VENOUS THROMBOEMBOLISM

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- Define DVT and PE and understand the basic pathophysiology
- Know risk factors for VTE in the orthopedic patient
- Understand evidence-based prevention strategies
- Diagnose VTE in a timely fashion
- Understand treatment strategies for DVT/PE



Definitions

- Deep Vein Thrombosis (DVT)
 - A pathologic coagulation of blood within a deep vein in an extremity
 - Commonly in the lower extremity
 - Popliteal fossa or proximal at highest risk of embolization
- Pulmonary Embolus (PE)
 - A pathologic coagulation of blood within a pulmonary artery
 - Ranges from small/subsegmental to massive



Pathophysiology

- Coagulation
 - Blood transforms from liquid to fibrin based clot
 - Relies on interplay of endothelium, platelets, and circulating coenzymes
 - Hemostasis is a balance between clot formation and dissolution
 - Pathologic coagulation = thrombosis



Ahsan ZS, Firoozibadi R. 2020. Venous Thromboembolic Disease in Patients with Skeletal Trauma. Tornetta, Paul, III, Rockwood and Green's Fractures in Adults 9e, Wolters Kluwer, 2020



Pathophysiology

- Virchow's Triad
 - Endothelial injury
 - Stasis
 - Hypercoagulable state
- All three often present in patients with skeletal trauma



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Traumatic Risk Factors

- Polytrauma
 - Increasing Injury Severity Score → Increased rates of VTE
- Blood transfusion
- Spinal cord injury
- Chest injury
- Head injury





Fracture Specific Risk Factors

- Orthopedic trauma patients have 69% incidence of VTE in the absence of prophylaxis
- Pelvis and Acetabular fractures at greatest risk
- More proximal lower extremity fractures = greater risk
 - 40% femoral shaft
 - 43% tibial plateau
 - 22% tibial shaft
 - 12.5% tibial plafond





Non-traumatic Risk Factors

- Age > 55 years
- Obesity
- Diabetes mellitus
- Malignancy
- Coagulopathy
- Tobacco use
- Oral contraceptives, hormone replacement





<u>Risk Assessment</u>

- Caprini Index
 - Establishes composite individual risk
 - Stratifies patients into low (0-2 pts), moderate (3-4), high (5-8), or highest risk (>8)
 - Major lower extremity fracture = high risk
 - Moderate risk or greater may warrant chemoprophylaxis

Each Risk Factor Represents 1 Point	Each Risk Factor Represents 2 Points	Each Risk Factor Represents 3 Points	Each Risk Factor Represents 5 Points
• Age 41-60 yrs	• Age 60-74 yrs	Age over 75 yrs	Elective major lower extremity arthroplasty
Minor surgery planned	Minor surgery (>60 min)	• Major surgery lasting 2-3 hrs	• Hip, pelvis, or leg fracture (<1 mo)
History of prior major surgery	Arthroscopic surgery (>60 min)	 BMI >50 (venous stasis syndrome) 	• Stroke (<1 mo)
Varicose veins	Laparoscopic surgery (>60 min)	History of SVT, DVT/PE	Multiple trauma (<1 mo)
History of inflammatory bowel disease	Previous malignancy	Family History of DVT/PE	Acute spinal cord injury (paralysis) (<1 mo)
 Swollen legs (current) 	Central venous access	Current cancer or chemotherapy	Major surgery lasting over 3 hrs
• Obesity (BMI >30)	Morbid obesity (BMI >40)	Positive factor V	 For Women Only (Each Represents 1 Point) Oral contraceptives or hormone replacement therapy Pregnancy or postpartum (<1 mo) History of unexplained stillborn infant, recurrent spontaneous abortion (≥3), premature birth with toxemia or growth-restricted infant
 Acute myocardial infarction (<1 mo) 		Leiden	
• Congestive heart failure (<1 mo)			
• Sepsis (<1 mo)		Positive prothrombin 202104	
 Serious lung disease including pneumonia (<1 mo) 		Elevated serum homocysteine	
 Abnormal pulmonary function (COPD) 		Positive lupus anticoagulant	
 Medical patient currently on bed rest 		Elevated anticardiolipin antibodies	
• Leg plaster cast or brace		 Heparin-induced thrombocytopenia (HIT) 	
Other risk factors		Other thrombophilia	

