

Thromboprophylaxis: Is Aspirin Enough?

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Objectives



- Burden of venous thromboembolism (VTE)
- Current evidence regarding aspirin for thromboprophylaxis
- Suggested thromboprophylaxis algorithm



Burden of VTE



- Pulmonary embolism (PE) is a significant cause of preventable death
- Deep vein thrombosis (DVT) can cause significant dysfunction

Stop the Clot, Spread the Word™





KNOW THE RISKS

Blood clots do not discriminate by age, gender, ethnicity or race. Blood clots can affect anyone. Three major risk factors are:



Burden of VTE

- Pulmonary embolism (PE) is a significant cause of preventable death
- Deep vein thrombosis (DVT) can cause significant dysfunction
- The cost for treatment of blood clots and associated complications in the US is >\$10 billion annually



- Major orthopaedic fracture is an independent risk factor for VTE
- 7-fold increased risk for VTE, despite thromboprophylaxis





Burden of VTE

Thromboprophylaxis Options



Anticoagulant



- Inhibits fibrin clot formation
- Inhibits blood clotting components
- LMWH targets antithrombin
- Direct oral anticoagulants target specific clotting factors

Antiplatelet



- Inhibits platelet aggregation
- Inhibits blood clotting components
- Aspirin (acetylsalicylic acid) is a COX-1 inhibitor



ORIGINAL ARTICLE

Aspirin or Low-Molecular-Weight Heparin for Thromboprophylaxis after a Fracture

Major Extremity Trauma Research Consortium (METRC)*



- Pragmatic, multicenter, randomized, noninferiority trial (n=12,211)
- Operative extremity fracture proximal to metatarsal or carpal bones
 AND
- Pelvis or acetabulum fracture, treated operatively or non-operatively



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• Treatments:

LMWH: 30 mg subcutaneously, twice per day ASA: 81 mg orally, twice per day

- Duration based on hospital protocol
- Open-label (patients, clinicians NOT blinded)





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Major Extremity Trauma Research Consortium (METRC)*



- Aspirin is **noninferior** to LMWH in preventing **all-cause mortality** after ortho trauma
- No difference:
 - Death due to PE or PE
 - Bleeding, wound dehiscence, infection, proximal DVT
- Difference:

LMWH favored in distal DVT (0.9% vs 1.5%, 95%CI: 0.2 – 1.0)



Risk-stratified thromboprophylaxis effects of aspirin versus low-molecular-weight heparin in orthopedic trauma patients: A secondary analysis of the PREVENT CLOT trial

J Trauma Acute Care Surg Volume 96, Number 4

- Do the PREVENT CLOT results apply to patients at highest risk of thrombosis?
- Classification: Stratified based on Caprini Score into 4 quartiles
- Analysis:
 - Intention-to-treat
 - Win ratio using a hierarchical outcome: Mortality, PE, DVT, bleeding



Risk-stratified thromboprophylaxis effects of aspirin versus low-molecular-weight heparin in orthopedic trauma patients: A secondary analysis of the PREVENT CLOT trial

- Thromboembolic outcomes were similar with LMWH or aspirin across stratified groups including high risk, medium-high risk, low-medium risk, or low risk
- Aspirin was favored when patient satisfaction was considered

Caprini Score Value	Risk Factor
1 point	Age 41–60 years
	Body mass index $>30 \text{ kg/m}^2$
	History of myocardial infarction
	Congestive heart failure
	Cerebrovascular disease
	Diabetes
	Oral contraceptives or hormone replacement therapy Abdominal injury
	Thoracic injury
2 points	Age 61–74 years
	Prior cancer diagnosis
	Immobilization due to restricted weight bearing
	Fracture of the tibia
	Head injury
3 points	Age ≥75 years
	Previous venous thromboembolism
5 points	Multi-trauma (Injury Severity Score ≥ 16) ²⁰
-	Fracture of the femur, pelvis, or acetabulum Spinal cord injury

