Update in Pulmonary Embolism and Chronic Thromboembolic Pulmonary Hypertension

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Challenges in Pulmonary & Critical Care: 2013

Faculty Disclosure

No relevant relationships to disclose
Objectives

- Review the diagnosis of pulmonary embolism (PE) and chronic thromboembolic pulmonary hypertension (CTEPH) with emphasis on the role of the ventilation perfusion (VQ) scan
- Review the current management of PE
- Explain surgical and new therapeutic options for CTEPH

On a scale of 1 to 5:
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What is the Best Indication for Thrombolytic Therapy in Acute PE?

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What is the Best Test for Chronic Thromboembolic Disease PH?

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What is the Mortality for Pulmonary Thromboendarterectomy?

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Diagnosis of Acute PE
PE Diagnosis

To diagnose, you must suspect
- Symptoms non-specific
- Setting: +history VTE, cancer, trauma, postop, etc.

Not quite true, incidental PE discovered on CTA 3% in 1 analysis

Thromb Res 2010; 125:518-22

Wells Score

- 1 point for cancer and hemoptysis
- 1.5 pts: hx VTE, postop or immobile, HR>100
- 3 pts: clinical signs of DVT, clin judgement
- Probability score: 0-1 low, 2-6 intermed, 7+ high

Thromb Haemost 2000; 83:416–420
D-dimer

- Sensitive > 95%: Helpful to exclude PE in low to moderate risk patient
- Non-specific (40%): cannot be used to confirm diagnosis

CTA

- Has become primary diagnostic test for acute PE but varies with PE extent & CPTP
- PPV: 97% with main or lobar, 68% with segmental, but only 25% with isolated sub-segmental pulmonary artery abnormalities
- PPV: 96% with high CPTP, 92% with moderate CPTP, but only 58% with low CPTP

CPTP=clinical pre-test probability
VQ Scan

- CTA has replaced for acute PE except ↑Cr
  - High probability +PE ≥ 85%
  - Normal scan (25%) excludes PE

- VQ remains test of choice for screening for CTE as cause of PH
  - CTA can be falsely negative

Treatment of Acute PE
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)

In patients with acute PE, we suggest LMWH or fondaparinux over
- IV UFH (Grade 2C for LMWH; Grade 2B for fondaparinux)
- and over SC UFH (Grade 2B for LMWH; Grade 2C for fondaparinux)

Grade 2B or 2C
Treatment

- In patients with acute PE, we recommend early initiation of VKA (eg, same day as parenteral therapy is started) over delayed initiation
- Continuation of parenteral anticoagulation for a minimum of 5 days and until the INR is 2.0 or above for at least 24 h
- Grade 1B

Treatment

- Acute PE associated with hypotension (eg, systolic BP < 90 mm Hg)
- If no high bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy
- (Grade 2C)
Treatment

- When a thrombolytic agent is used, we suggest short infusion times (e.g., a 2-h infusion)
- Administration through a peripheral vein over a pulmonary artery catheter
- Grade 2C
Treatment

- Acute PE associated with hypotension who have:
  - (i) contraindications to thrombolysis, or
  - (ii) failed thrombolysis, or
  - (iii) shock that is likely to cause death before systemic thrombolysis can take effect (eg, within hours)

- We suggest catheter-assisted thrombus removal or surgical pulmonary embolectomy over no such intervention

- Grade 2C

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Treatment

- In patients with acute PE and contraindication to anticoagulation, we recommend the use of an IVC filter

- In no CI to AC, IVC filter not recommended

- Grade 1B
Chronic Thromboembolic Pulmonary Hypertension (CTEPH)

WHO DIAGNOSTIC GROUPS

- Group 1: Pulmonary Arterial Hypertension
- Group 2: Pulmonary Venous Hypertension
- Group 3: PH in association with hypoxemia
- Group 4: PH in association with CTE
- Group 5: Miscellaneous

Mayo Clinic Florida PH Center

MCF Data: n = 1002

CTEPH

½ No history thromboembolism

Risk factors
  ➤ PE >> DVT
  ➤ Large perfusion defect

Up to 4% of acute PE develop CTEPH

Pengo V et al. NEJM 2004; 350:2257-64
CTEPH Survival

- MPAP > 30  
  30% at 5 years
- MPAP > 50  
  10% at 5 years

Viner SM Prog Cardiovasc Dis 1994;37:79
Piazza G NEJM 2011; 364:351-60

Diagnosis of CTEPH
Teaching Case

- 75 yo WF w/ dyspnea
- History: 2011 left DVT and PE treated with coumadin
- Co-morbidities
  - Mild COPD (Never smoker)
  - Systemic HTN

INITIAL EVALUATION

- WHO FC III
- BNP 581 pg/mL, ALT 76, INR 2.5
- Six-minute walk 383 m on O2
- ECHO: RAP 10, RVSP 97, MPAP 60
- Moderate RVE and RV hypokinesis; TAPSE 1.6 cm
FURTHER EVALUATION

- Chest CT with contrast (PE protocol) was normal except for some mild heterogeneous appearance of the pulmonary parenchyma (mosaicism)
- RHC was performed
  - MPAP 45 and PCWP 10 mmHg
  - PVR 7 Wood units
- WHAT SHOULD YOU DO NEXT?
Diagnosis

