# Thromboprophylaxis in the Orthopaedic Trauma Patient: What is Sufficient?

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# Disclosures

- **Scientific Advisory Committee**
  - Osteoporosis Canada
- **Institutional Research Funding**
  - Johnson & Johnson
- **Educational Engagements**
  - Stryker
- **Associate Editor**
  - Canadian Journal of Surgery

# Objective: What is Optimal?

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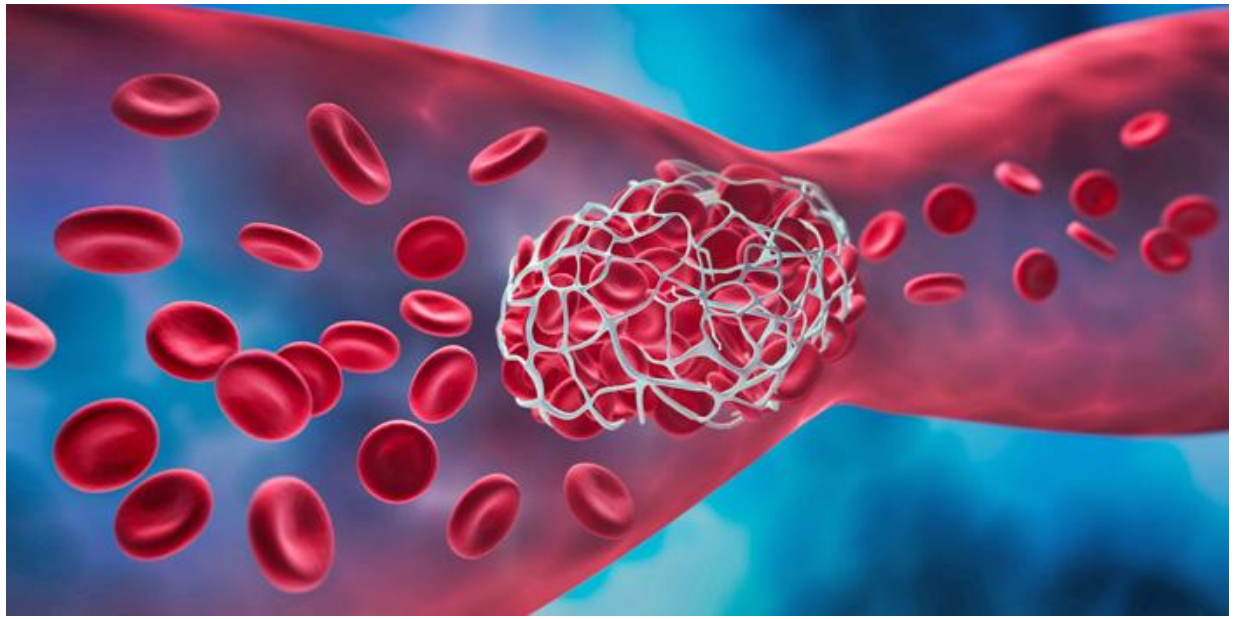
## To challenge you to consider the value of personalized thromboprophylaxis



# Burden of Venous Thromboembolism

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## Patient Experience

34 year old female
Proximal DVT POD 5

64 year old male
PE POD 7


82 year old female
Proximal DVT POD 3

18 year old male
PE POD 1

# Burden of VTE in Orthopaedics

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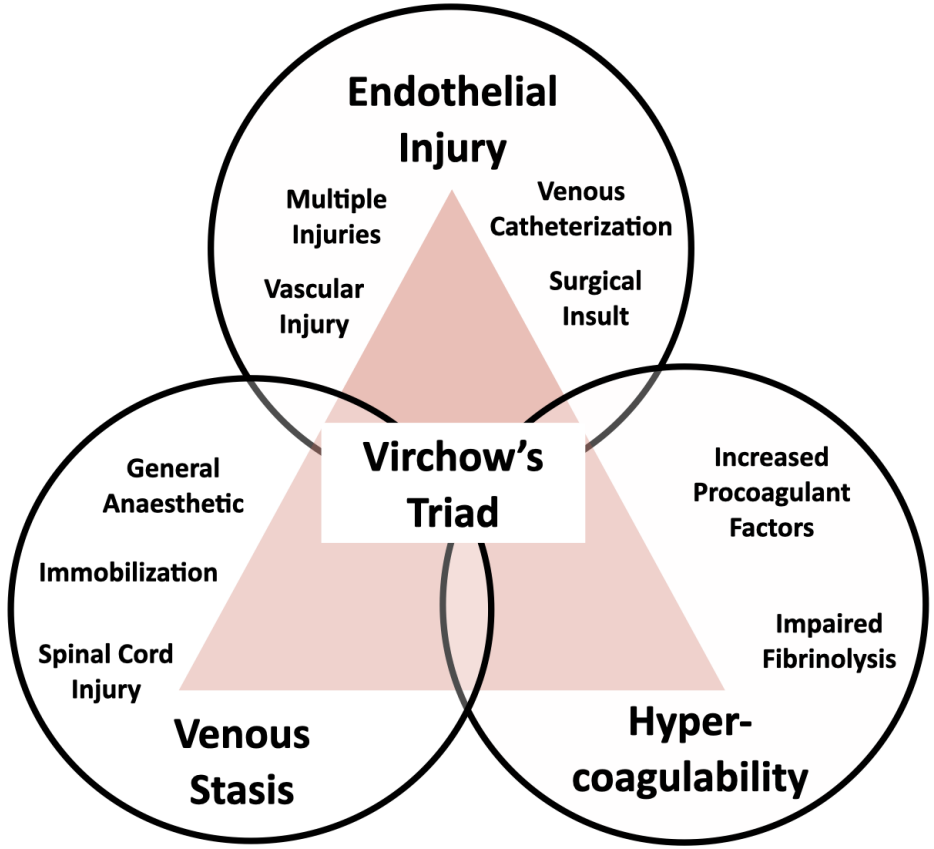
## Virchow's Triad

- Major orthopaedic fracture is an independent risk factor for VTE
- 7-fold increased risk for VTE, **despite thromboprophylaxis**
- There has been **no overall reduction in the rates of VTE in Orthopaedics**




Schneider, Rockwood & Green Ch 27, 2024

# Individualized Response to Trauma

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## What if we could measure

## individual coagulopathy in response to injury over time?

# Precision Medicine

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The **right intervention**

for the **right patient**

at the **right time**

# Precision Medicine Thromboprophylaxis

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The **right intervention**

*optimal thromboprophylaxis agent*

for the **right patient**

*based on individual risk and physiology*

at the **right time**

*optimal duration*

# Optimal Thromboprophylaxis?

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## Lack of Consensus on Optimal Agent

Summary of NICE guidelines for venous thromboembolic assessment

| Risk Factors |
|---|
| VTE |
| Active cancer or cancer treatment |
| Age >60 y |
| Critical care admission |
| Dehydration |
| Known thrombophilia |
| Obesity (BMI >30 kg/m$^2$) |
| ≥1 Significant medical comorbidities (e.g., heart disease; metabo or respiratory pathologic features; acute infectious diseases; in conditions) |
| Personal history or first-degree relative with a history of VTE eve |
| Use of hormonal replacement therapy |
| Use of estrogen-containing contraceptive therapy |
| Varicose veins with phlebitis |

Abbreviations: BMI, body ma
thromboembolic.

