Acute Respiratory Distress Syndrome, Fat Embolism, & Thromboembolic Disease in the Orthopaedic Trauma Patient

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Objectives

Acute Respiratory Distress Syndrome

Fat Embolism

Venous Thromboembolism

• Review – History – Diagnosis - Classification - Epidemiology Pathophysiology - Treatment

Acute Respiratory Distress Syndrome



Relatively clear CXR

Diffuse bilateral coalescent opacities

ARDS-History

ACUTE RESPIRATORY DISTRESS IN ADULTS

DAVID G. ASHBAUGH M.D. Ohio State ASSISTANT PROFESSOR OF SURGERY The Lancet · Saturday 12 August 1967

"The respiratory-distress syndrome in 12 patients was manifested by acute onset of tachypenia, hypoxemia and loss of compliance after a variety of stimuli; the syndrome did not respond to usual and ordinary methods of respiratory therapy"

Acute Respiratory Distress Syndrome The Berlin Definition

JAMA. 2012;307(23):2526-2533

Consensus definition with empirical evaluation

Timing- Within 1 week of clinical insult or new/worsening respiratory symptoms

Chest Xray- Bilateral opacities- not fully explained by effusions,

collapse or nodules

Origin of edema- Respiratory failure not fully explained by cardiac failure, fluid overload- Needs objective assessment (echo)

Oxygenation-

Mild- $200 \text{mmHg} < PaO2/FiO2, \leq 300 \text{mmHg w} / PeeP \text{ or } CPAP \geq 5 \text{ cm } H2O$ Moderate- $100 \text{ mmHg} < PaO2/FiO2, \leq 200 \text{ mmHg w} / PEEP \geq 5 \text{ cm } H2O$ Severe- $PaO2/FiO2 \leq 100 \text{ mmhg w} / PEEP \geq 5 \text{ cm } H2O$

Outcomes with Berlin Definition

- Severity of ARDS found to be associated with worse mortality and duration of requiring mechanical ventilation.
 - Mortality increase with level of oxygenation
 - Mild- 27%
 - Moderate- 32%
 - Severe- 45%
 - Mechanical ventilation requirements
 - Mild- 5 days
 - Moderate- 7 days
 - Severe- 9 days

ARDS Epidemiology

Incidence and Outcomes of Acute Lung Injury

Gordon D. Rubenfeld, M.D., Ellen Caldwell, M.S., Eve Peabody, B.A., Jim Weaver, R.R.T., Diane P. Martin, Ph.D., Margaret Neff, M.D., Eric J. Stern, M.D., and Leonard D. Hudson, M.D. N ENGL J MED 353;16 OCTOBER 20, 2005

Incidence

 78.9 per 100,000
 person-years

-190,600 cases per years in US

- 38.5% in hospital mortality rate

-74,500 associated deaths per year in US

Epidimiology

Age associated increase in Incidence
15-19 yo' s- 16 per 100,000
75-84 yo' s- 306 per 100,000

Age associated increase in Mortality
15-19 yo' s- 24%
>85 yo' s- 60%

Causes

- Sepsis
- Aspiration
 Trauma
 Transition
 Embolism
 - Burns
- Systemic inflammatory process
- Multi-organ failure
 - Drug overdose
- Stem-cell transplant

Pathophysiology



Pathology Slide of Alveoli



- ARDS patient
- Injury to Type I (and Type II) pneumocytes
 - Decreased surfactant production
- Plasma protein leak
 - Inactivate surfactant with increase in proteinaceous material in alvioli (albumin and fibrin)

Slide from personal collection of Dr Rodney A. Schmidt MD (UW Pathology)

Differential Diagnosis

 Underlying lung disease
 – Pulmonary fibrosis, chronic interstitial lung disease

• Cardiogenic pulmonary edema

• Diffuse alveolar hemmorage

Pneumonia

ARDS Treatment

Supportive care

- Nutritional support
 - GI prophylaxis
 - Glucose control
- Sedation/paralysis
- VTE prophylaxis
- Hemodynamic monitoring
- Control causes of sepsis
 - Prevent aspiration/pneumonia
- Treat underlying injuries/organ dysfunction
- Prone positioning

