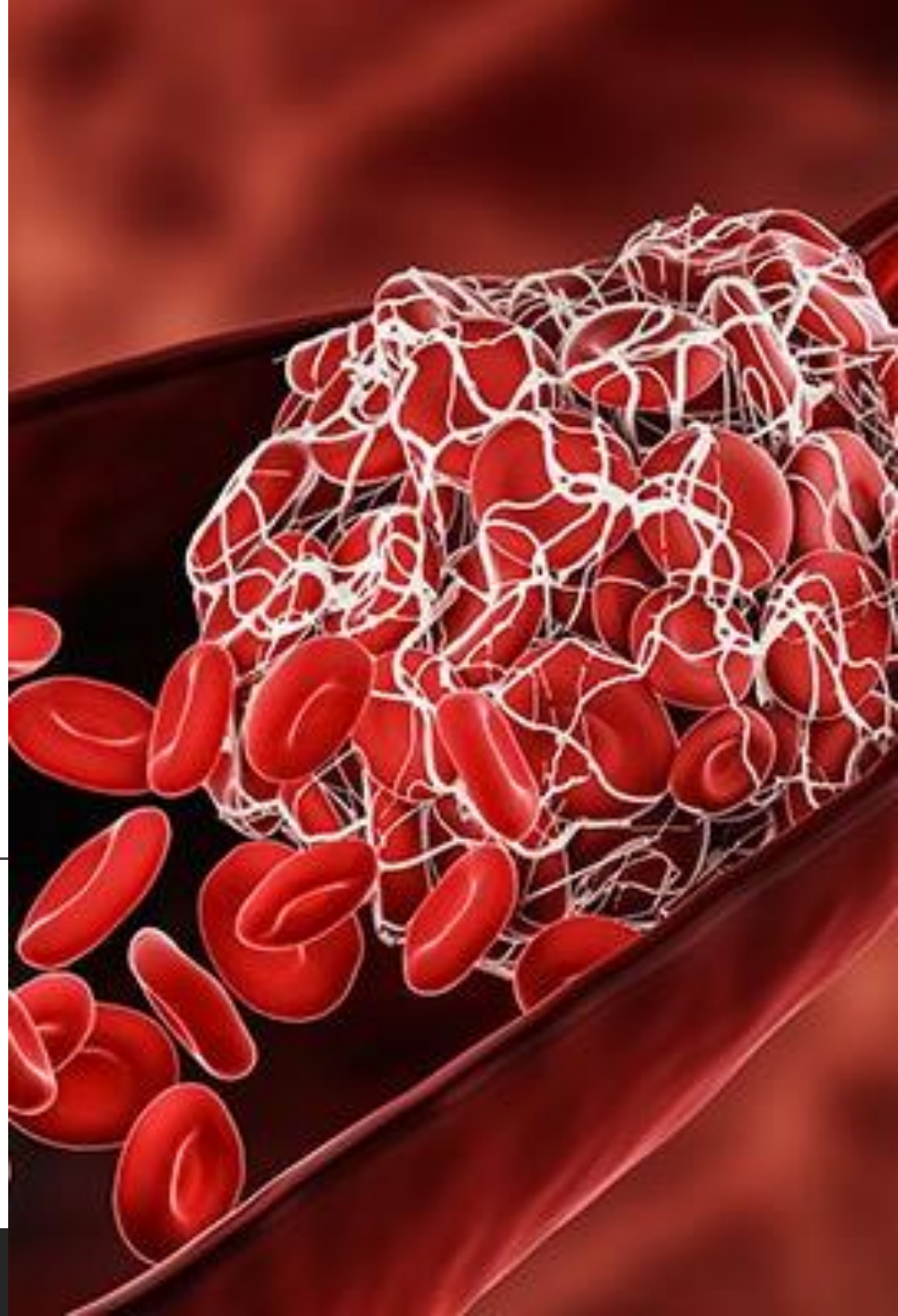
Giving aspirin a shot to prevent a clot?

Aspirin vs standard of care for prevention of venous thromboembolism following orthopedic surgery

JERRICA LILLEY, PHARMD

PGY2 PHARMACOTHERAPY RESIDENT

UIW FEIK SCHOOL OF PHARMACY



Financial Disclosure

NO FINANCIAL CONFLICTS OF INTEREST TO DISCLOSE

Pharmacy Technician Learning Objectives

1. Identify factors that increase the risk of venous thromboembolism after orthopedic surgery

2. List medications that may be used for venous thromboembolism prophylaxis

3. Recognize the role of aspirin in venous thromboembolism prevention in the setting of orthopedic surgery

Pharmacist Learning Objectives

1. Compare and contrast guideline recommended venous thromboembolism prophylaxis agents in the setting of orthopedic surgery

2. Identify risks and benefits of guideline recommended venous thromboembolism prophylaxis agents

3. Given a patient case, develop a treatment plan for a patient undergoing surgical repair of fracture

4. Given a patient case, develop a treatment plan for a patient undergoing total hip arthroplasty or total knee arthroplasty

Abbreviations

VTE: Venous thromboembolism

DVT: Deep vein thrombosis

PE: Pulmonary embolism

THA: Total hip arthroplasty

TKA: Total knee arthroplasty

HFS: Hip fracture surgery

POD: Postoperative day

LMWH: Low molecular weight heparin

UFH: Unfractionated heparin

ASA: Aspirin

DOAC: Direct-acting oral anticoagulant

Trick or Treat

What is the first indication that comes to mind for the use of aspirin?

Nobody has responded yet.

Hang tight! Responses are coming in.

Background

THA & TKA

THA and TKA are frequently performed major orthopedic surgeries

- > 1 million performed annually
- Rates expected to increase with aging population

High risk of VTE compared to other surgical interventions

Median time to diagnosis:

- TKA: 7 days
- THA: 17 days

The Journal of Bone and Joint Surgery. 2015;97(17):1386-1397
Chest. 2012 Dec;142(6):1698-1704
European Heart Journal Supplements (2024) 26 (Supplement 1), i102–i107

Traumatic Fracture Repair

Trauma increases risk of VTE

6 million fractures treated annually in US

> 2 million hospital admissions following traumatic events

Hip and femur fractures associated with high risk of VTE development

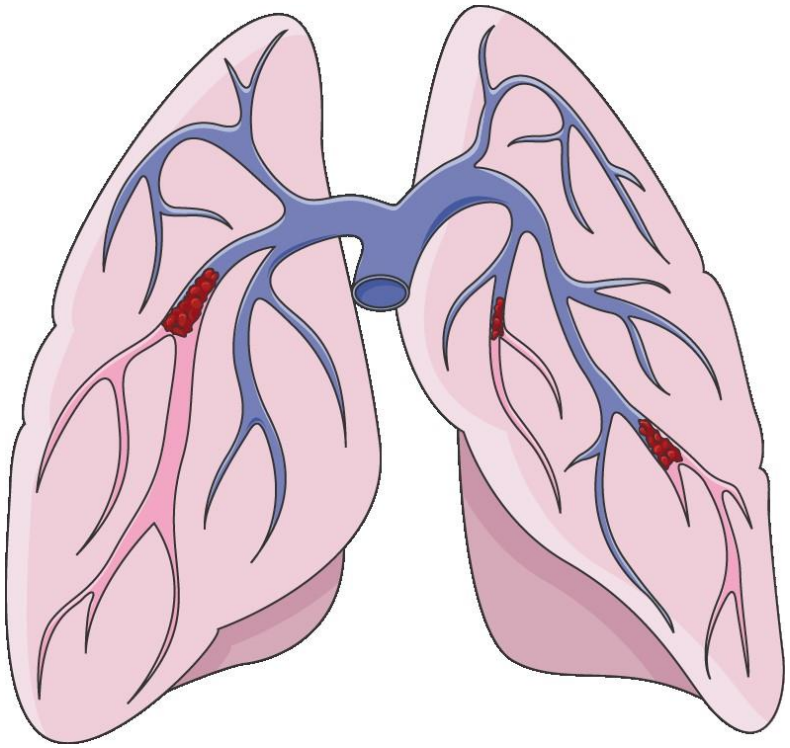
N Engl J Med 2023;388:203-13.