CHEST

ANTITHROMBOTIC THERAPY AND PREVENTION OF THROM

**Prevention of VTE in Orthopedic Surgery Patients**

Plymouth Hospitals NHS
NHS Trust

**GUIDELINES FOR VENOUS THROMBOEMBOLISM (VTE) PROPHYLAXIS IN ORTHOPAEDICS AND TRAUMA**

DEVELOPED BY: Mr J Keenan, Dr T Nokes and Dr T Gale

Thrombosis Canada
Thrombose Canada

**Practice Management Guidelines for the Prevention of Venous Thromboembolism in Trauma Patients: The EAST Practice Management Guidelines Work Group**

Duration of increased VTE risk is **unknown**

# Chemoprophylaxis Options

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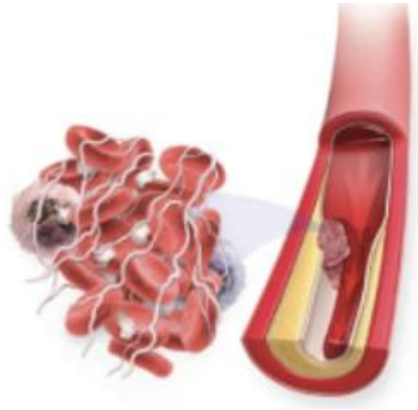
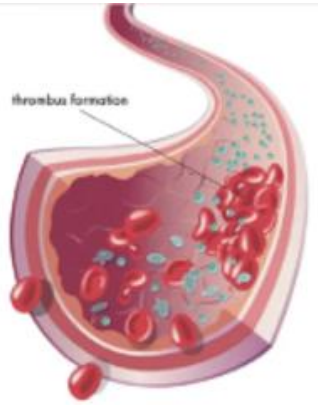
## Anticoagulant



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

## Antiplatelet




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

# Aspirin for Thromboprophylaxis?

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ORIGINAL ARTICLE

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

Major Extremity Trauma Research Consortium (METRC)*

The NEW ENGLAND JOURNAL of MEDICINE

- 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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- Randomization on 1:1 ratio, stratified by treatment site
- **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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- 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 to 1.0)

# Role for Personalized Thromboprophylaxis

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## Individual Risk Assessment – TRiP (cast) Score

| | Score |
|---|---|
| **Trauma (choose 1 – most severe trauma)** | |
| High-risk<br>Fibula and/or tibia shaft fracture; tibial plateau fracture; Achilles tendon rupture | 3 |
| Intermediate-risk<br>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<br>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<br><35<br>≥35 and <55<br>≥55 and <75<br>≥75 | <br>0<br>1<br>2<br>3 |
| Male sex | 1 |
| BMI<br>≥25 and <35 kg/m$^2$<br>≥35 kg/m$^2$ | <br>1<br>2 |
| Family history of VTE (first-degree relative) | 2 |
| Personal history of VTE 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 puerperium | 3 |
| Other immobilization within the past 3 months | 2 |
| Hospital admission, bedridden or flight >6 hr; lower limb paralysis or surgery within the past 3 months | 2 |
| **Comorbidity** | |
| Heart failure, rheumatoid arthritis, chronic kidney disease, COPD, IBD | 1 |
| Chronic venous insufficiency (varicose veins) | 1 |

BMI: body mass index; COPD: chronic obstructive pulmonary disease; hr: hours; IBD: inflammatory bowel disease; VTE: venous thromboembolism.

### TRiP Cast Score

Risk stratification based on:

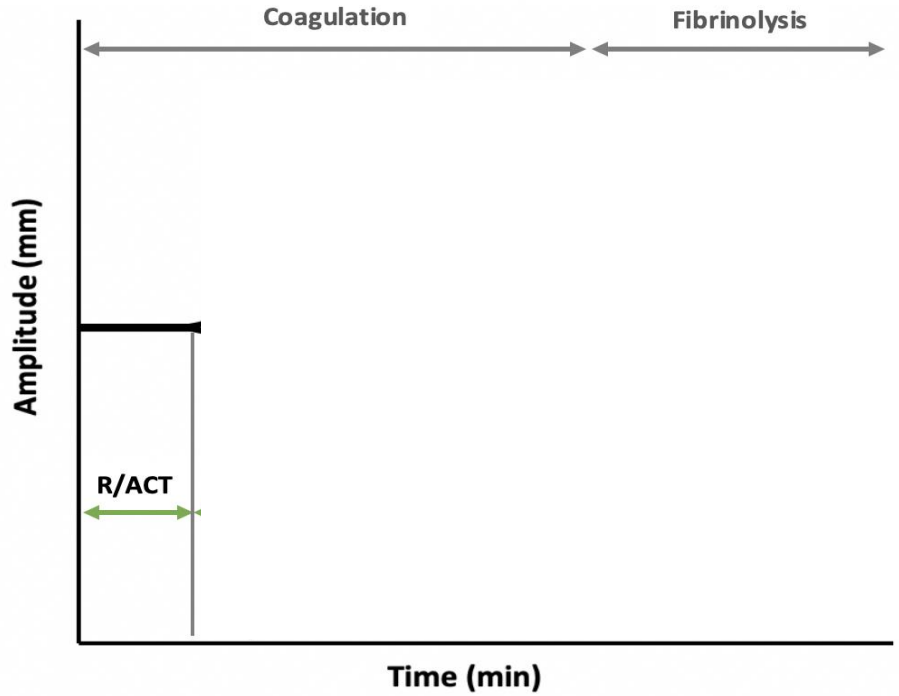
- Type of injury
- Type of immobilization
- Age
- Sex
- Known risk factors