Respiratory specific

- Ventilator support
 - Fully supported ventilator mode
 - Low tidal volume ventilation
 - High PEEP
 - Intermittent recruitment measure
 - High % inspired O2
- All carry their own potential associated complications
- Ongoing area of research

Complications of ARDS

- Delirium
- VTE
- Stress ulcers
- Pressure ulcers
- Catheter associated infections
 UTI's

Ventilator associated – Pneumonia ~2x incidence as compared to pts without ARDS on ventilator – Mechanical trauma from ventilator settings (barotrauma)

Key Clinical Factors

- Early identification and initiation of supportive care are essential.
 - Remember VTE prophylaxis and nutritional support
- Patients with ARDS have high mortality rates as well as extended period of ventilator support
- Pulmonary status may limit ability for positioning patient for procedures

- 68 year old F involved in MVC with bilateral femur fractures and traumatic head injury.
- Portable X-ray in Trauma bay after ET tube placed



• Worsening respiratory status and vent settings in ICU waiting for operative stabilization of bilateral femurs and clearance by neurosurgery.



Fat Emboli Syndrome (FES)



FES-History

First described in 1861 by Zenker, F. A.
 Fat desposits in the lungs of postmortum accident patients

 Clinical description by Bergmann, E. B. 1873

- Confusion, dyspnea, and petechiae

Classic Triad

Definition

- Syndrome
 1) hypoxemia
 2) respiratory insufficiency
 3) neurologic impairment
 4) +/- petechial rash
- Usually within the first 24-72 hours
- In the setting of
 Long bone or pelvic fracture
 No other etiology- PE, ARDS

FES Epidemiology

Incidence

-0.5% to 8.5% of all fracture patients

- Possibly up to 35% in patients with long bone fracture
- Uncommon in young patients and isolated upper extremity injuries

- Mortality

• 2.5% to 8.5%

Fat Embolism Syndrome: A 10-Year Review

Eileen M. Bulger, MD; Douglas G. Smith, MD; Ronald V. Maier, MD; Gregory J. Jurkovich, MD Arch Surg. 1997;132(4):435-439.

- Incidence- 27 patients identified
 - 0.9% of patients with long bone fractures
 - Mean Injury Severity score of 9.5
 - 52% single long-bone fracture
 - 48% multiple long-bone fractures
 - Sign or Symptom associated with diagnosis of FES
 - Hypoxia (96%)
 - Tachycardia (heart rate > 120 beats per minute (93%)
 - Temperature higher than 39 degrees C (70%)
 - Unexplained anemia (67%)
 - Mental status changes (59%)
 - Petechiae (33%)

Fat Embolism Syndrome: A 10-Year Review

Eileen M. Bulger, MD; Douglas G. Smith, MD; Ronald V. Maier, MD; Gregory J. Jurkovich, MD Arch Surg. 1997;132(4):435-439.

- Overall mortality rate of 7%.
- Author conclusions
 - FES is a diagnosis of exclusion
 - FES is rare and may be masked by associated injuries
 - No association between FES and fracture pattern or location was found
 - Early intramedullary fixation did not increase the incidence or severity of FES
 - FES management remains primarily supportive

Pathophysiology

Two major theories on how injury occurs with FES

– Mechanical

 Gauss, H. 1924. The pathology of fat embolism. Arch. Surg. 9:593-605

– Physiochemical

 Lehman, E. P., Moore, R. M. 1927. Fat embolism including experimental production without trauma. Arch. Surg. 14:621-62

Mechanical



Physiochemical

- High amounts of unbound fatty acids (as occurs with a fracture) in the blood stream leads to toxic metabolites that effects pulmonary, cerebral and coetaneous tissue.
 - Experimentally seen w/ injection of fatty acids into dogs resulting in pulmonary failure (Cahill, J. M. 1974)
- Amount of fatty acids released is the blood stream appears proportional to the magnitude of injury. (McNamara, J. D. 1972)

Prevention of FES

Early immobilization

- With both operative fixation or temporary stabilization (Riska EB et al. 1982)



- Corticosteroids
 - Controversial- unknown dose or duration
 - Meta-analysis by Bederman et al. 2009 shows may prevent hypoxia and FES but NO mortality benefit

Treatment of FES

Supportive therapy

Oxygen
Maintain a high PaO2 level
May require mechanical ventilation

– Hydration

- Corticosteroids?