- Chest CT with contrast for PE study can be falsely negative for CTE
- V/Q scan remains gold standard for screening

Tunariu N et al. VQ more sensitive than CTA. J Nucl Med 2007;48:680-4
Treatment of CTEPH
CTEPH

Treatment

- Anticoagulation
- Endarterectomy (PTEA)
- IVC filter
- Riociguat for inoperable cases


Treatment

- We recommend extended anticoagulation over stopping therapy (Grade 1B)
- We suggest pulmonary thromboendarterectomy over no pulmonary thromboendarterectomy (Grade 2C)

CHEST 2012; 141(2)(Suppl):7S–47S
CTEPH Surgical Candidacy

- Symptomatic: FC ≥ II
- Increased MPAP ≥ 26 mmHg
- PVR 800 to 1000 dyne/sec/cm⁵
- Surgically accessible disease
- Absent Contraindications: Severe lung disease


CTEPH Selection Group

- Determine eligibility for endarterectomy
- Cardiovascular surgery, pulmonary, cardiology, critical care, cardiac anesthesia, transplantology and chest radiology
- Monthly meetings

Fedullo Am J Respir Crit Care Med 2011; 183:1605-13
Teaching Case

- Diagnosis was Group 4 CTEPH
- Treatment was successful PTEA

Pulmonary Thromboendarterectomy

- Midline incision
- Surgery time 4-5 hrs with circulatory arrest at 16 degrees
- Sequential approach to R then L
- 2 to 3 mm endarterectomy (vessel 4)
- Avoid pleural space-no chest tube
UCSD RESULTS

- N = 500
- Surgical Time
  - Bypass 219 minutes
  - Circ Arrest 36 min
- ICU Stay 96 hours (Vent 24 hrs)
- 22 deaths (4.4%)


Methylprednisolone

- AIM: preventing lung injury following PEA
- RCPCT in Chest January 2012
- No benefit
- AE: Hyperglycemia requiring insulin

Anesthesia Recommendations

- Paucity of evidence-based guidelines
- Regional and general techniques described
- Avoid conditions that elevate PVR: hypoxia, acidosis, hypercarbia and hypothermia
- Low TV and PEEP but avoid hypercarbia
- Keep CVP > 10 mmHg, Maintain SR


Managing Right Ventricular Failure

- Rewarm if hypothermic post-op
- Correct acidosis and hypoxemia
- Control arrhythmias

PH and RV FUNCTION

Ventricular Interdep  
Syst Dysfunction  
Diast Dysfunction

Arrhythmia  
TR

LV Dysfx  
Low CO  
Shunt  
Congestion

Circulatory Failure  
Hypoxemia

HSM, ascites  
Perip Edema


Managing Right Ventricular Failure

- Adequate MAP
  - Dobutamine 2 – 5 mcg/kg/min
  - Milrinone 0.375 – 0.75 mcg/kg/min

- Hypotensive Patients
  - Dopamine 5 – 15 mcg/kg/min
  - Epinephrine 0.01 – 0.1 mcg/kg/min
  - Norepinephrine 0.01 – 0.1 mcg/kg/min

Managing Right Ventricular Failure

Vasodilators
- Inhaled NO 10 – 20 ppm
- Inhaled epoprostenol
- Iloprost every 2 hrs
- Tyvaso (inhaled treprostinil) every 6 hrs

PH Drugs and Bleeding
- Prostacyclins inhibit PLT aggregation
- Potentially could increase bleeding
- Inhaled: treprostinil, prostacyclin
- Infusion: treprostinil, epoprostenol

Targets for Current Therapy in CTEPH

Nitric Oxide Pathway

Arginine

Nitric Oxide Synthase

Nitric Oxide

cGMP

Exogenous Nitric Oxide

Phosphodiesterase Type-5

Phosphodiesterase Type-5 Inhibitors

Vasodilatation and Antiproliferation


RIOCI GUAT

- 261 patients with inoperable CTEPH
  - MCRDBPCT over 16 weeks
  - Primary: 6MWD improved 46 meters
  - Secondary Outcomes
    - Improved: WHO FC, BNP, PVR
    - Not improved: Time to clinical worsening
RIOCIGUAT

- 443 patients for Group 1 PAH
- MCRDBPCT over 12 weeks
- Primary: 6MWD improved 36 meters
- Secondary Outcomes
  - Improved: FC, BNP, TTCW, and PVR
  - SE: HA 27%, Dyspepsia 19%, Edema 17%

Lung Transplant

- Acute morbidity and mortality high
- Survival curves merge with other disease groups long-term
- Rarely need HLT
Bibliography


Post-Test Question 1

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Which of the statements below describes your approach to diagnosing and treating patients with PE and CTEPH?

1. I do not manage patients with PE and CTEPH, nor do I plan to this year.
2. I did not manage patients with PE and CTEPH before this course, but as a result of attending this course I’m thinking of managing it now.
3. I do manage patients with PE and CTEPH and this course helped me change my treatment methods.
4. I do manage patients with PE and CTEPH and this course confirmed that I don’t need to change my treatment methods.
Discussion and Questions