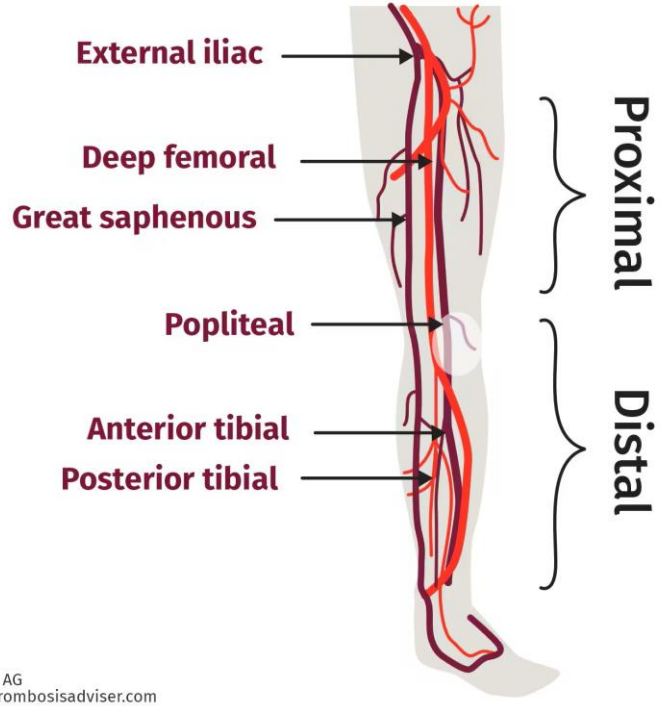
Venous Thromboembolism

Pulmonary embolism

Deep vein thrombosis

- Proximal
- Distal





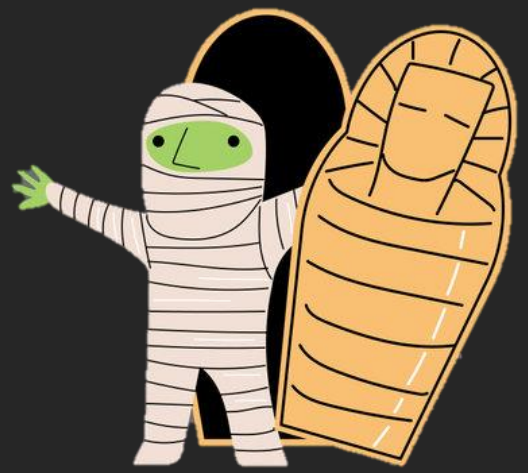
Virchow's Triad

Venous stasis

Vascular damage

Hypercoagulable state

Venous Stasis



- Acute medical illness requiring hospitalization
- Surgery
- Paralysis
- Immobility
- Obesity

Pharmacotherapy: A Pathophysiologic Approach, 11e. McGraw-Hill Education; 2020

Vascular Damage

- Major orthopedic surgery
- Trauma
- Indwelling venous catheters

Pharmacotherapy: A Pathophysiologic Approach, 11e. McGraw-Hill Education; 2020

Hypercoagulable State

- Malignancy
- Factor V Leiden
- Protein C, S, or antithrombin deficiency
- Pregnancy (up to 6 weeks postpartum)
- Medications
  - Estrogen-containing medications
  - Tamoxifen
  - Raloxifene

Pharmacotherapy: A Pathophysiologic Approach, 11e. McGraw-Hill Education; 2020

Enhanced VTE Risk Factors

Patient-related risk factors

- Age ≥ 40
- Female
- BMI > 30
- Malignancy
- History of VTE

Procedure/Injury-related risk factors

- TKA/THA (bilateral > unilateral)
- Fracture to hip, pelvis, or long bones
- General anesthesia ≥ 30 minutes
- Prolonged immobilization
- Use of tourniquet

BMC Musculoskeletal Disorders. 2015;16:24
Circulation. 2003;107(23):I9-I16

Trick or Treat

Which scoring tool is used to predict VTE risk in patients undergoing orthopedic surgery?

0

A. Padua Prediction Score (A)

B. Caprini Score (B)

C. CHADS-VASc Score (C)

D. None of the above (D)

Which scoring tool is used to predict VTE risk in patients undergoing orthopedic surgery?

0

A. Padua Prediction Score **(A)** 0%

B. Caprini Score **(B)** 0%

C. CHADS-VASc Score **(C)** 0%

D. None of the above **(D)** 0%

Which scoring tool is used to predict VTE risk in patients undergoing orthopedic surgery?