FES with Facture Care

• Overall remains controversial

Definitive Care vs Damage Control

Early immobilization is preventative



The timing of fracture treatment in polytrauma patients: relevance of damage control orthopedic surgery*

Hans-Christoph Pape, M.D.^{a,†}, Peter Giannoudis, M.D.^b, Christian Krettek, M.D.^a The American Journal of Surgery 183 (2002) 622–629

Three principle factors that control clinical course
1. Initial degree of injury (1st hit)
2. Individual biological response
3. Type of Treatment (2nd hit)

DCO intervenes here to provide-

Temporary stability, decrease blood loss, help with pain control, and allow for the 1st hit and initial biological response to occur with a reduced 2nd hit as compared to definitive fixation. Definitive fixation occurs at a delayed date.

Reaming and FES

The biology of intramedullary reaming Roman Pfeifer, Richard Sellei, Hans-Christoph Pape*

- Any intramedullary pressure increase of more that 40mmHG is associated with fat emboli.
 - Includes guide wire insertion
 - Highest pressure at initial insertion
 - Solid fat have been seen w/ pressures > 200mmHg
- Pressure while reaming depends on
 - Compressive force while reaming
 - Sharpness of reamer
 - Drill speed
 - Reamer head shape
 - Conical w/ large flutes is better Muller CA et al. 2000

Adult Respiratory Distress Syndrome, Pneumonia, and Mortality following Thoracic Injury and a Femoral Fracture Treated Either with Intramedullary Nailing with Reaming or with a Plate

BY MICHAEL J. BOSSE, M.D.[†], CHARLOTTE, NORTH CAROLINA, ELLEN J. MACKENZIE, PH.D.[‡], BALTIMORE, BARRY L. RIEMER, M.D.[§], PITTSBURGH, PENNSYLVANIA, ROBERT J. BRUMBACK, M.D.[¶], MELISSA L. MCCARTHY, M.S.[‡], ANDREW R. BURGESS, M.D.[¶], DAVID R. GENS, M.D.[¶], AND YUTAKA YASUI, PH.D.[#], BALTIMORE, MARYLAND

> THE JOURNAL OF BONE AND JOINT SURGERY VOL. 79-A, NO. 6, JUNE 1997

 No difference in pulmonary complications or mortality in patients with femur fractures treated with reamed nails vs plate fixation

Reamed Versus Unreamed Intramedullary Nailing of the Femur: Comparison of the Rate of ARDS in Multiple Injured Patients

> By The Canadian Orthopaedic Trauma Society J Orthop Trauma • Volume 20, Number 6, July 2006

No difference in reamed vs. unreamed nailing

Case Examples

• 57 yo male involved in forklift accident with R open GA III-B tibia-fibula fracture.



Initially taken for I&D, spanning external fixation and antibiotic bead placement on injury day 1 and transferred to the floor post-op.



 POD #2 developed mental status changes, desaturation to 89% on 4L NC and transferred to ICU. CT done which showed filling voids concerning for FES. Found to have patechial rash diffusely over body. No other clear etiology.



- Patient was treated with supportive oxygen with recovery of his mental status and pulmonary status over next 4 days.
- Discharged from ICU to floor on HD #6.
- Underwent staged management of his fracture with antibiotic spacer placement and eventual bone transport.