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

# Thrombelastography (TEG)

## Viscoelastic Assay

- A whole-blood assay which provides a comprehensive analysis of hemostasis:
  - **Clot initiation** (R-time/ACT)

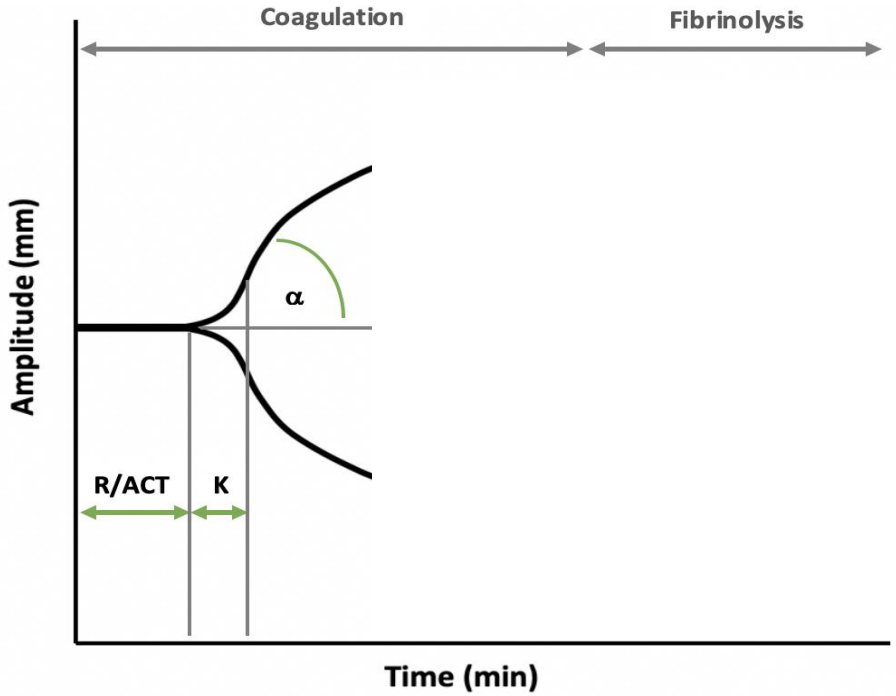



Gonzalez et al (2017) Crit Care Clin; Cotton et al (2012) J Trauma Acute Care Surg; Gary et al (2016) JOT; Liu et al (2016) Med; You et al (2021) Can J Surg

# Thrombelastography (TEG)

## Viscoelastic Assay

- A whole-blood assay which provides a comprehensive analysis of hemostasis:
  - **Clot initiation** (R-time/ACT)
  - **Clot propagation** (K-time, α-angle)

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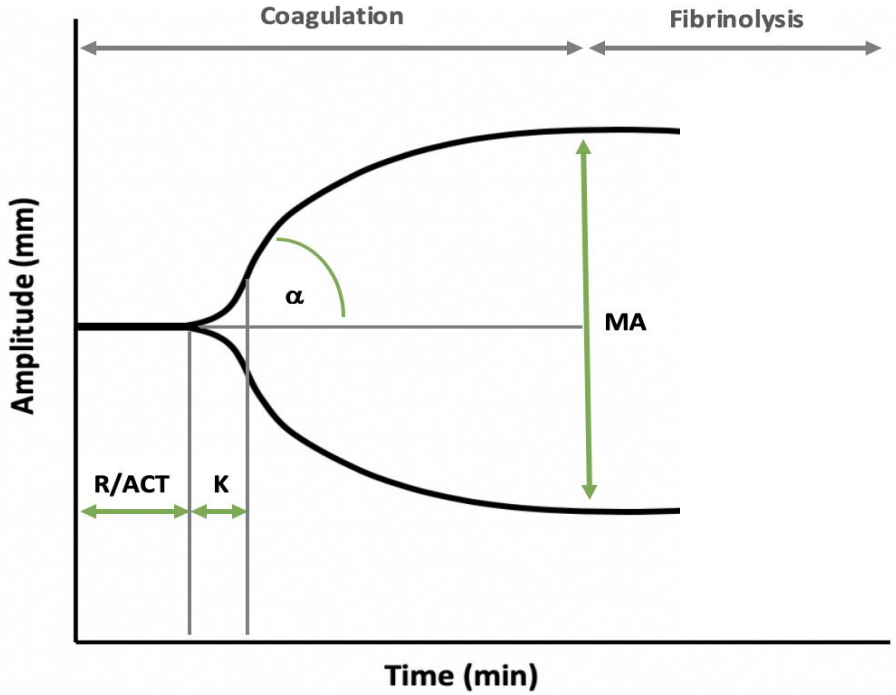


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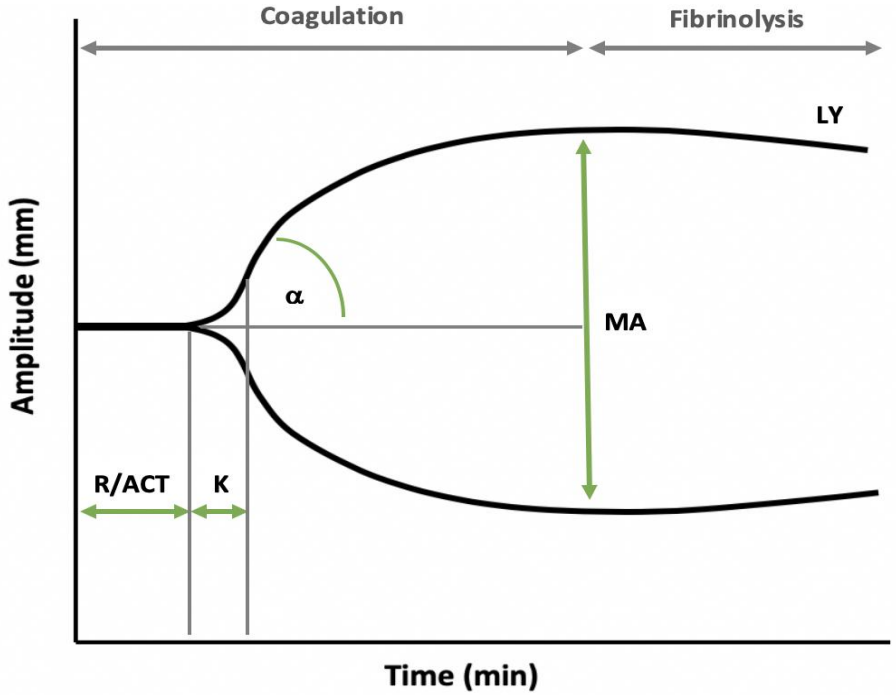
  - **Clot propagation** (K-time, α-angle)
  - **Clot Strength** (Maximal Amplitude [MA])
  - **Fibrinolysis** (LY-30)