0

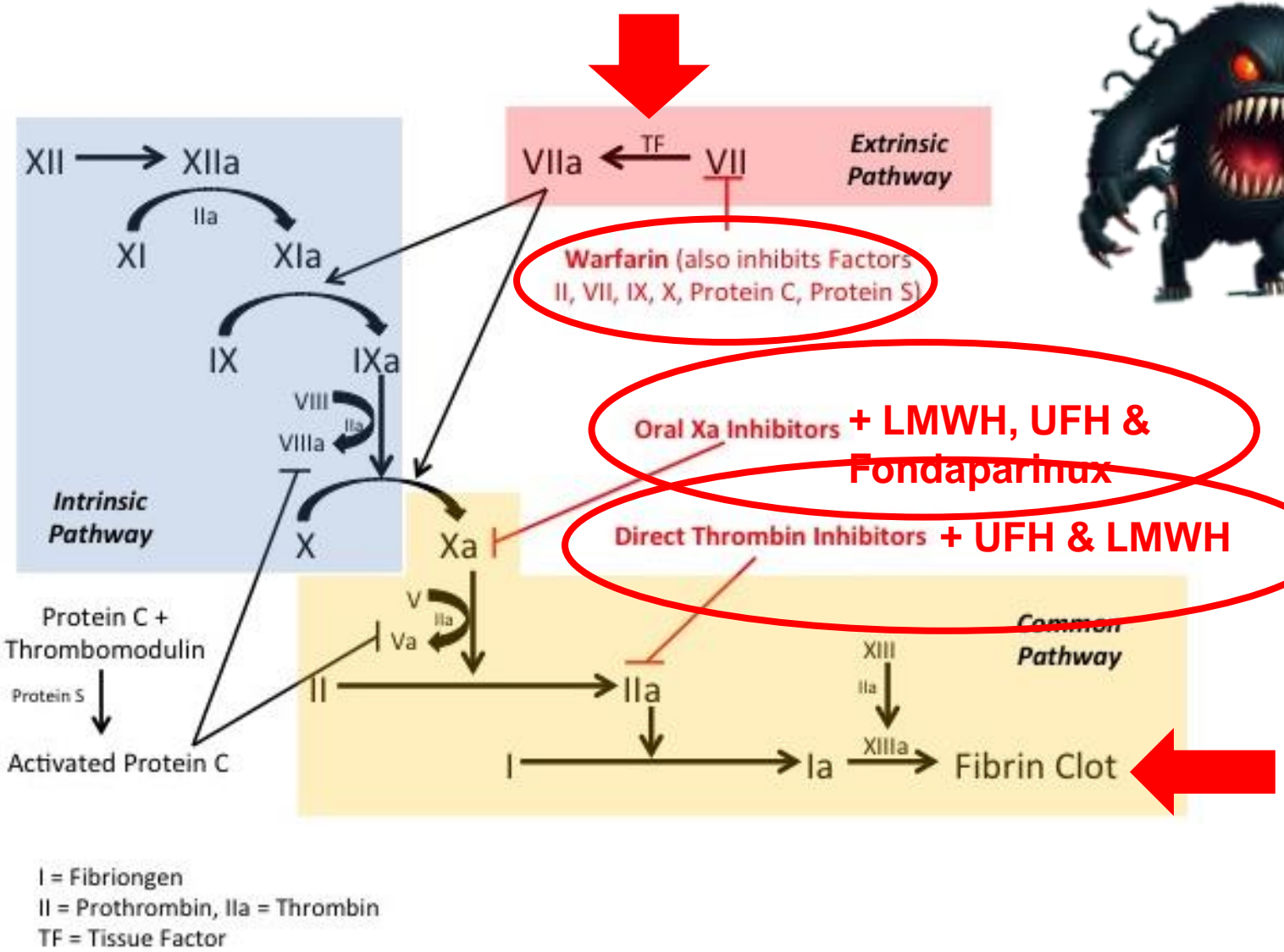
A. Padua Prediction Score **(A)** 0%

B. Caprini Score **(B)** 0%

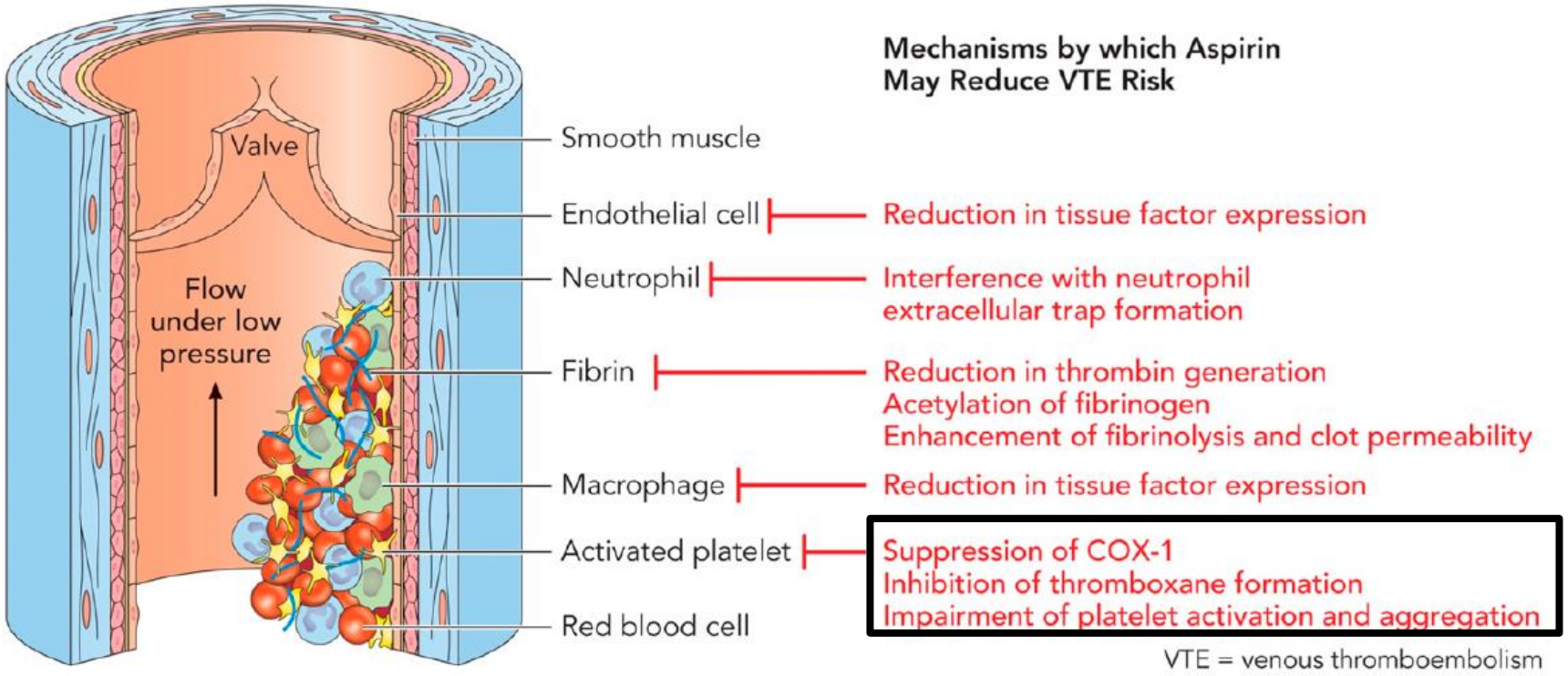
C. CHADS-VASc Score **(C)** 0%

D. None of the above **(D)** 0%

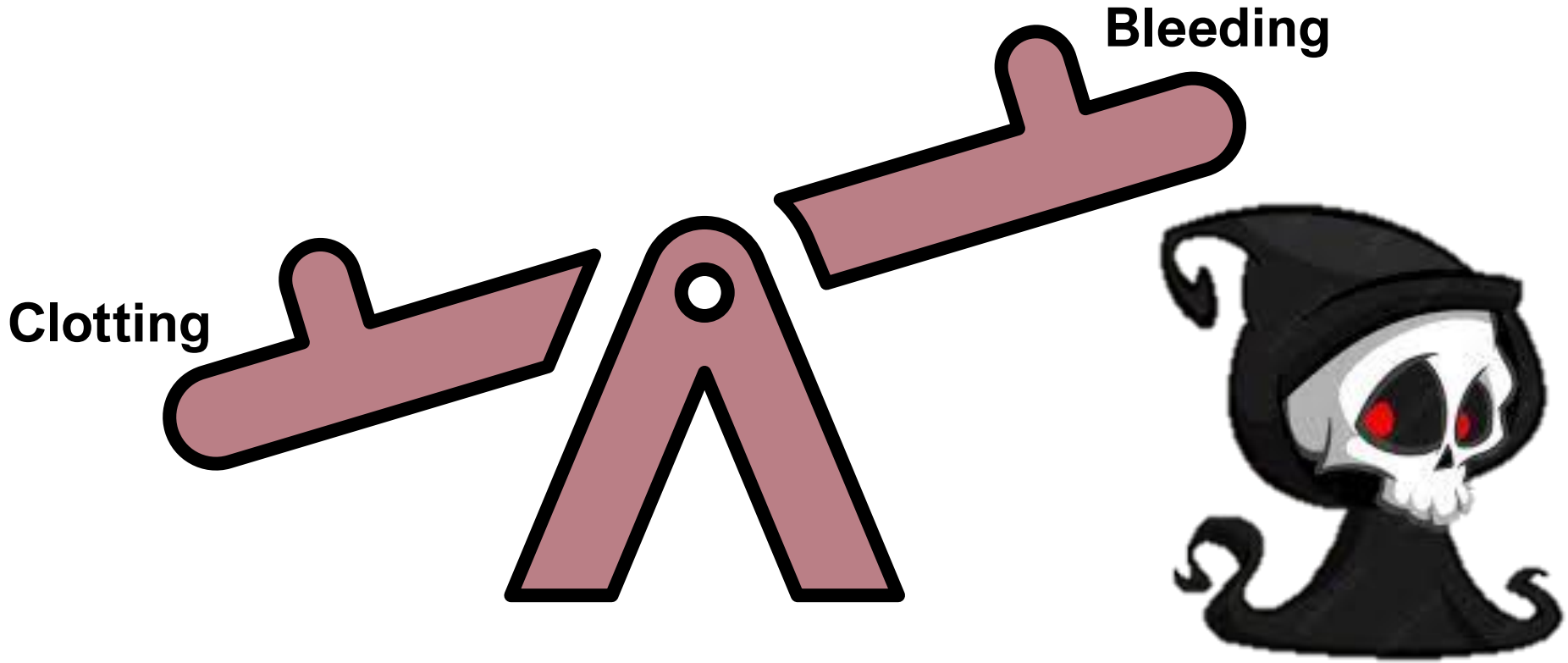
Coagulation Cascade

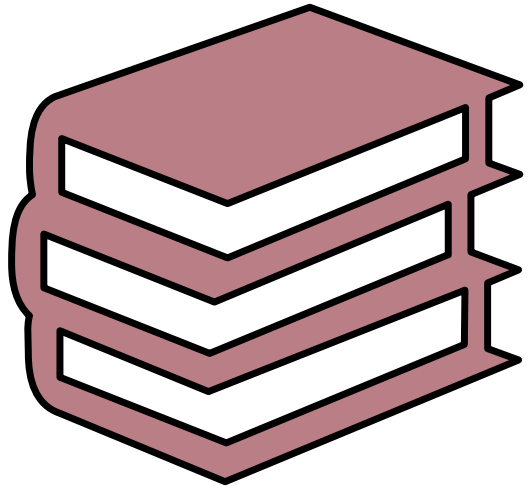


Role of Aspirin in VTE Prophylaxis



Risk vs Benefit





Guideline Recommendations

2012 CHEST Guidelines

THA & TKA

- Recommend use of LMWH, fondaparinux, apixaban, dabigatran, rivaroxaban, UFH, warfarin, or aspirin for 10 to 14 days rather than no prophylaxis (Grade 1B)
- LMWH preferred over alternatives:
  - Fondaparinux, DOAC, UFH (Grade 2B)
  - Warfarin or aspirin (Grade 2C)

Chest. 2012 Dec;142(6):1698-1704

2012 CHEST Guidelines

Hip fracture surgery

- Recommend use of LMWH, fondaparinux, UFH, warfarin, or aspirin for 10 to 14 days rather than no prophylaxis (Grade 1B)
- LMWH preferred over alternatives:
  - Fondaparinux or UFH (Grade 2B)
  - Warfarin or aspirin (Grade 2C)

Chest. 2012 Dec;142(6):1698-1704

2012 CHEST Guidelines

Major orthopedic surgery

- Recommend extending thromboprophylaxis for up to 35 days rather than for only 10 to 14 days (Grade 2B)

Lower leg injury

- Recommend no prophylaxis in patients with isolated lower leg injury requiring leg immobilization (Grade 2C)

Chest. 2012 Dec;142(6):1698-1704

2012 CHEST Guidelines

Statement included with recommendations:

- “One panel member believed strongly that aspirin alone should not be included as an option.”

Grade 1B, 2B, and 2C recommendations

- Moderate to low quality of evidence

Evidence for aspirin use

- Older data
- Unreliable methods of DVT screening, lack of blinding, risk of bias

American Society of Hematology 2019 Guidelines

THA or TKA

- Suggests using aspirin or anticoagulants
- When anticoagulants are used, suggests using DOAC over LMWH
- Suggests using LMWH over warfarin or UFH

Hip fracture surgery