Full mental status and pulmonary recovery.
Clinical Case

HPI: 20 y/o female, suicide attempt by trying to walk into traffic:

- Open L femoral shaft fracture
- Closed L tibial shaft fracture
- Closed R femoral shaft fracture
- Pulmonary contusion
- 12cm R scapular laceration/degloving
- Head lacerations

- PMHx: Asperger's, depression, gender dysphoria

Patient received appropriate chemoprophylaxis with enoxaparin 30mg SC. No missed doses.

On hospital day 2, patient taken for I&D L femur, IMN of all three fractures.

- Open L femoral shaft fracture
- Closed L tibial shaft fracture
- Closed R femoral shaft fracture









 Post-operatively, patient was extubated but found to have decreased mental status and hypoxemia requiring re-intubation.

CT –PE protocol showed a small apical segmental pulmonary embolus

 MRI brain obtained showing diffuse punctate foci of restricted diffusion in "star field" pattern consistent with Fat Emboli Syndrome

– Echo demonstrated patent foramen ovale

Patient treated with heparin drip, high dose statin, supportive care in ICU

- Patient failed extubation attempts

required tracheostomy

Remaining Hospitalization:

- Mental status slowly improved
- Hospital Acquired PNA
- Dischargd to inpatient Rehab

Case- Learning Points

- Long bone fractures with Classic Triad:
 - Respiratory Changes (dyspnea, tachypnea, hypoxemia)
 - Neurological Abnormalities (range from confusion to seizures)
 - focal neurological signs, hemiplegia, aphasia, apraxia, visual field disturbances, and anisocoria
 - Petechial Rash (conjuctiva, oral mucous, neck & axilla)
 - appears within the first 36 h and is self-limiting
 - Generally disappearing completely within 7 days
 - Treatment- Supportive care

Venous Thromboembolism (VTE)

Deep Vein Thrombosis (DVT) & Pulmonary embolism (PE)

DVT

• Clotting of blood that obstruct a deep vein in an extremity.

Most commonly seen in the lower extremities

- Can be obstructive or non-obstructive

PE

• Clotting of blood that obstructs a veins of any degree in the lungs.

Ranges from blockage of small subsegmental pulmonary arteries to segmental and massive emboli blocking an entire pulmonary artery.

History

• DVT

Described as far back as 1271
Guillaume de Saint Pathus- described a case of calf swelling that extended up the leg of a 20 year old cobbler.

- 1676: Wiseman- DVT is a consequence of an alteration of blood.

- 1793: Hunter - occlusion of the vein by blood clots Galanaud, JP et al. 2013

History

• **P**E

 Discovery largely credited to Rudolph Virchow in 1858

He described two types of PE occurrence
 DVT that embolizes to the lung
 Blockage in a pulmonary artery distal as a result of stagnant blood flow

 Virchow R. Die Cellularpathologic in Ihrer Begrudung auf Physiologische und Pathologische Gewebelehre. Berlin: A. Hirschwald, 1858

Etiology

- Virchow Triad 1858
 - Hemostasis
 - Immobilization, occlusion, tournaquet use
 - Endothial injury
 - Direct trauma or pressure from injury
 - Hypercoagulable state
 - Genetic, activation of clotting cascade, depression of thrombolytic enzymes
 - Virchow's overarching hypothesis of VTE has remained largly unchanged in 150+ years, with expansions of the definitions of each contributing factor



Antithrombotic Therapy for VTE Disease

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Clive Kearon, MD, PhD; Elie A. Akl, MD, MPH, PhD; Anthony J. Comerota, MD; Paolo Prandoni, MD, PhD; Henri Bounameaux, MD; Samuel Z. Goldhaber, MD, FCCP; Michael E. Nelson, MD, FCCP; Philip S. Wells, MD; Michael K. Gould, MD, FCCP; Francesco Dentali, MD; Mark Crowther, MD; and Susan R. Kahn, MD

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Occurrence of non fatal, symptomatic VTE rates after major orthopaedic surgery
- 4.3% (1.5% PE, 2.8% DVT) – No prophylaxis
- 1.8% (0.55% PE, 1.25% DVT)- LMWH
In cumulative postoperative period of 0-35 days