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# Thrombelastography (TEG) and VTE

JB&JS OPEN ACCESS

## Thrombelastography as a Predictive Tool for Thromboembolic Events After Extremity Trauma

A Secondary Analysis of PREVENT-CLOT

Cory K. Mayfield, MD, Nathan N. O'Hara, PhD, MHA, Prism S. Schneider, MD, PhD, Renan C. Castillo, PhD, Robert V. O'Toole, MD, Katherine P. Frey, PhD, RN, William Obremskey, MD, MPH, Deborah M. Stein, MD, MPH, Reza Firoozabadi, MD, Stephen J. Warner, MD, PhD, Madhav A. Karunakar, MD, FAOA, Joshua L. Gary, MD, FAOA, and METRC

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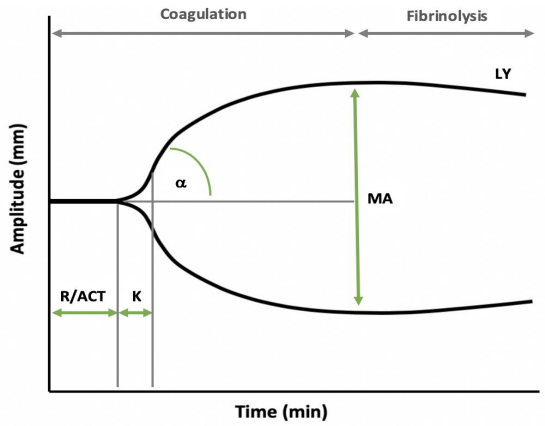



OTA Highlight Paper

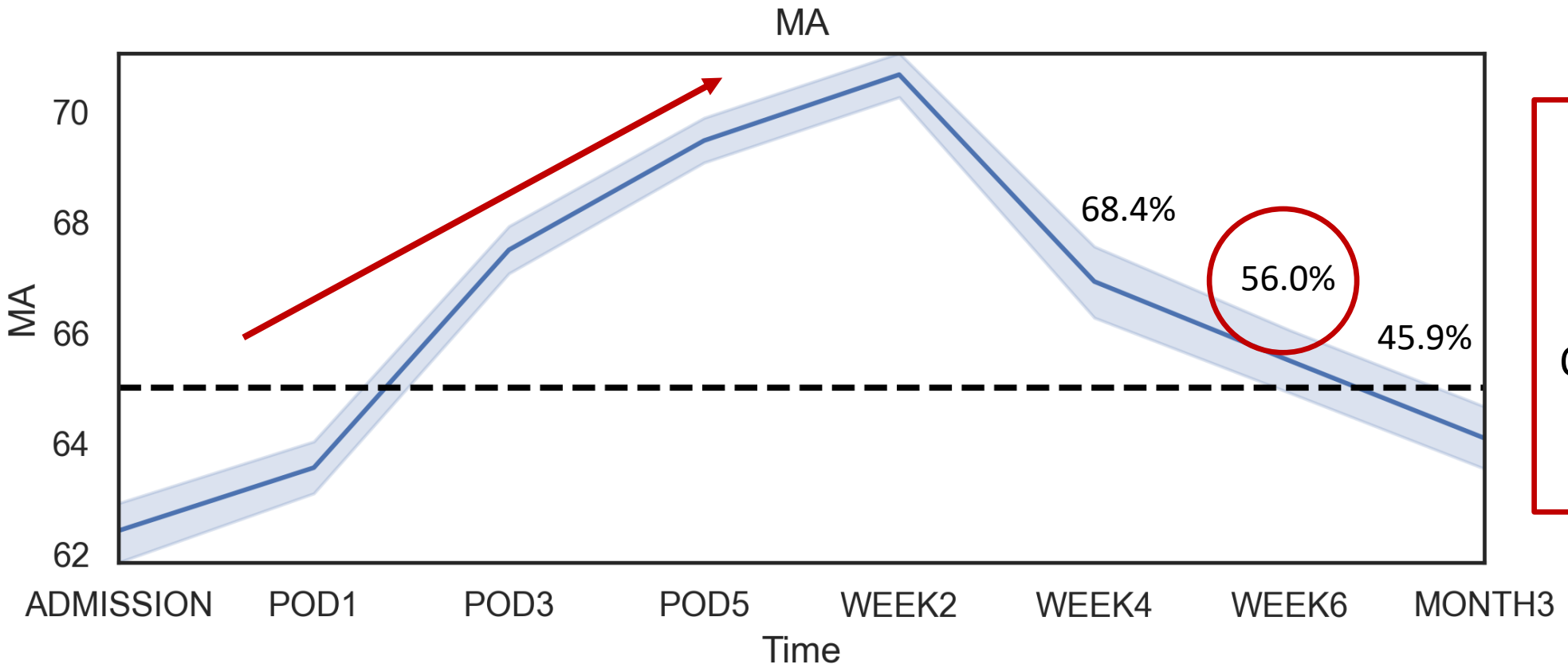
## Can Thrombelastography Predict Venous Thromboembolic Events in Patients With Severe Extremity Trauma?

*Joshua L. Gary, MD,* Prism S. Schneider, MD, PhD,* Matthew Galpin, RC,* Zayde Radwan, MD,* John W. Munz, MD,* Timothy S. Achor, MD,* Mark L. Prasarn, MD,* and Bryan A. Cotton, MD†*