- Suggests using pharmacological prophylaxis over no pharmacological prophylaxis
- Suggests using LMWH or UFH

Blood Adv (2019) 3 (23): 3898–3944

Guideline Recommended Agents

Drug	Dose	Considerations
UFH	5,000 units subcutaneously every 8-12 hours	No renal dose adjustments Contraindicated if history of HIT
Enoxaparin	30 mg subcutaneously every 12 hours 40 mg subcutaneously every 24 hours	CrCl < 30 mL/min: 30 mg every 24 hours Contraindicated if history of HIT
Fondaparinux	2.5 mg subcutaneously every 24 hours	Contraindicated: - Body weight < 50 kg - CrCl < 30 mL/min Safe to use with history of HIT

HIT: Heparin-induced thrombocytopenia

Guideline Recommended Agents

Drug	Dose	Considerations
Rivaroxaban	10 mg PO daily	Avoid use if CrCl < 30 mL/min Avoid use with hepatic dysfunction
Apixaban	2.5 mg PO BID	No renal or hepatic dose adjustments required for this indication
Dabigatran	220 mg PO daily	Must be dispensed in original container Avoid use if CrCl < 30 mL/min
Warfarin	Target INR 2-3	Bridge to target INR Contraindicated in pregnancy Requires frequent monitoring
Aspirin	81 mg PO daily - BID	Avoid use in severe liver disease

Trick or Treat

Which of the following are options for VTE prophylaxis following orthopedic surgery?

0

A. Enoxaparin

B. Aspirin

C. Clopidogrel

D. Rivaroxaban

E. Ticagrelor

Which of the following are options for VTE prophylaxis following orthopedic surgery?

0

A. Enoxaparin 0%

B. Aspirin 0%

C. Clopidogrel 0%

D. Rivaroxaban 0%

E. Ticagrelor 0%

Which of the following are options for VTE prophylaxis following orthopedic surgery?

0

A. Enoxaparin 0%

B. Aspirin 0%

C. Clopidogrel 0%

D. Rivaroxaban 0%

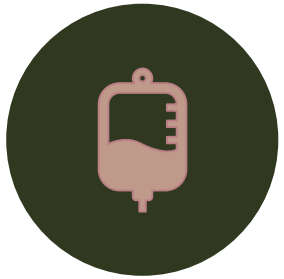
E. Ticagrelor 0%

Benefits of aspirin

Low cost

Easy to access

Oral route

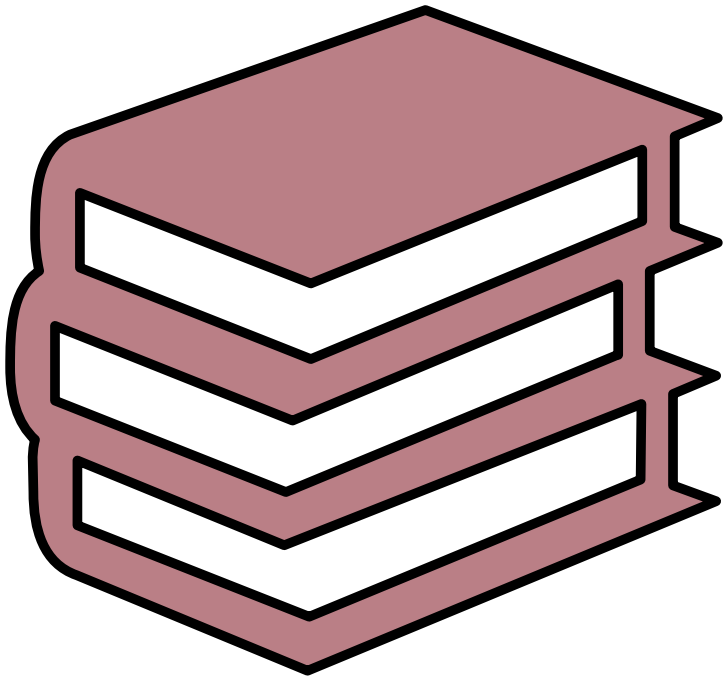


Lower bleed risk?

Clinical Question

Is aspirin a safe and effective option for VTE prophylaxis following THA, TKA, or fracture repair surgery?