Epidemiology

- Different orthopedic injuries carry different rates of VTE
 - PE- as high as 61% in pelvic ring injuries
 - Ankle fractures VTE rate from 0.26-40 %
 - <u>Lapidus</u> et al 2013 reported 514 VTE events (1.1%) in 36,388 patients who underwent 45,968 orthopaedic procedures
 - DVT rate increase associated with increased ISS

DVT Diagnosis

- Wells Score- DVT assessment

- Paralysis, paresis or recent orthopedic casting of lower extremity (1 point)
- Recently bedridden (more than 3 days) or major surgery within past 4 weeks (1 point)
- Localized tenderness in deep vein system (1 point)
- Swelling of entire leg (1 point)
- Calf swelling 3 cm greater than other leg (measured 10 cm below the tibial tuberosity) (1 point)
- Pitting edema greater in the symptomatic leg (1 point)
- Collateral non varicose superficial veins (1 point)
- Active cancer or cancer treated within 6 months (1 point)
- Alternative diagnosis more likely than DVT (Baker's cyst, cellulitis, muscle damage, superficial venous thrombosis, post phlebitic syndrome, inguinal lymphadenopathy, external venous compression) (-2 points)

3-8 Points: High probability1-2 Points: Moderate probability-2-0 Points: Low Probability

Wells PS et al. 1997

PE Diagnosis

- Well's score for PE
 - Symptoms of DVT (3 points)
 - No alternative diagnosis better explains the illness (3 points)
 - Tachycardia with pulse > 100 (1.5 points)
 - Immobilization (>= 3 days) or surgery in the previous four weeks (1.5 points)
 - Prior history of DVT or pulmonary embolism (1.5 points)
 - Presence of hemoptysis (1 point)
 - Presence of malignancy (1 point)

Score > 6 High probability Score > 2 Moderate probability Score < 2 Low Probability

Wells PS et al. 2000

Diagnostic Studies

• DVT-

– Venous Ultrasound- non-invasive

 D-dimer-limitations due to elevation w/ many factors- rule out test.

• **P**E

- CT (PE protocol)- contrast study
- VQ scan
 - pregnant patients or pts allergic to contrast
- Venography- uncommon

Prevention of VTE

Mechanical

and/or

Chemical

Mechanical Prophylaxis

- Mobilization, Mobilization, Mobilization
 - Increase venous flow
- Sequential compressive devices (SCD's)
 - Increase venous return and fibrinolysis
- Vena Cava Filters- for PE
 - Block emboli
- Compression Stockings
 - Reduce stasis

Mechanical

- All have varying levels of efficacy in orthopaedic patients and limitations to use
 - Ability to apply therapy in setting of injury • Mobilization, SCD's and stockings - Patient adherencemobilization, SCD's and stockings - Invasiveness of the intervention • IVC filter Availability & Cost • All

Chemical Prophylaxis

- Aspirin
- Heparin (unfractonated)
- Low Molecular Weight Heparin (LMWH)
- Coumadin (warfarin)
- Fondaparinux
- Rivaroxaban
- Argatroban

Aspirin

- Irreversibly inhibits platelets
 Blocks cyclo-oxygenase-lactivity
 - Reduced thromboxane A-2 which allows platelets to aggregate
 - Platelet turnover is ~10%/day
 - So return of normal platelet activity in 7-10 days

- Advantages
 - Inexpensive, oral, no monitoring
- Disadvantages
 - Irreversible, GI intolerance, unclear efficacy w/ VTE

Heparin

- Increases Anti-Thrombin III Activity
 - Inbibits factors IIa, III, Xa
 - Overall decreases clotting cascade response
- Advantages
 - Reversible w protamine sulfate
- Disadvantages
 - Variable half-life, injectable, Heparin-induced thrombocytopenia (HIT), bleeding

