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

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January 2016
Objectives

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

Acute Respiratory Distress Syndrome
Fat Embolism
Venous Thromboembolism
Acute Respiratory Distress Syndrome

Relatively clear CXR

Diffuse bilateral coalescent opacities
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- 200mmHg < PaO2/FiO2, ≤ 300mmHg w/ PEEP or CPAP ≥ 5cm H2O
Moderate- 100 mmHg < PaO2/FiO2, ≤ 200 mmHg w/ PEEP ≥ 5 cm H2O
Severe- PaO2/FiO2 ≤ 100mmhg w/ PEEP ≥ 5 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
- 78.9 per 100,000 person-years
- 38.5% in hospital mortality rate

- 190,600 cases per years in US
- 74,500 associated deaths per year in US
Epidemiology

– 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
  • Transfusion
  • Embolism
  • Burns
• Systemic inflammatory process
• Multi-organ failure
• Drug overdose
• Stem-cell transplant
Pathophysiology

Lung Injury

- Alveolar & Vessel damage
  - IL-1
  - IL-6

- Fluid accumulation in lung interstitium and alveoli

- Decreased lung compliance
- Decreased gas exchange
- Increase pulmonary arterial pressure

Cytokines
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 hemorrhage

• 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 deposits in the lungs of postmortem 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

- 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%)
– 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
Mechanical

Fracture

Fat liberated from bone

Fat uptake by venous system

Fat causes obstruction

Skin/eyes

Petechiae

Lungs

Hypoxia

Patent Foramen Ovale

Brain

Confusion
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
Three principle factors that control clinical course

1. Initial degree of injury (1^{st} hit)
2. Individual biological response
3. Type of Treatment (2^{nd} hit)

DCO intervenes here to provide-
- Temporary stability, decrease blood loss, help with pain control, and allow for the 1^{st} hit and initial biological response to occur with a reduced 2^{nd} hit as compared to definitive fixation. Definitive fixation occurs at a delayed date.
Reaming and FES

• Any intramedullary pressure increase of more than 40mmHg is associated with fat emboli.
  – Includes guide wire insertion
  – Highest pressure at initial insertion
  – Solid fat have been seen with 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
No difference in pulmonary complications or mortality in patients with femur fractures treated with reamed nails vs plate fixation.

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** (conjunctiva, 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 sub-segmental 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

• PE
  – 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

Etiology

- Virchow Triad – 1858
  - Hemostasis
    - Immobilization, occlusion, tourniquet use
  - Endothelial 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 largely unchanged in 150+ years, with expansions of the definitions of each contributing factor
Epidemiology

• 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 %
  - Lapidus 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 probability
1-2 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.

• PE
  – 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 adherence-
    - mobilization, SCD’s and stockings
  - Invasiveness of the intervention
    - IVC filter
  - Availability & Cost
    - All
Chemical Prophylaxis

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

- Irreversibly inhibits platelets
  - Blocks cyclo-oxygenase-1 activity
    - 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
  – Inhibits 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 $< 50,000$
  - Previous head bleed
Ideal Agent!

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

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
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!

• Special thanks to
  – Dr Rodney A. Schmidt MD- Pathology
    • University of Washington Medical Center
  – Dr Stephanie Cheng MD- Chest Radiology
    • University of Washington Medical Center
References

References

References

• For questions or comments, please send to ota@ota.org