Literature Evaluation



Aspirin or Rivaroxaban for VTE Prophylaxis after Hip or Knee Arthroplasty (EPCAT II Trial)

ANDERSON ET AL. 2018

N Engl J Med. 2018;378:699-707

EPCAT II

Objective

- Determine safety and efficacy of extended prophylaxis with aspirin compared to rivaroxaban for prevention of VTE following THA or TKA

Study Design

- Multicenter
- Double-blind
- Randomized
- Non-inferiority

N Engl J Med. 2018;378:699-707

EPCAT II

Inclusion

- Age 18 years or older
- Elective unilateral hip or knee arthroplasty (primary or revision)

Exclusion

- Hip or lower limb fracture within 3 months
- Metastatic cancer
- History of major bleeding, active peptic ulcer disease, platelets < 100,000/L or significant hepatic disease
- CrCl < 30 mL/min
- Need for long-term anticoagulation

*N Engl J Med.*2018;378:699-707

EPCAT II

Intervention

- Rivaroxaban 10 mg by mouth once daily POD 0/1 through POD 5 followed by:
  - TKA: Aspirin 81 mg by mouth once daily for 9 days (14 days total)
  - THA: Aspirin 81 mg by mouth once daily for 30 days (35 days total)

Comparator

- TKA: Rivaroxaban 10 mg by mouth once daily from POD 0/1 through POD 14
- THA: Rivaroxaban 10 mg by mouth once daily from POD 0/1 through POD 35

N Engl J Med. 2018;378:699-707

EPCAT II - Outcomes

Primary Outcomes

- Efficacy: Adjudicated symptomatic VTE, defined as DVT involving popliteal vein or more proximal veins or PE within 90 days
- Safety: Bleeding, including major or clinically relevant nonmajor bleeding

Secondary Outcomes

- Death
- Myocardial infarction
- Stroke
- Wound infection

EPCAT II – Statistical Analysis

Estimated 1% baseline rate of VTE in rivaroxaban group

- Minimally clinically importance difference 1%
- 1% noninferiority limit

1696 patients to provide 90% power

- Increased to 3426 to account for patients lost to follow up

EPCAT II – Baseline Characteristics

Characteristic	Rivaroxaban (N = 1717)	Aspirin (N = 1707)
Age – yr.	62.7	62.9
Male – n (%)	833 (48.5)	804 (47.1)
BMI	31 ± 6.6	31.1 ± 6.8
Risk factors – n (%)		
- Previous VTE	44 (2.6)	37 (2.2)
- Cancer	38 (2.2)	42 (2.5)
- Current smoker	157 (9.1)	162 (9.5)
Time in operating room – Hours	1.4	1.4
Length of hospital stay – Days	3.4	3.6

EPCAT II – Results

Outcomes	Rivaroxaban (N = 1717)	Aspirin (N = 1707)	Difference (95% CI)	Noninferiority P value
Primary outcomes				
Efficacy: Adjudicated symptomatic VTE within 90 days	12 (0.70%)	11 (0.64%)	0.06% (-0.55 to 0.66)	< 0.001
Safety: Major or clinically relevant nonmajor bleeding	17 (0.99%)	22 (1.29%)	0.3% (-1.07 to 0.47)	

Aspirin not superior to rivaroxaban: P = 0.84

EPCAT II – Results

Outcomes	Rivaroxaban (N = 1717)	Aspirin (N = 1707)
Secondary outcomes		
Death	0	1 (0.1%)
Myocardial infarction	1 (0.1%)	2 (0.1%)
Stroke/transient ischemic attack	0	0
Wound infection	58 (3.4%)	44 (2.6%)
Distal DVT (not included in outcomes)	5	8

EPCAT II

Strengths

- Double-blinded study design
- Only evaluated symptomatic VTEs
- Used standardized algorithm to evaluate symptomatic patients

Limitations

- Outcome excluded distal DVTs
- Allowed for continuation of aspirin if taking prior to randomization
- Real world applicability of 5-day lead in with DOAC

*N Engl J Med.*2018;378:699-707

EPCAT II - Conclusions

Extended VTE prophylaxis with aspirin was noninferior to rivaroxaban with regards to safety or efficacy following unilateral THA or TKA

Primary outcome excluded distal DVTs, but reported occurrences were infrequent

Patient population had low baseline risk of VTE

Effect of Aspirin vs Enoxaparin on Symptomatic Venous Thromboembolism in Patients Undergoing Hip or Knee Arthroplasty: The CRISTAL Randomized Trial

SIDHU ET AL. 2022

JAMA. 2022;328(8):719-727

CRISTAL

Objective

- Determine if aspirin monotherapy is noninferior to LMWH in preventing symptomatic VTE within 90 days of primary THA or TKA

Study Design

- Multicenter
- Open-label
- Cluster-randomized
- Crossover

JAMA. 2022;328(8):719-727

CRISTAL

Inclusion

- Age 18 years or older
- Primary TKA or THA for osteoarthritis

Exclusion

- Preoperative anticoagulation for any indication, including DAPT
- Medical contraindication
  - Bleeding disorder
  - Clotting disorder
  - Allergy

JAMA. 2022;328(8):719-727

CRISTAL

Intervention

- Aspirin 100 mg by mouth once daily

Comparator

- Enoxaparin 40 mg subcutaneously once daily
- Reduced dose to enoxaparin 20 mg subcutaneously once daily if:
  - Body weight < 50 kg
  - eGFR < 30 mL/min/1.73 m^2

JAMA. 2022;328(8):719-727

CRISTAL - Outcomes

Primary Outcome

- Symptomatic VTE within 90 days of surgery

Secondary Outcomes

- Joint-related readmission
- Joint-related reoperation
- Major bleeding events including those resulting in readmission, reoperation, or death
- Mortality within 90 days
- Joint-related reoperation within 6 months
- Adherence rates assessed by audits

CRISTAL – Statistical Analysis

Estimated 2% event rate

- Set 1% noninferiority margin

Required 15,562 patients to provide 90% power

- Allowed for 27% loss to follow up
- 251 patients per cluster

Interim analysis

- 2-sided significance level of 0.001 to detect between-group superiority difference for primary outcome
- If between-group superiority difference found, study would be discontinued

JAMA. 2022;328(8):719-727

CRISTAL – Baseline Characteristics

Characteristic	Aspirin (N = 5675)	Enoxaparin (N = 4036)
Age, median (IQR)	67 (61-74)	68 (61-74)
Male, n (%)	2467 (43.5)	1733 (42.9)
BMI, median (IQR)	30.5 (26.9-35.1)	30.6 (26.9-34.9)
American Society of Anesthesiologists Classification, n (%)		
- Class I	315 (5.6)	201 (5)
- Class II	3219 (56.9)	2221 (55.1)
- Class III	2074 (36.7)	1582 (39.2)
- Class IV	47 (0.8)	29 (0.7)
Previous VTE	276 (5.2)	240 (6.3)
Preoperative aspirin, n (%)	817 (15.4)	584 (15.2)

CRISTAL – Procedure Type

Procedure	Aspirin (N = 5675)	Enoxaparin (N = 4036)
Unilateral TKA	2973 (52.4)	2113 (52.4)
Unilateral THA	2066 (36.4)	1494 (37)
Bilateral TKA	547 (9.6)	385 (9.5)
Bilateral THA	89 (1.6)	44 (1.1)

CRISTAL - Results

Patient enrollment discontinued after second interim analysis

Outcome	Aspirin (N = 5416)	Enoxaparin (N = 3787)	Estimated treatment difference, % (95% CI)	P value
Primary Outcome				
Any symptomatic VTE within 90 days	187 (3.5%)	69 (1.8%)	1.97 (0.54 to 3.41)	0.007
Components of primary outcome				
PE within 90 days	58 (1.1%)	21 (0.6%)	0.44 (-0.19 to 1.08)	0.17
Any DVT within 90 days	140 (2.6%)	50 (1.3%)	1.61 (0.54 to 2.68)	0.003
Above-knee DVT	12/5415 (0.2%)	6 (0.2%)	0.06 (-0.11 to 0.23)	0.49
Below-knee DVT	129/5415 (2.4%)	45 (1.2%)	1.49 (0.49 to 2.50)	0.004