Low Molecular Weight Heparin

Derivative of Heparin molecule
 Inhibits factor Xa

Advantages

- No monitoring, reversible with protamine, longer half-life than heparin, less risk of HIT
- Disadvantages
 - Cost, injectable, requires wt based/creatinine clearance based dosing, bleeding

Coumadin (Warfarin)

- Blocks Vit K dependant enzymes in clotting cascade.
 - Factors II, VII, IX, X, Protein C &S

- Advantages
 - Oral, inexpensive, reversible by Vit K or FFP
- Disadvantages
 - Requires close monitoring, effected by Vit K intake, bleeding, medication interactions

Others

- Fondaparinux Indirect factor Xa inhibitor
 - High bleeding complication rate, Cost
 - No monitoring required

- Rivaroxaban Direct Xa inhibitor
 Bleeding complications rate, Cost
 No monitoring required
- Continued difficulty with reversibility, cost, availability
- Ongoing research into their role in VTE prophylaxis in orthopaedics

Others

Argatroban - direct thrombin inhibitor
 Used in patients with HIT
 Dabigatran- oral direct thrombin inhibitor

• Issues with use

- Continuous infusion requiring monitoring
- Reversible
- Cost
- Bleeding

Other Factors

- Potential contraindication to chemical VTE prophylaxis
 - Spinal cord injury
 - Solid organ injury
 - Uncontrolled bleeding
 - Medication allergy
 - Upcoming operation
 - Platelet count < 50,000</p>
 - Previous head bleed

Ideal Agent!

- Want a VTE prophylaxis agent that is:
 - Inexpensive
 - Oral
 - Reversible
 - Doesn't require monitoring
 - No medication interactions
 - Low bleeding osk

VTE Treatment

• DVT

- Anticoagulation- prevent further DVT/PE
 - LMWH, Warfarin (INR 2-3),
 - Maybe factor Xa inhibitor or direct thrombin inhibitor

- Duration of therapy is dependent on

- If first DVT
- Provoked vs unprovoked
- Associated w/ Malignancy
- Associated w/ genetic disorder
- Remains unknown but ranges from 30 days to indefinite. Requires a discussion about risks.

VTE Treatment

- PE
 - Depends on hemodynamic stability
 - Stable patient-
 - Treat very similar to DVT + supplemental Oxygen.
 - Unstable patient- treat like a patient in shock
 - Anticoagulation
 - Supportive care with
 - » Repiratory support-
 - » Fluids
 - » Vasopressors
 - Invasive interventions-
 - » Thrombolytic therapy, Embolectomy,
 - » Surgical or catheter based
 - » IVC filter

Outcomes

30-Year Mortality After Venous Thromboembolism A Population-Based Cohort Study

Kirstine Kobberøe Søgaard, MD; Morten Schmidt, MD; Lars Pedersen, PhD; Erzsébet Horváth–Puhó, PhD; Henrik Toft Sørensen, DMSc *Circulation* September 2, 2014

- Mortality rate ratio (MRR) at 30 years

- DVT 1.55 (CI 1.53 1.57)
- PE 2.77 (CI 2.74 2.81

– People with VTE have a higher 30 year mortality

• PE reoccurrence rate

- 8 % six months, 13 % one year, 23 % five years,
30 % 10 years
den Exter, PL et al. 2013

Recommendations

 The next section will go over recommendations from major groups regarding orthopedic patients and specific procedure. This is a resource for you to review.

OTA Recommendations

Venous Thromboembolism Prophylaxis in Orthopaedic Trauma Patients: A Survey of OTA Member Practice Patterns and OTA Expert Panel Recommendations

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

Most recent guidelines put out by the OTA specific to Orthopedic Trauma patients

Based on 185 OTA members who responded to a survey of their clinical practices regarding VTE prophylaxis and in conjunction with an expert panel they put forth 13 recommendations