*J Orthop Trauma* • Volume 30, Number 6, June 2016

# Optimal Duration?

## Maximal Amplitude – Measure of Clot Strength




*significantly increased MA from POD 3 to 6 weeks

Over 50% remained hypercoagulable at 6 weeks

# Optimal Agent?

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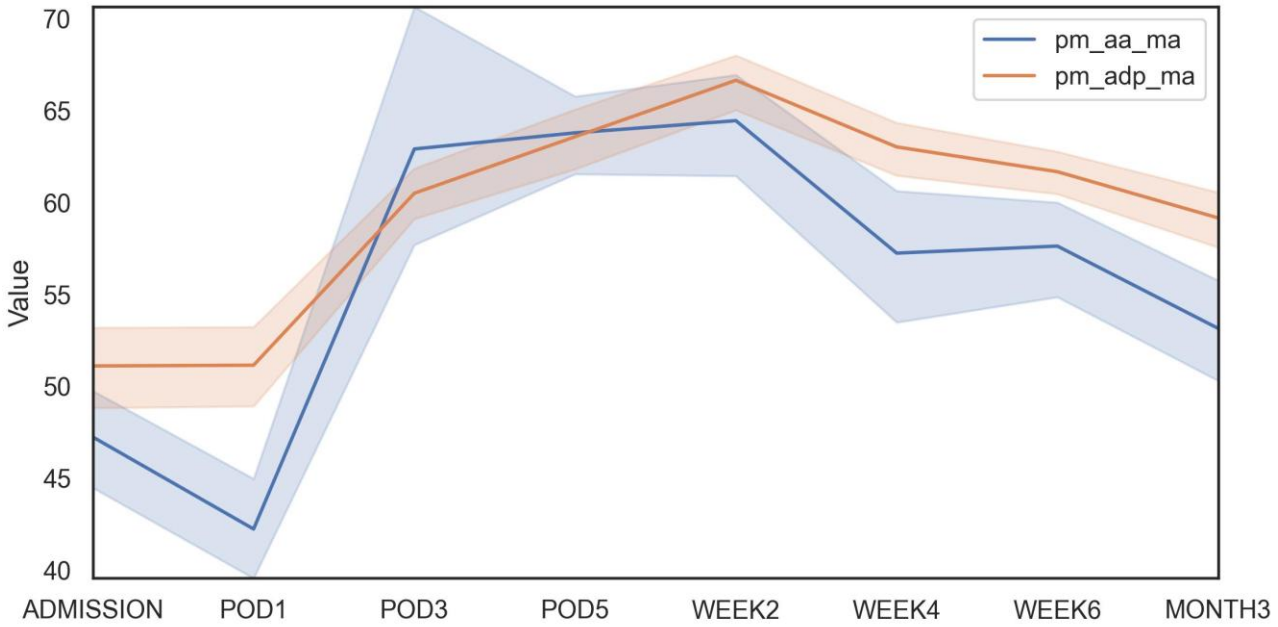
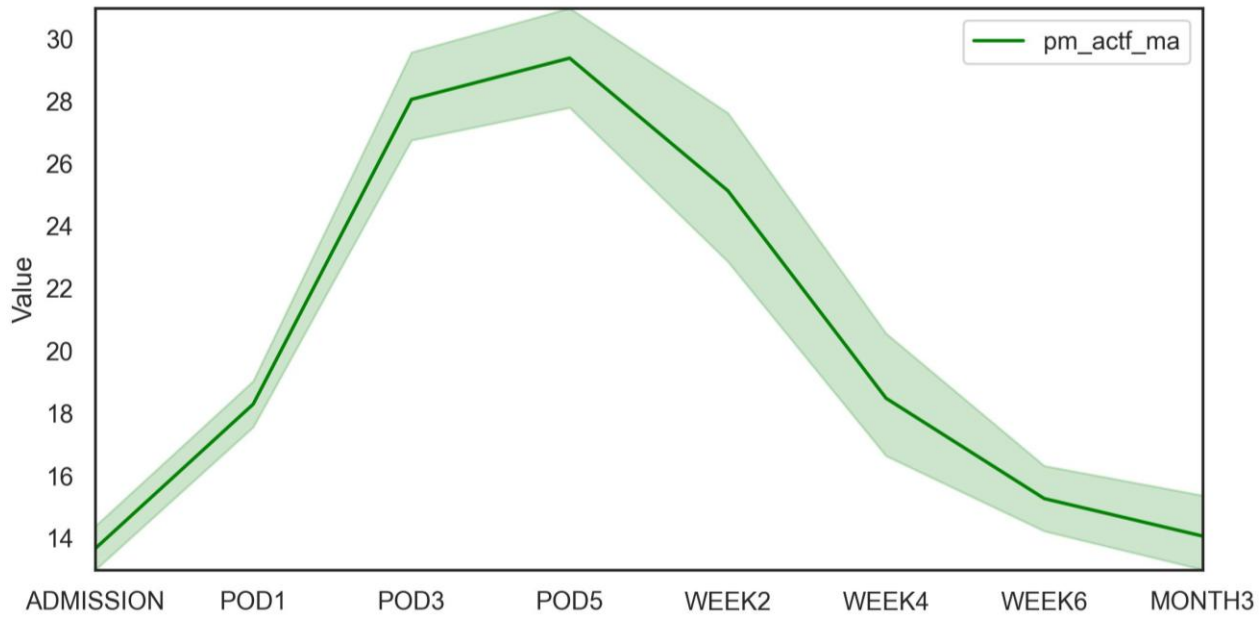
## TEG-Based Platelet Mapping Can Measure Pathophysiology