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- Three primary modalities
 - Mechanical Prophylaxis
 - Inferior Vena Cava Filters
 - Chemoprophylaxis



- Mechanical Prophylaxis
 - Intermittent Pneumatic Compression (IPC)
 - Stimulates venous flow in the extremities
 - May be as effective as LMWH
 - Per the American College of Chest Physicians (ACCP), chemoprophylaxis superior to mechanical alone
 - Combined IPC and chemoprophylaxis superior to either alone



- Mechanical Prophylaxis
 - Compressive Stockings
 - Minimize venous stasis
 - Multiple RCTs to suggest decreased incidence of DVT/PE



- Inferior Vena Cava Filter
 - In theory prevents migration of DVT to the pulmonary artery
 - Mixed evidence regarding efficacy
 - Numerous complications if left long term
 - ACCP recommends against use of IVC filters in polytrauma patients



- Chemoprophylaxis
 - Unfractionated Heparin (UFH)
 - Binds to antithrombin III \rightarrow inactivates thrombin, factor Xa
 - Half life of 1-2 hours (dosed 2-3 times daily)
 - Reversible with protamine
 - Heparin Induced Thrombocytopenia (HIT) a potential complication



- Chemoprophylaxis
 - Low-Molecular-Weight Heparin (LMWH)
 - Also binds antithrombin III, but reduced anti-factor IIa activity
 - Half life of 4-5 hours (dosed once or twice daily)
 - Lab monitoring not required
 - Superior to UFH in terms of PE risk reduction
 - Concerns over wound drainage/bleeding complications
 - HIT still possible, but lower risk compared to UFH



- Chemoprophylaxis
 - Fondiparinux
 - Indirect factor Xa inhibitor
 - Half life of 17 hours (once daily administration)
 - No risk of HIT
 - Superior reduction of VTE compared to LMWH in hip fracture patients



- Chemoprophylaxis
 - Aspirin
 - Irreversible inhibitor of cyclooxygenase (COX)
 - Inhibits platelet aggregation for 8-9 days
 - Arthroplasty literature shows decreased VTE and fewer complications compared to other agents
 - Not well studied in the trauma population



- Chemoprophylaxis
 - Novel Oral Anticoagulants (NOACs)
 - Dabigatran: selective inhibition of thrombin
 - Rivaroxaban, Apixaban, Edoxaban: inhibit factor Xa
 - Half life of 5-15 hours
 - Efficacy not well studied in trauma population
 - Concerns include bioavailability of oral agents in hospitalized patients, bleeding complications, limited reversibility



H. Claude Sagi, MD, FACS,* Jaimo Ahn, MD, PhD,‡ David Ciesla, MD,† Cory Collinge, MD,§ Cesar Molina, MD,|| William T. Obremskey, MD,§ and Oscar Guillamondegui, MD||, the Orthopaedic Trauma Association Evidence Based Quality Value and Safety Committee

J Orthop Trauma • Volume 29, Number 10, October 2015

- 24 Item questionnaire to members of OTA
- Found wide variability in surgeon practices
 - Many practices not evidence based
- Expert panel constructed evidence-based guidelines



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1. Chemical prophylaxis: The optimal form of VTE prophylaxis is LMWH and should be initiated in patients with musculoskeletal injury with additional risk factors within 24 hours, provided there are no contraindications. *Rating: Strong*.

2. LMWH is optimally held for 12 hours before and after surgery. Rating: Strong.

3. The use of ULDH, aspirin (and other antiplatelet medications), and warfarin are recommended over no prophylaxis when LMWH is contraindicated, not available, or prohibitive to patient due to cost or choice. *Rating: Moderate*.

4. We recommend combined prophylaxis with early and consistent use of calf pneumatic compression devices and LMWH over either regimen alone, provided that no contraindication to either modality exists. *Rating: Strong*.