Thromboprophylaxis for Hip Fracture

Serial thrombelastography from admission to 3 months

Demographic Variable	n = 294
Age, years	77.3 (11.1)
Sex, % Female	65.5%
Clinical Frailty Scale	4.4 (1.9)
Surgery Type, % Arthroplasty	44.9%







Maximal Amplitude – Measure of Clot Strength



Platelet Contribution to Coagulopathy



Platelet Mapping – AA Pathway



Platelet Contribution to Coagulopathy



Platelet Mapping Can Measure Antiplatelet Effect



pm_aa_ma

Pathophysiology of Hypercoagulability

Platelet Mapping Can Measure Pathophysiology



Platelet Activation

Fibrinogen Function



Role for Personalized Thromboprophylaxis

Individual Risk Assessment – TRiP (cast) Score

	Score
Trauma (choose 1 – most severe trauma)	
High-risk	
Fibula and/or tibia shaft fracture; tibial plateau fracture; Achilles tendon rupture	3
Intermediate-risk	
Bi or tri-malleolar ankle fracture; patellar fracture; ankle dislocation; Lisfranc injury; severe knee sprain (with edema/ hemarthrosis); severe ankle sprain (grade 3)	2
Low-risk	
Single malleolar ankle fracture; patellar dislocation; (meta)tarsal bone(s) or forefoot fracture; non-severe knee sprain or ankle sprain (grade 1 or 2); significant muscle injury	1
Immobilization, cast	
Upper-leg	3
Lower-leg	2
Foot (ankle free) or any semi-rigid without plantar support	1
Other or bracing with plantar support	0
Patients' characteristics	
Age in years	
<35	0
≥35 and <55	1
≥55 and <75	2
≥75	3
Male sex	1
BMI	
≥25 and <35 kg/m ²	1
≥35 kg/m²	2
Family history of VIE (first-degree relative)	2
Personal history of VIE or known major thrombophilia	4
Current use of oral contraceptives or estrogenic hormone therapy	4
Cancer diagnosis within the past 5 years	3
Pregnancy or puerpenum Other immediation within the next 0 menths	3
Other immobilization within the past 3 months	
Comorbidity	2
Comorbiancy	
Heart failure, rneumatoid artinritis, chronic kidney disease, COPD, IBD	1
Chronic venous insuniciency (vancose veins)	1

TRiP Cast Score

Risk stratification based on:

- Type of injury
- Type of immobilization
- Age
- Sex
- Known risk factors

Patients with a score of **7 or more** would likely benefit from thromboprophylaxis

Role for Personalized Thromboprophylaxis

Individual Risk Assessment – Trauma Embolic Scoring System

Table 1 Components of the Trauma Embolic Scoring System (TESS) and their associated scores (adapted from Rogers *et al*¹⁴

Predictor	TESS score		
Age (years)			
18–29	0		
30–64	1		
≥65	2		
Injury Severity Score			
1–9	0		
10–16	3		
17–25	3		
>25	5		
Pre-existing obesity			
No pre-existing obesity	0		
Pre-existing obesity	1		
Ventilation days			
No ventilation days	0		
Ventilator days	4		
Lower extremity fracture			
No lower extremity fracture	0		
Lower extremity fracture	2		





In surgically treated patients, if OR delayed consider pharmacologic thromboprophylaxis up to 12 hours pre-operatively







- Current clinical and basic science evidence suggests that ASA (aspirin) is appropriate for prevention of PE and proximal DVT
 - Noninferior to LMWH
 - Oral medications are preferred by patients
- Individual assessment and risk stratification still recommended
 - Contraindications to Aspirin: Allergy, prior gastrointestinal ulcer, thrombocytopenia
 - **Contraindications to Anticoagulants:** Allergy, acute or chronic renal failure for direct oral anticoagulants





Remaining Questions:

- BID vs. daily dosing?
- Oral anticoagulant for thromboprophylaxis?
- Duration of thromboprophylaxis?
- Clinical significance of distal DVT?



Acknowledgements



Thank you!













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