathology preliminary read is adenocarcinoma of uterus. She had complication of intraoperative bleeding with some hypotension and ultimately underwent open TAHBSO. Bleeding vessel was clipped and hemostasis was achieved with resulting hemoglobin 10 g/dL and creatinine is 1.5 mg/dL (CrCL>50)

Your team gets blood sugars and pain under control and is asked to make VTE recommendations. Which of the following do you choose?

A. IPC
B. UFH + IPC
C. Fondaparinux
D. Enoxaparin + IPC
E. Enoxaparin + IPC/GCS with plans for Extended Prophylaxis after discharge x4 weeks
F. Enoxaparin + IPC/GCS in hospital with plans for Extended Prophylaxis with Apixiban on discharge

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Extended Prophylaxis in Surgical Cases

CHEST® JOURNAL

OFFICIAL PUBLICATION OF THE AMERICAN COLLEGE OF CHEST PHYSICIANS

ACP IMKSAP 18

	Cancer surgery		LMWH for 4 wk
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	Isolated lower leg fracture repairs		None
	Knee arthroscopy with no previous VTE		Early ambulation

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Case 4 Plus…

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E. Enoxaparin + IPC/GCS with plans for Extended Prophylaxis with Enoxaparin after discharge x4 weeks
F. Enoxaparin + IPC/GCS in hospital with plans for Extended Prophylaxis with DOAC on discharge

ORIGINAL ARTICLE

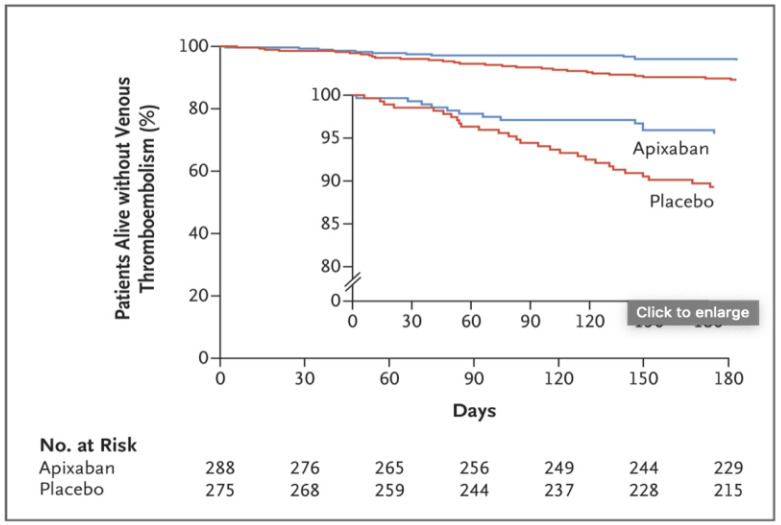
Apixaban to Prevent Venous Thromboembolism in Patients with Cancer

Marc Carrier, M.D., Karim Abou-Nassar, M.D., Ranjeeta Mallick, Ph.D., Vicky Tagalakis, M.D., Sudeep Shivakumar, M.D., Ariah Schattner, M.D., Philip Kuruvilla, M.D., Danny Hill, M.D., Silvana Spadafora, M.D., Katerine Marquis, M.D., Mateya Trinkaus, M.D., Anna Tomiak, M.D., et al., for the AVERT Investigators*

February 21, 2019
N Engl J Med 2019; 380:711-719
DOI: 10.1056/NEJMoa1814468
Chinese Translation 中文翻译

Apixaban for Thromboprophylaxis in Cancer

Published Feb 20, 2019 - Written by Carla Rothaus



- Advanced cancer with lymphoma, pancreas, and gynecologic cancers
- Few colorectal and prostate
- Beware of bowel obstruction/vomiting/absorption in certain malignancies

Case 5

65 y/o male admitted for CHF exacerbation and has been in ED overflow for 8 hours. PMhx significant for acute on chronic systolic dysfunction with ICM 40% . Repeat echo-pending. Other PMhx: DM, HTN,HLP, BMI >30. Your therapies include Lasix and is having a nice response. Oxygenation improved to 94% on RA and urine output is @ 1 Liter so far on Lasix .

1. Enoxaparin
2. UFH
3. Fondaparinux
4. SCDS only
5. Ambulate and Reassess

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Equation #2

Intermediate Risk Factors + > 48 hrs.
+ immobility from baseline= VTE Prophylaxis

- MI
- Acute COPD/Acute respiratory Failure
- CHF
- Active infection
- Severe dehydration
- Age greater than 65 y/o
- BMI>30
- Nephrotic syndrome
- Hormonal therapies
- CVL
- Previous CVA with paresis

Case 6

- 65 y/o female with insulin dependent diabetes, HTN, and COPD admitted with UTI with septic shock with BP 70/50 . Overnight she was started on CRRT due to anuria, pressors, and IV antibiotics

Appropriate VTE prophylaxis includes

A. Enoxaparin with IPC
B. Enoxaparin
C. Fondaparinux with GCS
D. Unfractionated heparin with IPC
E. Unfractionated heparin

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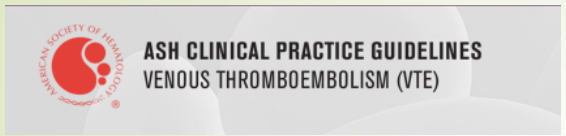

Review of Learning Points

- Know how to navigate Cerner VTE Prevention Order-set
- Know how to navigate moderate risk patients and decipher who needs VTE prophylaxis and who does not
- Know 9 Strong VTE Risk factors
- Be familiar with Intermediate Risk Factors
- Know what populations of surgical patients need extended prophylaxis
- Be aware of possible future role for DOACS in VTE Prevention for Cancer patients
- Think outside the box and document