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J Orthop Trauma • Volume 29, Number 10, October 2015

5. We recommend the use of pneumatic compression devices when chemical prophylaxis is contraindicated. *Rating: Strong.*

6. We recommend surgeons consider and discuss with patients prolonged VTE chemoprophylaxis in patients with risk factors. *Rating: Consensus*.

7. We do not recommend chemical prophylaxis in patients with isolated lower extremity fractures and **"no other risk factors"** for VTE who are able to independently mobilize. *Rating: Moderate*.

8. We recommend prolonged prophylaxis (approximately 4 weeks) in patients at a high risk for VTE (elderly patients with a proximal femur and multiple trauma patients). *Rating: Strong*.

9. We do not recommend the routine use of screening protocols for DVT in the asymptomatic patient with musculoskeletal injury. *Rating: Strong*.



7. We do not recommend chemical prophylaxis in patients with isolated lower extremity fractures and **"no other risk factors"** for VTE who are able to independently mobilize. *Rating: Moderate*.

Other Risk Factors

- 1. Older than 40 years
- 2. Obesity (body mass index > 30)
- 3. Previous history of VTE (personal or familial)
- 4. History of malignancy
- 5. History of smoking
- 6. Hormonal birth control
- 7. Nonambulatory status
- 8. Spinal cord injury
- 9. Proximity of injury to the axial skeleton
- 10. Tourniquet use
- 11. Immobilization
- 12. Other hypercoagulability conditions (protein C and S deficiency)



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10. Patients thought to be at a high risk for pulmonary embolus or a documented VTE/PE with contraindications to acceptable anticoagulant should be considered candidates for IVC filter placement. *Rating: Moderate.*

11. We do not recommend the routine use of IVC filters for low-risk patients to prevent PE. Rating: Strong.

12. Although patients with hemodynamically stable solid-organ injuries can safely be anticoagulated after 24 hours, provided there is no on-going blood loss, consultation with the general/trauma/acute care surgeon is recommended. *Rating: Moderate*.

13. Although patients with closed head injuries and stable serial head CT scans can safely be anticoagulated after 24–48 hours provided the neurological examination has not worsened, consultation with the neurosurgeon is recommended. *Rating: Consensus*.



A Double-Blind, Randomized Controlled Trial of the Prevention of Clinically Important Venous Thromboembolism After Isolated Lower Leg Fractures

Rita Selby, MBBS, FRCPC, MSc,*† William H. Geerts, MD,* Hans J. Kreder, MD, MSc,‡ Mark A. Crowther, MD, MSc,§ Lisa Kaus,* and Faith Sealey, RN,* on behalf of the D-KAF (Dalteparin in Knee-to-Ankle Fracture) Investigators J Orthop Trauma • Volume 29, Number 5, May 2015

- 265 patients with below-knee fractures
- Randomized to 14 days of LMWH vs placebo
- Doppler of bilateral proximal leg veins at 14 days and 3 months
- Overall incidence of clinically important VTE (CIVTE) was 1.9%
 - no significant difference between groups
- Due to low incidence of CIVTE, trial recruitment was stopped early

Chemoprophylaxis for Venous Thromboembolism in Operative Treatment of Fractures of the Tibia and Distal Bones: A Systematic Review and Meta-analysis

> Joseph T. Patterson, MD and Saam Morshed, MD, PhD J Orthop Trauma • Volume 31, Number 9, September 2017

- Metanalysis of 5 randomized trials describing chemoprophylaxis of VTE after operative management of fractures of the tibia and distal bones
- Assessed the incidence of any VTE vs clinically important VTE (CIVTE)
- Incidence of *any* VTE was significantly reduced with chemoprophylaxis
- No significant difference in CIVTE between LMWH and placebo



The Incidence of Venous Thromboembolism Following Pelvic and Lower Extremity Trauma Despite Adherence to Modern Prophylactic Protocols

Jason A. Lowe, MD,^{a,b} Sean M. Mitchell, MD,^b Sumit Agarwal, MD, MBA,^c and Clifford B. Jones, MD^d

