Management of Pulmonary Embolism
Where are we now?

Pulmonary Vascular Disease Center

Pulmonary Arterial Hypertension

Pulmonary Embolism

High Altitude PH

WHO class II/III PH

Hereditary Hemorrhagic Telangiectasia (HHT)

Pulmonary Embolism

- 700,000 cases VTE in US/year
- 80,000 deaths/year
- 3 month mortality: 17%
- All specialties
Pathophysiology

RV: pressure, time, volume

Impact of increased afterload
Case

- You are called to the ED for the evaluation of a 22 year old women:
  - CC: Chest Pain and SOB
    Graduate Student at CSU and an avid mountain biker.
    Calf pain 1 week ago and had some trouble completing a mountain bike race this weekend
    PMH: No previous medical problems
    No Meds                   FH: Mother ? DVT

Case

- Vitals: P- 98, R- 24, T-37, BP 94/60, SaO2-90%
  Gen: Mild distress due to pluritic chest pain
  Pulm: No rale or wheeze
  CV: JVD- 8 cm, II/VI SEM, no edema

CT angiography
Troponin: 1.2
BNP: 230

Case
She was started on UF heparin in ED
Attending calls you to discuss the case
– Should this patient receive thrombolysis?
  • Systemic or Catheter Directed?
– Should she get an IVC filter?

The patient wants to know
– How long does she have to stay on medication
– Will she have any long term sequela

Topics
• Thrombolytics for Pulmonary Embolism
• IVC filters
• Duration of Anticoagulation
• Chronic Thromboembolic Disease (CTEPH)
Thrombolysis and Pulmonary Embolism

- UPET- 1970,
  - 160 patients with PE, UK vs. Heparin.
  - Improved hemodynamics and VQ at 24 hours.
  - No difference between groups at 5 days.
- 8 other similar trials using various agents (SK, rt-PA) with same findings.

Jama Dec 21 1970  214: 12

Thrombolytics: Stratification

- Massive
  - Hemodynamic definition
    - SBP < 90 for 15 minutes
    - Pressor requirement
- Sub-massive
  - RV enlargement
  - Pulm Htn
  - Tri or BNP elevation
  - CT evidence of PH
Massive PE

Enoxaparin and Heparin versus Heparin Alone in Massive Pulmonary Embolism: A Randomized Controlled Trial

RCT Single Center

N= 8

P=0.03

Sub-massive PE

Peitho

n=1006, Tenectaplace vs. Heparin

1- Death or “hemodynamic collapse”
2.6% vs. 5.6%  OR- 0.44  p=0.02

Death: 1.2% vs. 1.8%  p=0.42
“Hemodynamic Collapse”- 1.6% vs. 5%  p=0.002
**Bleeding**

Major Bleeding: 11.5% vs. 2.4%

Bleeding (extra cranial): 6.3% vs. 2.4%  \( p<0.001 \)

Hemorrhagic CVA: 10 pts vs. 1 pt (2.4% vs. 0.2%)

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**Moderate Pulmonary Embolism Treated With Thrombolysis**

From the “MOPET1” Trial:

Sharifi et al.  *Am J Cardiol* 2012

n = 121,  Single Center

“safe dose” (50 mg tPA) vs. Heparin

Primary - Pulmonary Hypertension at 22 months

57% vs. 16%

???

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**Catheter Directed Thrombolysis**

MC-RCT: USAT vs. UFH

n = 59

10-20 mg tPA over 15 hrs

Primary: RV/LV 0.3 vs .032 \( p<0.001 \)

Secondary: No major bleeding events
IVC Filters

Venous ligation

The New England Journal of Medicine

NEW ENGLAND SURGICAL SOCIETY
THROMBOSIS OF THE DEEP VEINS OF THE LOWER LEG, CAUSING PULMONARY EMBOLISM

* Collins et al reported IVC ligation 1943

IVC plication
IVC filters

- Mobin-Uddin umbrella filter 1969
- Greenfield
  - IVC filter 1971

Filter Types

- Greenfield
- Birds Nest
- Vena Tech
- Trap Ease
- Opt Ease
- Optional/Retrievable

[Image of IVC filters]

[Image of Filter Types]

[Graph: Twenty-one-Year Trends in the Use of Inferior Vena Cava Filters]

Stein AM J Med 2011
Indications for IVC filters

1. Can not anti-coagulate
2. Failure of Anticoagulation
3. The next one will kill you!!

Outcome

**NNT= 33**

**No difference in mortality or major bleeding**

**3.2.1.**

**A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis**

**Abstract**

Using a two-by-two factorial design, we randomly assigned 400 patients with proximal deep-vein thrombosis who were at risk for pulmonary embolism, death, and major venous thromboembolism to receive low-molecular-weight heparin (enoxaparin, 195 patients) or unfractionated heparin (4.2 percent), had had asymptomatic pulmonary embolism (odds ratio, 0.38; 95 percent confidence interval, 0.10 to 1.38). At two years, 37 patients assigned to the filter group (20.8 percent), as compared with 21 patients assigned to the no-filter group (11.6 percent), had had recurrent deep-vein thrombosis (odds ratio, 0.22; 95 percent confidence interval, 0.05 to 0.90). There were no significant differences in mortality or major bleeding were analyzed at day 12 and at two years.