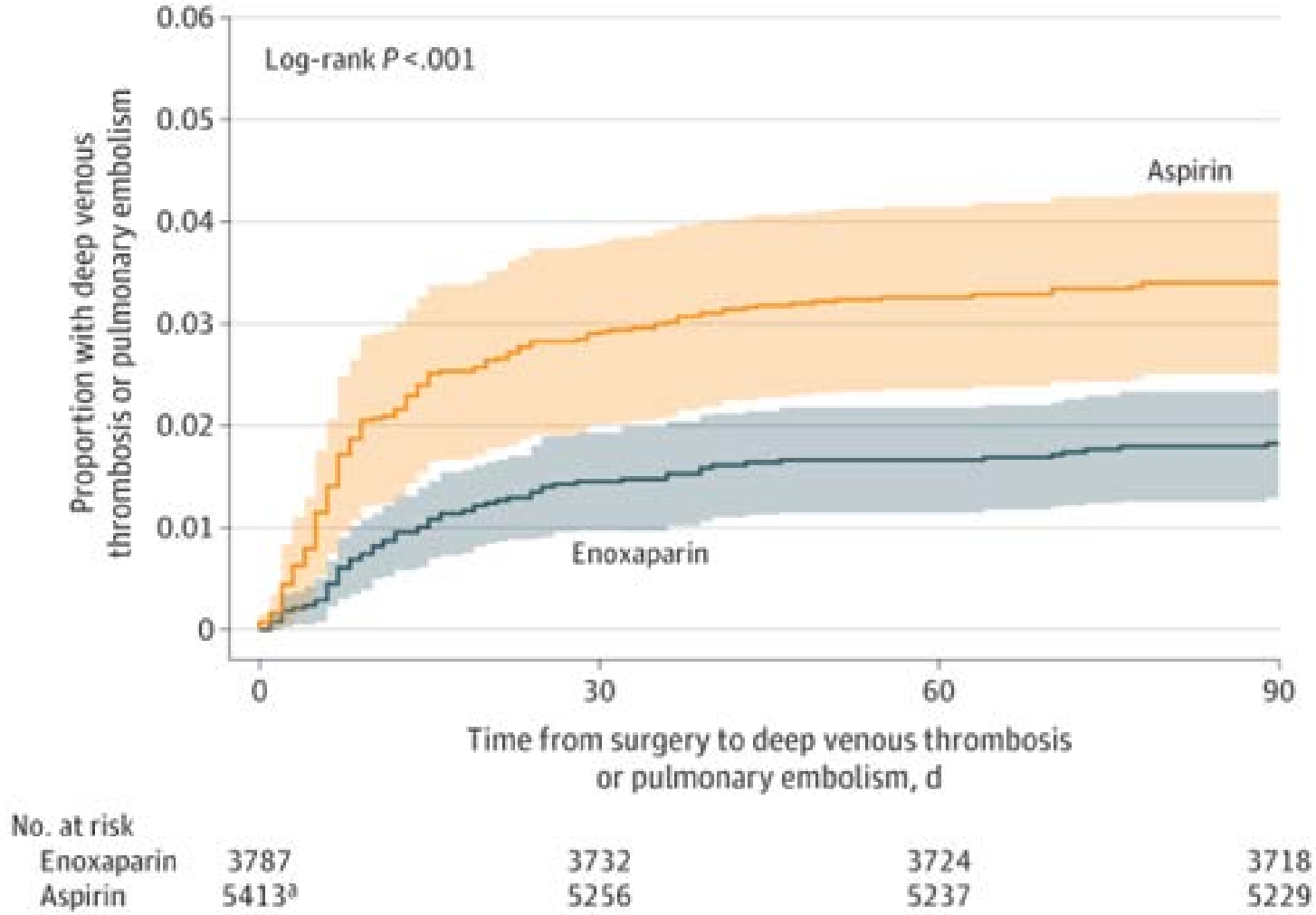
CRISTAL - Results

Median time to VTE, days (IQR)

- Aspirin: 7.5 (5-9)
- Enoxaparin: 12 (7-25)

NNH = 58

No statistically significant differences in secondary outcomes



CRISTAL

Strengths

- Evaluated use of aspirin in initial postoperative period
- Baseline characteristics well matched between groups

Limitations

- Open-label study design
- Risk of selection bias
- 5.2% loss to follow-up
- Differences in US dosing

JAMA. 2022;328(8):719-727

CRISTAL – Conclusions

When used within 24 hours postoperatively, aspirin resulted in higher rates of symptomatic VTE compared to enoxaparin in patients undergoing THA or TKA

Primary outcome mainly due to occurrence of distal DVT

Open-label study design may have impacted results

Patient population had low baseline risk of VTE

JAMA. 2022;328(8):719-727

Trick or Treat

What component of the primary outcome drove the discontinuation of the CRISTAL Trial?

A. Mortality

B. Pulmonary Embolism

C. Proximal DVT

D. Distal DVT

What component of the primary outcome drove the discontinuation of the CRISTAL Trial?

A. Mortality 0%

B. Pulmonary Embolism 0%

C. Proximal DVT 0%

D. Distal DVT ✓ 0%

What component of the primary outcome drove the discontinuation of the CRISTAL Trial?

A. Mortality 0%

B. Pulmonary Embolism 0%

C. Proximal DVT 0%

D. Distal DVT ✓ 0%

Aspirin or Low-Molecular-Weight Heparin for Thromboprophylaxis after a Fracture (PREVENT CLOT)

O'TOOLE ET AL. 2023

N Engl J Med 2023;388:203-213

PREVENT CLOT

Objective

- Examine safety and efficacy of aspirin for thromboprophylaxis compared to LMWH in patients with a major extremity fracture

Study Design

- Multicenter
- Randomized
- Open-label
- Non-inferiority

N Engl J Med 2023;388:203-213

PREVENT CLOT

Inclusion

- Age 18 years or older
- Extremity fracture treated operatively
  - Upper extremity from shoulder to wrist
  - Lower extremity from hip to midfoot
- Fracture of pelvis or acetabulum treated operatively or nonoperatively

Exclusion

- Presentation > 48 hours after injury
- ≥ 3 doses of thromboprophylaxis prior to consent
- History of VTE within previous 6 months
- Chronic blood clotting disorder
- Receipt of therapeutic anticoagulation at time of admission
- CrCl < 30 mL/min

N Engl J Med 2023;388:203-213

PREVENT CLOT

Intervention

- Aspirin 81 mg by mouth twice daily

Comparator

- Enoxaparin 30 mg subcutaneously twice daily

Duration

- Could end at discharge or continue based on site-specific clinical protocol

Adherence

- Received at least 80% of assigned in-hospital doses
- If prescribed at discharge, had to be same enrollment group

N Engl J Med 2023;388:203-213

PREVENT CLOT - Outcomes

Primary Outcome

- Death from any cause at 90 days

Secondary Efficacy Outcomes

- Cause-specific death (related to PE, possibly related to PE, or unlikely to be related to PE)
- Nonfatal PE
- DVT (any, proximal, or distal)

PREVENT CLOT - Outcomes

Secondary Safety Outcomes

- Bleeding complications
  - Symptomatic bleeding into critical area or organ
  - Bleeding causing ≥ 2 g/dL drop in Hgb within 24 hours and led to transfusion of ≥ 2 units whole blood or packed red blood cells
  - Bleeding that led to reoperation
- Wound complications
  - Wound drainage, hematoma or seroma that led to reoperation
- Infection
  - CDC criteria for deep incision or organ-space infection leading to surgical treatment

PREVENT CLOT – Statistical Analysis

- Noninferiority margin for death from any cause of 0.75 percentage points
- Sample size of 12,200 patients to provide 95% power
- Evaluated primary outcome using treatment-specific Kaplan-Meier estimators
- Assessed noninferiority with upper boundary of two-sided 96.2% CI

N Engl J Med 2023;388:203-213

PREVENT CLOT – Baseline Characteristics

Characteristic	Aspirin (N = 6101)	Enoxaparin (N = 6110)
Age – yr ± SD	44.5 ± 18	44.7 ± 17.6
Male, n (%)	3832 (62.8)	3769 (61.7)
BMI, median (IQR)	27.1 (23.6-31.8)	27.4 (23.7-32.3)
Risk factor, n (%)		
- Previous VTE	43 (0.7)	46 (0.8)
- Cancer	140 (2.3)	166 (2.7)
- Current smoker	2099 (34.4)	2139 (35)
Medication prior to injury, n (%)		
- Estrogen or oral contraceptive	112 (1.8)	107 (1.8)
- Aspirin	496 (8.1)	476 (7.8)
- Clopidogrel or other antiplatelet	1355 (22.2)	1288 (21.1)