### Platelet Activation




**Antiplatelet Agents**

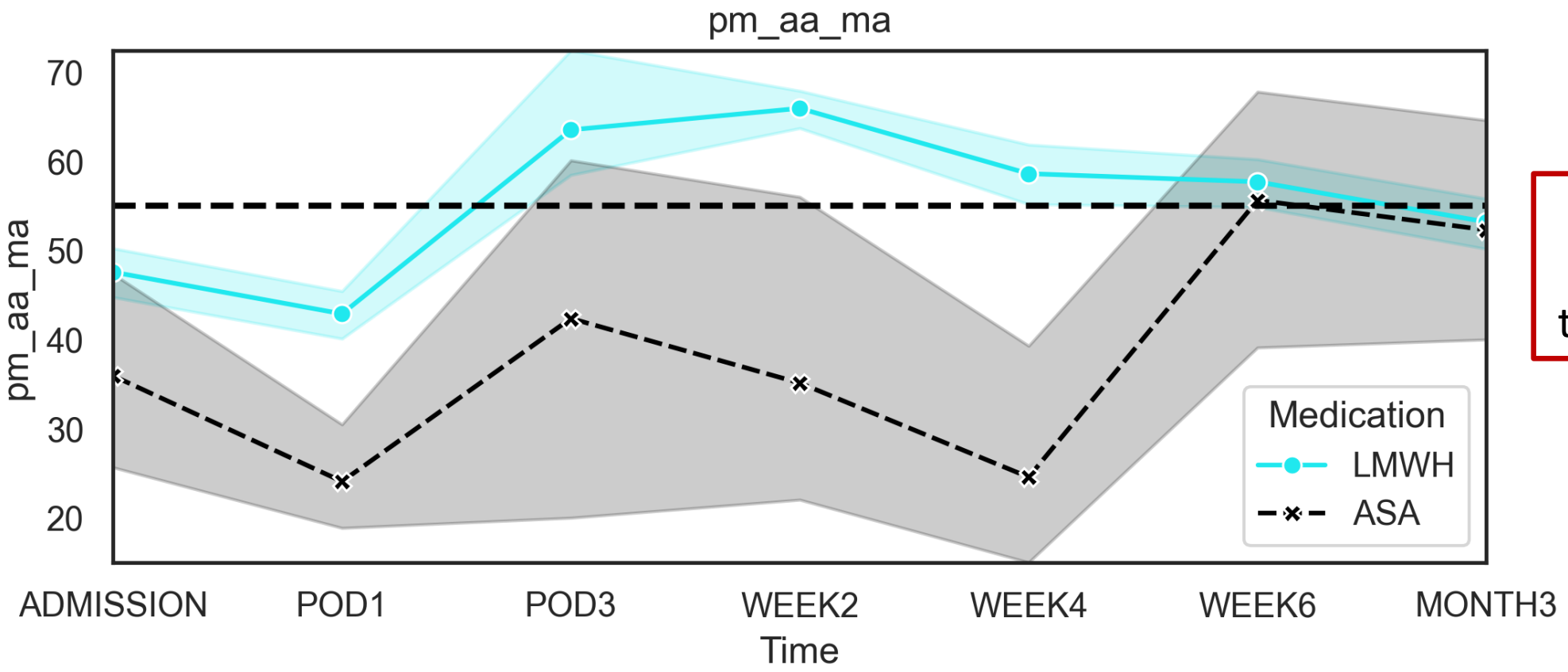
### Fibrinogen Function




**Anticoagulant Agents**

# Measure Thromboprophylaxis Efficacy?

## Platelet Mapping Can Measure Antiplatelet Effect




n = 13 (4.4%)
with aspirin
thromboprophylaxis

# Novel Therapeutic Targets

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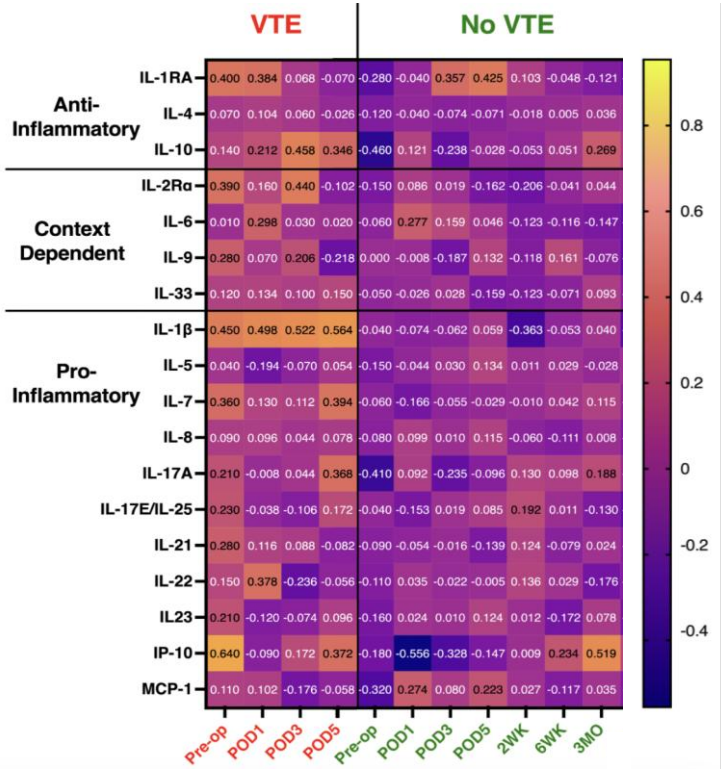
## Individual Pathophysiology

### Inflammatory Cytokines



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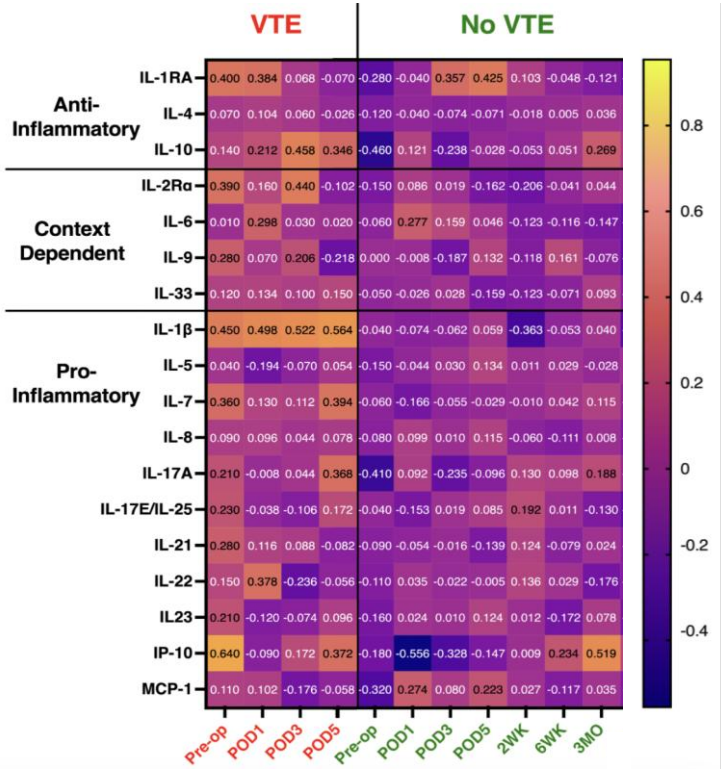


## PRECISE Study

320 patients (mean age = 36.2 [11.1], 72.2% male)
**35 VTE events in 33 patients (10.3%)**

MCP-1: a significant **positive** predictor of VTE (p = 0.008)
IL-13: a significant **negative** predictor of VTE (p < 0.001)