Useful VTE Prophylaxis Guideline Websites

PREVENTING VENOUS THROMBOEMBOLIC DISEASE IN PATIENTS UNDERGOING ELECTIVE HIP AND KNEE ARTHROPLASTY

> EVIDENCE-BASED GUIDELINE AND EVIDENCE REPORT

September 24, 2011 http://www.orthoguidelines.org/topic?id=1006

THE DIAGNOSIS AND TREATMENT OF ACUTE ACHILLES TENDON RUPTURE

GUIDELINE AND EVIDENCE REPORT

Adopted by the American Academy of Orthopaedic Surgeons Board of Directors December 4, 2009

http://www.orthoguidelines.org/topic?id=1000

MANAGEMENT OF HIP FRACTURES IN THE ELDERLY

EVIDENCE- BASED CLINICAL PRACTICE GUIDELINE

Adopted by the American Academy of Orthopaedic Surgeons Board of Directors September 5, 2014

http://www.orthoguidelines.org/topic?id=1017
Highlighted Chest Guidelines

Antithrombotic Therapy for VTE Disease

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

Clive Kearon, MD, PhD; Elie A. Akl, MD, MPH, PhD; Anthony J. Comerota, MD; Paolo Prandoni, MD, PhD; Henri Bounameaux, MD; Samuel Z. Goldhaber, MD, FCCP; Michael E. Nelson, MD, FCCP; Philip S. Wells, MD; Michael K. Gould, MD, FCCP; Francesco Dentali, MD; Mark Crowther, MD; and Susan R. Kahn, MD

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2.2.1. In patients with a high clinical suspicion of acute VTE, we suggest treatment with parenteral anticoagulants compared with no treatment while awaiting the results of diagnostic tests (Grade 2C).

2.5.1. In patients with acute DVT of the leg, we suggest LMWH or fondaparinux over IV UFH (Grade 2C) and over SC UFH (Grade 2B for LMWH; Grade 2C for fondaparinux).

2.13.1. In patients with acute DVT of the leg, we recommend against the use of an inferior vena cava (IVC) filter in addition to anticoagulants (Grade 1B).

2.13.2. In patients with acute proximal DVT of the leg and contraindication to anticoagulation, we recommend the use of an IVC filter (Grade 1B).

2.14. In patients with acute DVT of the leg, we suggest early ambulation over initial bed rest (Grade 2C).

- 3.1.4. In patients with an unprovoked DVT of the leg (isolated distal [see remark] or proximal), we recommend treatment with anticoagulation for at least 3 months over treatment of a shorter duration (Grade 1B). After 3 months of treatment, patients with unprovoked DVT of the leg should be evaluated for the risk-benefit ratio of extended therapy.
- In all patients who receive extended anticoagulant therapy, the continuing use of treatment should be reassessed at periodic intervals (eg, annually).
- 3.5. In patients who are incidentally found to have asymptomatic DVT of the leg, we suggest the same initial and long-term anticoagulation as for comparable patients with symptomatic DVT (Grade 2B).
- 4.1. In patients with acute symptomatic DVT of the leg, we suggest the use of compression stockings (Grade 2B).
- 5.1. In patients with acute PE, we recommend initial treatment with parenteral anticoagulation (LMWH, fondaparinux, IV UFH, or SC UFH) over no such initial treatment (Grade 1B).
- 5.2.3. In patients with a low clinical suspicion of acute PE, we suggest not treating with parenteral anticoagulants while awaiting the results of diagnostic tests, provided test results are expected within 24 h (Grade 2C).
- 5.9.1. In patients with acute PE who are treated with anticoagulants, we recommend against the use of an IVC filter (Grade 1B).
- 5.9.2. In patients with acute PE and contraindication to anticoagulation, we recommend the use of an IVC filter (Grade 1B).
- 9.1.1. In patients with acute upper-extremity DVT (UEDVT) that involves the axillary or more proximal veins, we recommend acute treatment with parenteral anticoagulation (LMWH, fondaparinux, IV UFH, or SC UFH) over no such acute treatment (Grade 1B).

Thank You!

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 Dr Rodney A. Schmidt MD- Pathology
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 University of Washington Medical Center

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