PREVENT CLOT – Baseline Characteristics

Characteristic	Aspirin (N = 6101)	Enoxaparin (N = 6110)
Injury Severity Score (ISS), n (%)		
- < 9	2522 (41.3)	2606 (42.7)
- 9-15	2715 (44.5)	2607 (42.7)
- >15	833 (13.7)	864 (14.1)
Location of fracture, n (%)		
- Lower extremity only	4093 (67.1)	4046 (66.2)
- Upper extremity only	724 (11.9)	741 (12.1)
- Lower and upper extremity	1253 (20.5)	1290 (21.1)
In-hospital days	5.3 ± 5.9	5.3 ± 5.4
Discharged on thromboprophylaxis, n (%)	5709 (93.6)	5427 (88.8)
Duration of thromboprophylaxis, median (IQR)	21 (19-21)	21 (14-21)

PREVENT CLOT – Results

Outcome	Aspirin (N= 6101)	Enoxaparin (N = 6110)	% Difference (96.2% CI)	Noninferiority P value
Primary outcome: Death from any cause				
Intention-to-treat population, n (%)	47 (0.78)	45 (0.73)	0.05 (-0.27 to 0.38)	< 0.001
Per-protocol population, n (%)	41 (0.75)	38 (0.72)	0.03 (-0.31 to 0.38)	

Aspirin not superior to LMWH: P = 0.63

PREVENT CLOT – Results

Outcome	Aspirin (N = 6101)	Enoxaparin (N = 6110)	% Difference (95% CI)
Secondary efficacy outcomes			
Any PE	90 (1.49)	90 (1.49)	0 (-0.43 to 0.43)
DVT			
- Any	151 (2.51)	103 (1.71)	0.80 (0.28 to 1.31)
- Proximal	74 (1.23)	59 (0.98)	0.25 (-0.12 to 0.62)
- Distal	87 (1.45)	52 (0.86)	0.58 (0.20 to 0.96)
Secondary safety outcome			
- Bleeding complications	834 (13.72)	869 (14.27)	-0.54 (-1.78 to 0.69)

No statistically significant difference found in cause-specific death, wound complications, or infection

PREVENT CLOT

Strengths

- Used standardized doses between treatment sites
- Evaluated mortality as primary outcome
- Evaluated safety outcomes

Limitations

- Open-label study design
- Did not include admission location or disposition
- Did not provide monitoring/adherence information
- No standardized duration of VTE prophylaxis

N Engl J Med 2023;388:203-213

PREVENT CLOT – Conclusions

When used for VTE prophylaxis following traumatic fractures, aspirin was noninferior to LMWH with regards to mortality

Higher rates of distal DVTs in patients receiving aspirin

Open-label study design may have impacted results

Patient population had low baseline risk of VTE

N Engl J Med 2023;388:203-213

Summary

	EPCAT II		CRISTAL		PREVENT CLOT	
Agents compared	Aspirin	Rivaroxaban	Aspirin	Enoxaparin	Aspirin	Enoxaparin
Symptomatic VTE at 90 days*	=		✗	✓	N/A	
Symptomatic PE at 90 days	=		=		=	
Symptomatic DVT at 90 days	=		✗	✓	✗	✓
Death from any cause at 90 days**	=		=		=	
Major bleed or clinically relevant nonmajor bleed	=		=		=	

*Primary outcome for EPCAT II & CRISTAL
**Primary outcome for PREVENT CLOT

Trick or Treat

Are you in favor of using aspirin for VTE prophylaxis following orthopedic surgery?

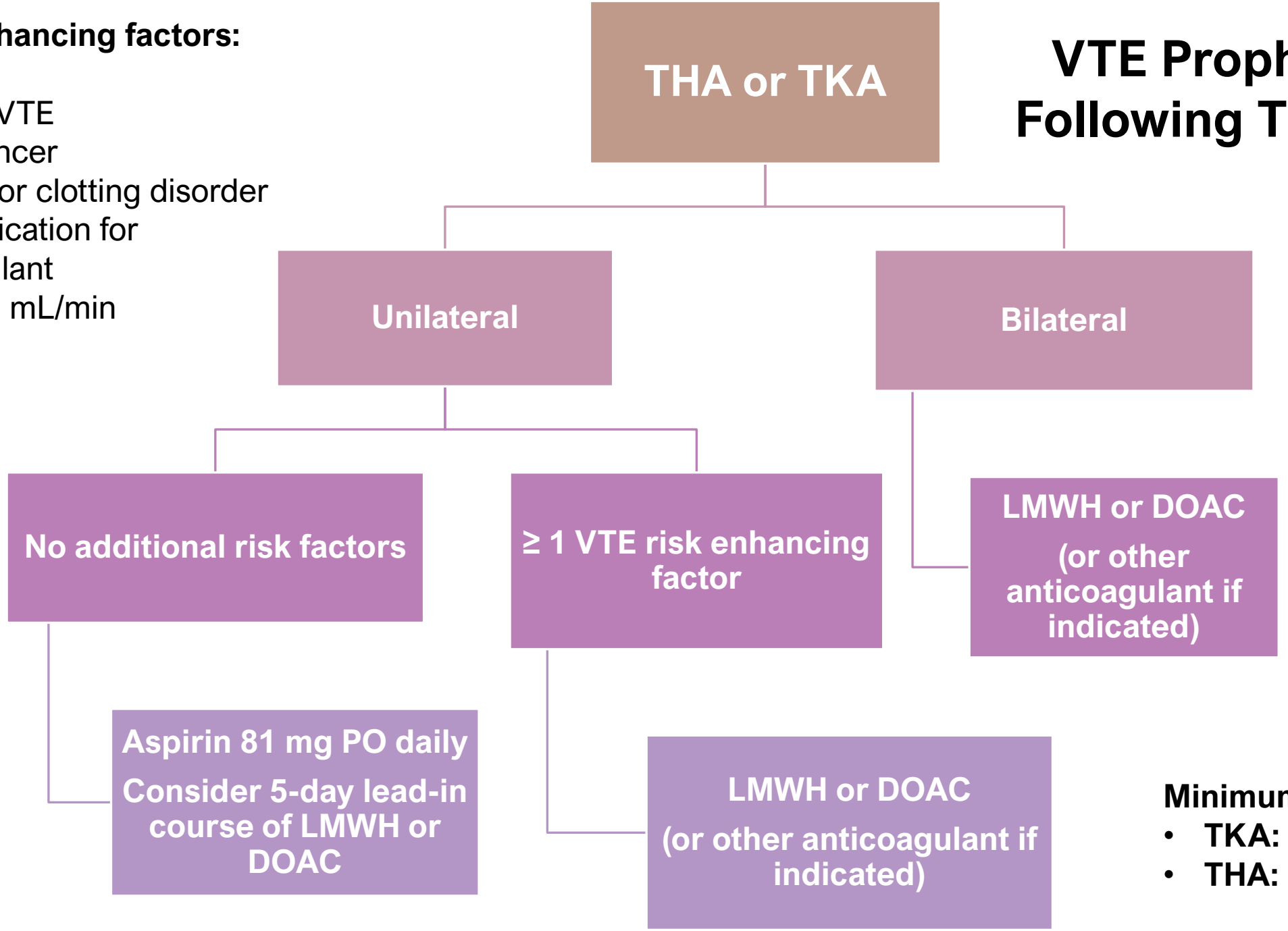
A. Yes 0%

B. No 0%

VTE Prophylaxis Following THA/TKA

VTE risk enhancing factors:

- BMI > 35
- Previous VTE
- Active cancer
- Bleeding or clotting disorder
- Other indication for anticoagulant
- CrCl < 30 mL/min



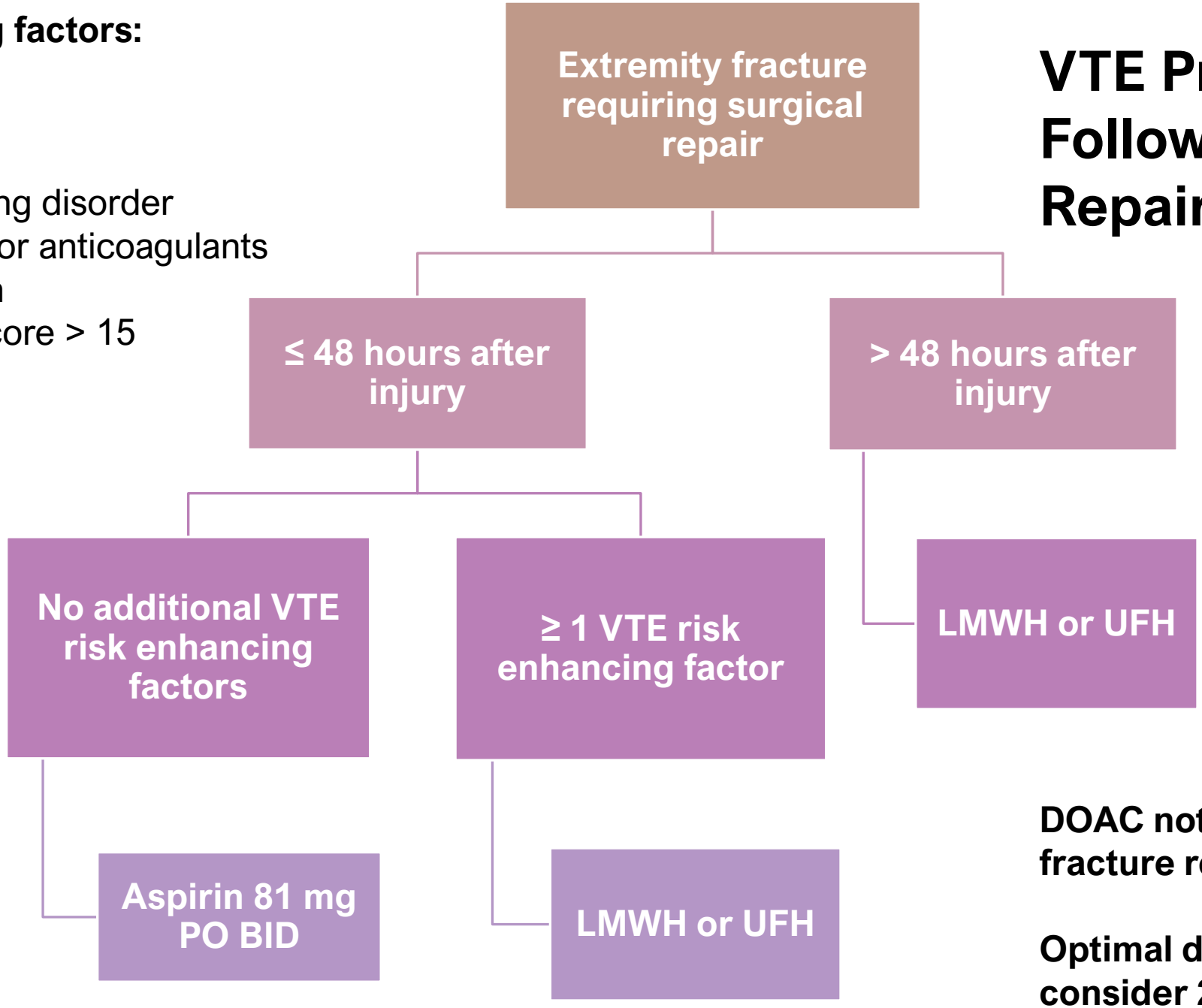
Minimum duration:

- **TKA: 14 days**
- **THA: 35 days**

VTE Prophylaxis Following Fracture Repair Surgery

VTE risk enhancing factors:

- BMI ≥ 30
- Previous VTE
- Active cancer
- Bleeding or clotting disorder
- Other indication for anticoagulants
- CrCl < 30 mL/min
- Injury Severity Score > 15



DOAC not indicated for hip fracture repair

Optimal duration unclear, consider 21 days

BOLO

PEPPER Trial

- Comparative Effectiveness of Pulmonary Embolism Prevention After Hip and Knee Replacement
- Primary or revision hip or knee arthroplasty
- Enteric coated aspirin vs low intensity warfarin (target INR 2) vs rivaroxaban for 30 days
- Primary outcomes: all-cause mortality, DVT, and PE

EPCAT III Trial

- VTE Prevention Following Total Hip and Knee Arthroplasty
- Elective THA or TKA
- Aspirin vs rivaroxaban + aspirin
- Primary outcomes: VTE, bleeding

Resources for Pharmacists

2012 CHEST Guidelines

- Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e278S-e325S.

2019 ASH Guidelines

- Anderson DR, Morgano GP, Bennett C, et al. American Society of Hematology 2019 guidelines for management of venous thromboembolism: prevention of venous thromboembolism in surgical hospitalized patients. Blood Adv. 2019;3(23):3898-3944.

2018 NICE Guidelines

- National Institute for Health and Care Excellence. Venous Thromboembolism in Over 16s: Reducing the Risk of Hospital-Acquired Deep Vein Thrombosis or Pulmonary Embolism. NICE guideline [NG89]. Available at: https://www.nice.org.uk/guidance/ng89. Accessed 11 October 2024.

Post-Test Questions

Post-Test Question 1

In a patient undergoing total hip or knee arthroplasty, which VTE prophylaxis agents are indicated for use in a patient with a CrCl < 30 mL/min? (Select all that apply)

a. Heparin 5,000 units subQ every 8 hours
b. Enoxaparin 40 mg subQ every 24 hours
c. Fondaparinux 2.5 mg subQ every 24 hours
d. Apixaban 2.5 mg PO BID

Post-Test Question 2

In the PREVENT CLOT and CRISTAL trials, aspirin was associated with lower instances of major bleeding or clinically relevant nonmajor bleeding compared to LMWH.

- A. True
- B. False


https://nypost.com/2023/05/30/robert-englund-done-playing-freddy-krueger-too-old-and-thick/

Post-Test Question 3

Freddy Krueger, a 62-year-old male, tripped and fell while running down Elm Street. He presented to the hospital immediately following his fall and was found to have a fracture to his femur (thighbone) that will require surgical repair. He has no known past medical history, normal renal function, and his BMI is 23. He has a fear of needles and would prefer not to give himself injections. What would you recommend for VTE prophylaxis?

a. Apixaban 2.5 mg PO BID
b. Warfarin with INR goal of 2-3
c. Aspirin 81 mg PO BID
d. Enoxaparin 40 mg subcutaneously once daily

Post-Test Question 4

After years of stalking children throughout the streets of Salem, Winifred Sanderson needs a total hip arthroplasty. She is 81 years old, with a past medical history significant for type 2 diabetes, hypertension, and atrial fibrillation (CHA_2DS_2-VASc = 5). She weighs 176 lbs and her BMI is 28.4. Her SCr is 1.5 mg/dL and her CrCl is 31 mL/min. What is the most appropriate regimen for VTE prophylaxis following her surgery?

a. Apixaban 2.5 mg PO BID
b. Warfarin with INR goal of 2-3
c. Aspirin 81 mg PO BID
d. Enoxaparin 40 mg subcutaneously once daily

https://disney.fandom.com/wiki/Winifred_Sanderson

Special Thanks

Faculty Mentor

- Sarah Berman, PharmD, BCCCP

Critique

- Tina Beck, PharmD, MSc, BCPS