**MCP-1**
Each increase in IQR (577 units) = **increased odds ratio for VTE** of 1.4 [1.09 to 1.80]

**IL-13**
Each increase in IQR (31 units) = **decreased odds ratio for VTE** of 0.5 [0.35 to 0.70]

# What is Sufficient?

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

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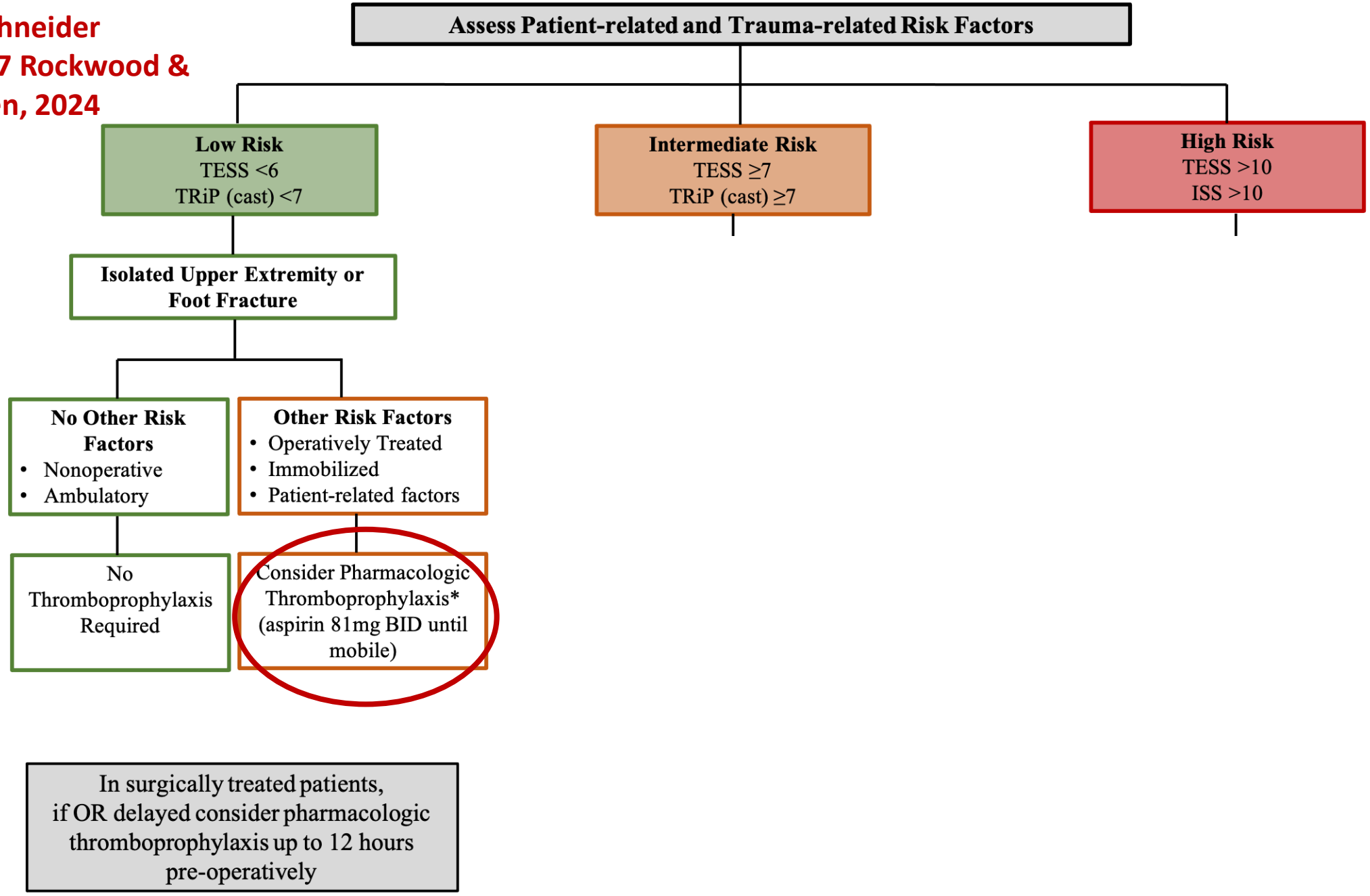


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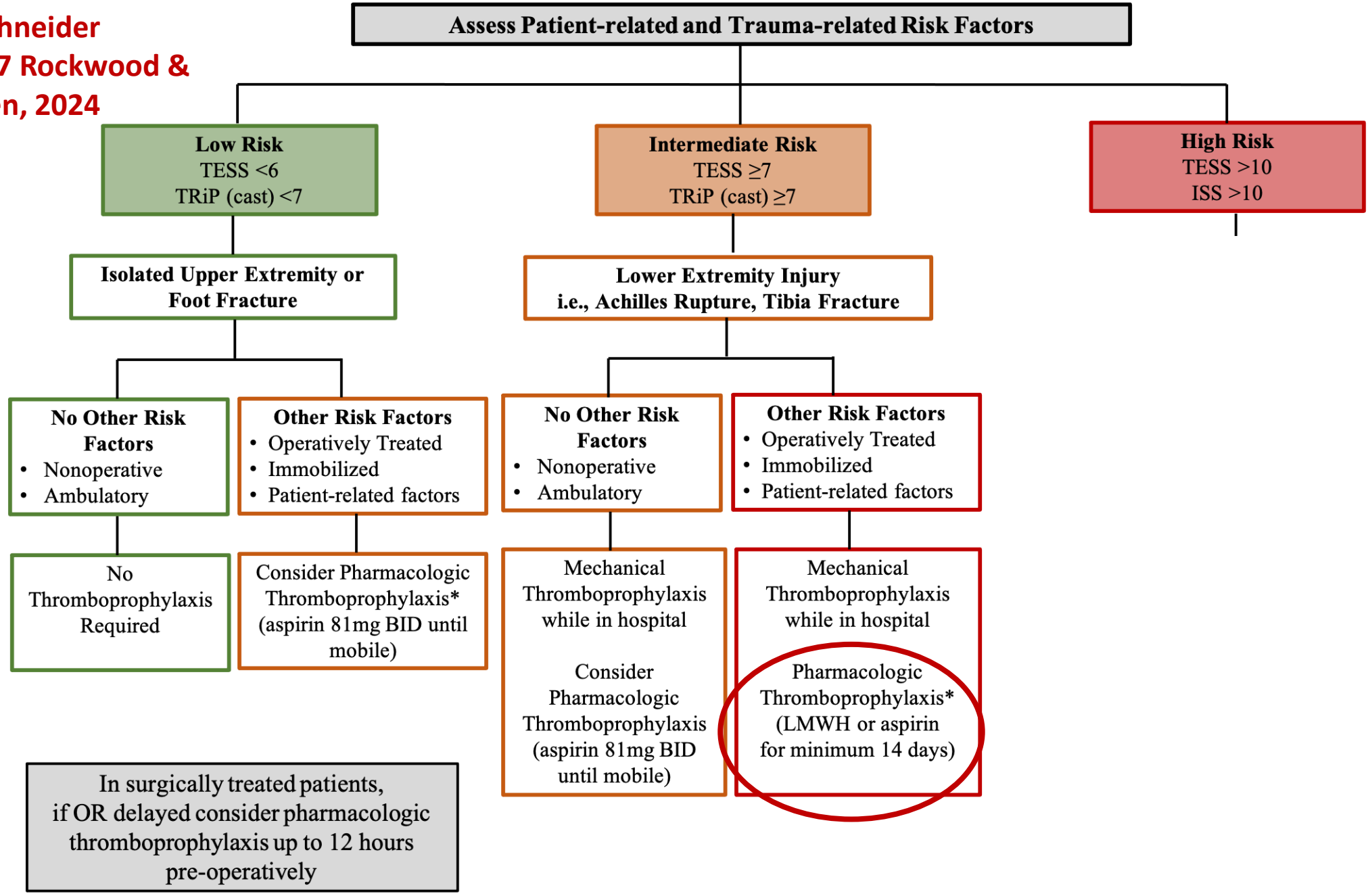