**Background**

In high-risk patients with proximal deep-vein thrombosis, the initial beneficial effect of intracaval filters became available in the late 1960s. According to Monreal and associates, filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis, without any difference in mortality. Our data also confirmed that low-molecular-weight heparin was as effective and safe as unfractionated heparin for the prevention of pulmonary embolism.

**Results**

N= 400 2x2 factorial study

+/‐ IVC filter     ‐/+ LMWH vs. IV UF heparin

Outcome:

PE, Death or major bleed
Day 12 and 2 years

**Outcome**

• 12 days: PE 1.1 % filter vs 4.8% no filter
• 2 years: DVT 20.8% filter vs 11.6% no filter

• No difference in mortality or major bleeding
• NNT= 33
8 yr. follow-up
  - PE 6.2% filter vs 15.1% no filter
  - DVT 35.7% filter versus 27.5% no filter
  - No difference in mortality or post thrombotic syndrome

Impact of Vena Cava Filters on In-hospital Case Fatality Rate from Pulmonary Embolism

Nationwide Inpatient Sample
2,010,500 patients - PE 1999-2008
In hospital case fatality rate: IVC +/-
Stable vs. Unstable
Lysis vs. no
DVT vs. no

Improved Mortality

Effect of a Retrievable Inferior Vena Cava Filter
Plus Anticoagulation vs Anticoagulation Alone
on Risk of Recurrent Pulmonary Embolism
A Randomized Clinical Trial

N = 399
1- PE 3 months
2 – PE 6 months, DVT, major bleeding, Filter complications
Filter- 3% No Filter- 1.5% r = 2.00 p = 0.5)

ACCP Guidelines 2012
– Do not use IVC filter if anti-coagulate . 1B
– Use IVC filter if unable to anti-coagulate. 1B
– Conventional course of anti-coagulation if filter placed. 2B

Preserve:
• “Predicting the Safety and Efficacy of Inferior Vena Cava Filters”
• Registry: 2100 patients, 60 centers, 5 years
• SIR and SVS
• A variety of filters

We need a RCT on filters
Major Bleed: 1.5% vs. 3%

2 years: 15.7% vs. 15.8%

9 months: 0.7% vs. 8.3%

N= 267

Duration of Anticoagulation

How long do you go?

The New England Journal of Medicine

N= 902
Followed 2 years
18% vs 9.5% recurrence
Major Bleed 0.2% vs. 1%

Three months versus one year of oral anticoagulant therapy for idiopathic deep venous thrombosis

N= 267
9 months: 0.7% vs. 8.3%
2 years: 15.7% vs. 15.8%
Major Bleed: 1.5% vs. 3%
Comparison of 1 month with 3 months of anticoagulation for a first episode of venous thromboembolism associated with a transient risk factor

N= 165
Assessed at 1 year
1 month: 6% vs. 3.7%  p=.05
Major Bleed: 0
Risk

- Annual Risk of Major Bleed VKA
  - 3%

Unprovoked

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<th>Duration</th>
<th>Strength of Recommendation</th>
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<td>3 months</td>
<td>Ib</td>
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3% annual risk VTE

15% at 5 years

10% VTE first year

30% at 5 years

Duration of Therapy: ACCP 2012 (9th Edition) PE

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Risk

Provoked

3% annual risk VTE

15% at 5 years

15% at 5 years

10% VTE first year

30% at 5 years
Duration of Anticoagulation

- Risk vs. Benefit

Stratification of risk

Clotting

Patient
Education and
Patient Goals

Alternative
and Novel
agents

Bleeding

New oral anticoagulants in the treatment of acute venous thromboembolism – a systematic review with Indirect comparisons

Hirschl et al, VASA 2014

- DOACS: Direct oral anticoagulants: oral Xai and DTI
  - Rivaroxaban, Apixaban, Dabigatran and Endoxaban

- 27,024 pts in trials
- No difference in recurrent VTE or survival
- Significant decrease in bleeding RR 0.31-0.81
- Lack reversal agents

Idarucizumab for Dabigatran Reversal

RE-VERSE Prospective Cohort

N= 90
a) Bleeding
b) Urgent Procedure
6.6 % vs. 11%
N = 403
1st unprovoked
2 year follow up
6.6 % vs. 11%
Risk reduction - 40%

Pulmonary Vascular Disease Center

Pulmonary Arterial Hypertension
Pulmonary Embolism
High Altitude PH
WHO class II/III PH
Hereditary Hemorrhagic Telangiectasia (HHT)

Case

- What did we do?
  - Sub-massive PE
  - Received 100mg tPA
  - No IVC filter
  - LMWH → Rivaroxaban
  - Remains on therapy at 6 months
  - No evidence of CTEPH on repeat echo