J Orthop Trauma • Volume 34, Number 8, August 2020

- Review of 11,313 trauma patients treated from 2010-2017 in a large multicenter health care system database
- Captured patients with ORIF of pelvis/acetabulum, femoral neck, and intertrochanteric fractures or intramedullary nailing (IMN) of the femur or tibia
- All patients in the study were on chemical and mechanical prophylaxis
 - LMWH or Warfarin
- Overall rate of VTE was 0.82% (0.39% DVT, 0.43% PE)
 - Pelvis/acetabulum 1.7%
 - Femoral IMN 1.33%



Diagnosis of DVT

- Symptoms
 - Clinically silent in many cases
 - Limb swelling
 - Homan's sign (calf pain with passive dorsiflexion of the ankle)
 - Tachycardia
 - Fever of unknown origin



Diagnosis of DVT

- Wells Score
 - 3-8 points = High probability
 - 1-2 points= moderate probability
 - -2-0 points= low probability

Deep Venous Thrombosis	
• Active cancer (treatment ongoing or within previous 6 mo, or palliative treatment)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
 Recently bedridden for 3 days or more, or major surgery within the previous 12 wks requiring general or regional anesthesia 	1
Localized tenderness along the distribution of the deep venous system	1
Entire leg swollen	1
• Calf swelling >3 cm compared to asymptomatic leg (measuring 10 cm below tibial tuberosity)	1
Pitting edema confined to the symptomatic leg	1
Nonvaricose collateral superficial veins	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT	-2
Total DVT score	Ь

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Diagnosis of DVT

- Testing modalities
 - D-Dimer
 - Poor specificity
 - Venography
 - Historical
 - Venous Doppler Exam
 - Good sensitivity/specificity, but user dependent
 - MRI
 - Expensive, high false positive rate



Diagnosis of PE

- Symptoms
 - Tachycardia
 - Shortness of breath
 - Chest pain
 - Hypoxia
 - Hemoptysis
 - Cyanosis



Diagnosis of PE

- Wells Score
 - > 6 points = High probability
 - 2-6 points= moderate probability
 - < 2 points= low probability

Pulmonary Embolism	Score
Clinical signs and symptoms compatible with DVT	3
PE judged to be the most likely diagnosis	3
 Surgery or bedridden >3 days during the past 4 wks 	1.5
Previous DVT or PE	1.5
Heart rate >100/min	1.5
Hemoptysis	1
Active cancer (treatment ongoing or within previous 6 mo or palliative treatment)	1
Total PE score	а

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Diagnosis of PE

- Testing modalities
 - Ventilation/Perfusion (V/Q) Scan
 - Historical gold standard
 - Remains useful for patients with contrast allergies or renal impairment
 - CT Pulmonary Angiography (CTPA)
 - Good sensitivity/specificity
 - Current gold standard



Treatment of DVT

- Based on anatomic location and individual risk factors
 - Proximal to calf \rightarrow aggressive treatment
- Typically 3 months of anticoagulation (sometimes indefinite)
 - Novel oral anticoagulants preferred to warfarin or LMWH
- Serial imaging of deep veins in patients at high risk of bleeding
 - No anticoagulation for stable thrombus



Review Article

Treatment of PE

Pulmonary Embolism in Orthopaedic Patients: Diagnosis and Management

Yelena Bogdan, MD J Am Acad Orthop Surg 2012;20:

586-595

- Subsegmental (proximal pulmonary artery not involved)
 - Rarely associated with cardiopulmonary complications
 - Low incidence of concomitant DVT or recurrent thromboemboli
 - Clinical surveillance recommended if no proximal DVT
- Clinically Relevant PE
 - Respiratory and hemodynamic support as needed
 - Thrombolytic therapy if low risk of bleeding
 - If elevated bleeding risk \rightarrow thrombus removal





- DVT/PE are common in patients with skeletal trauma
- Combined mechanical and chemical prophylaxis is recommended
- LMWH is commonly used in the trauma population
- IVC filters should be reserved for high risk patients with contraindications to an acceptable anticoagulant



Key References

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