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# Assess Patient-related and Trauma-related Risk Factors

## Low Risk
TESS <6
TRiP (cast) <7

### Isolated Upper Extremity or Foot Fracture

**No Other Risk Factors**
- Nonoperative
- Ambulatory

No Thromboprophylaxis Required

**Other Risk Factors**
- Operatively Treated
- Immobilized
- Patient-related factors

Consider Pharmacologic Thromboprophylaxis* (aspirin 81mg BID until mobile)

## Intermediate Risk
TESS ≥7
TRiP (cast) ≥7

### Lower Extremity Injury i.e., Achilles Rupture, Tibia Fracture

**No Other Risk Factors**
- Nonoperative
- Ambulatory

Mechanical Thromboprophylaxis while in hospital

Consider Pharmacologic Thromboprophylaxis (aspirin 81mg BID until mobile)

**Other Risk Factors**
- Operatively Treated
- Immobilized
- Patient-related factors

Mechanical Thromboprophylaxis while in hospital

Pharmacologic Thromboprophylaxis* (LMWH or aspirin for minimum 14 days)

## High Risk
TESS >10
ISS >10

### Hip, Pelvis, Acetabulum, Spine Fracture

**No Bleeding Risk**

Mechanical Thromboprophylaxis immediately

Pharmacologic Thromboprophylaxis* (LMWH or aspirin for minimum 28 days)

Consider DOAC in hip fracture

Consider extended duration in hip fracture

**Bleeding Risk****

Mechanical Thromboprophylaxis immediately

Pharmacologic Thromboprophylaxis as soon as bleeding risk reduced* (LMWH or aspirin for minimum 28 days)

Consider screening ultrasound q7 days

Consider IVC filter if bleeding risk persists or proximal DVT

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

# Optimal Thromboprophylaxis?

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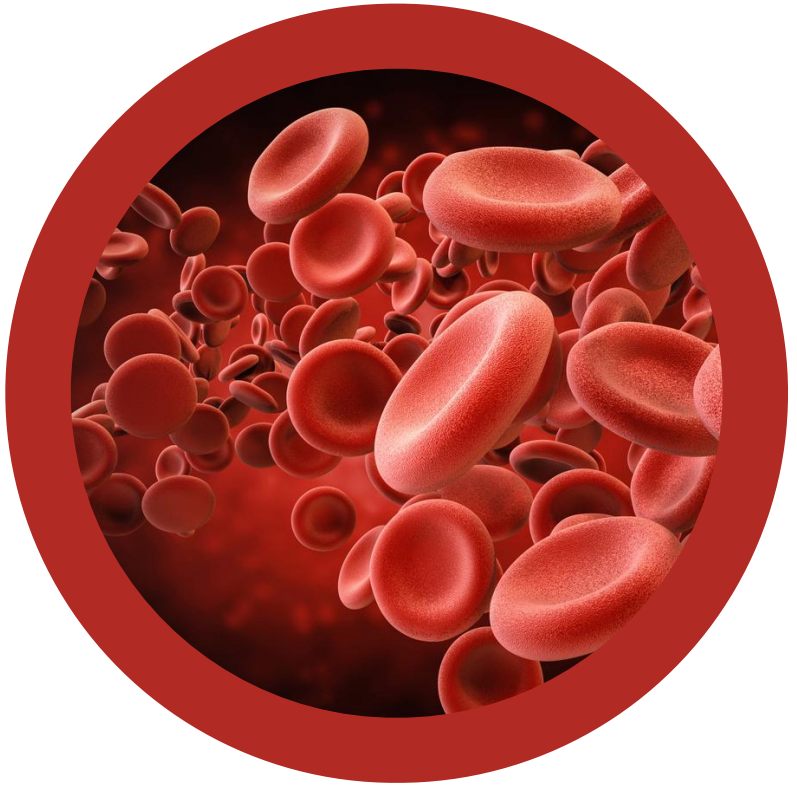
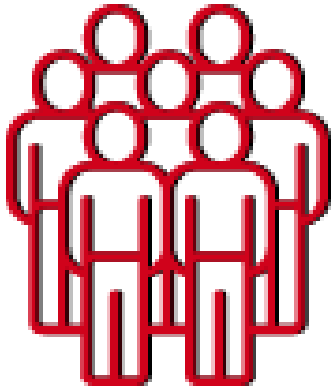
## Remaining Questions:

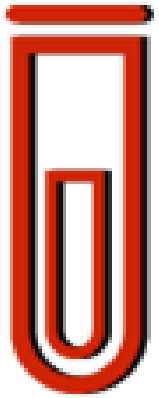
- Clinical significance of distal DVT?
- BID vs. daily dosing?
- LMWH followed by antiplatelet?
- Oral anticoagulant for thromboprophylaxis?
- Duration of thromboprophylaxis?
- Novel targets?



# Ongoing Research



Over 900
Participants



Over 8000
TEG Analyses

iiCP
Injury-induced Coagulopathy Program

TEG
Pelvis &
Acetabulum

TEG
Femur

TEG
MBD

TEG
Arthroplasty

# Acknowledgements

FOOTHILLS MEDICAL CENTRE
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## Thank you!

iiCP Injury-induced Coagulopathy Program

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