Chronic Thromboembolic Pulmonary Hypertension: Pathogenesis and Diagnosis

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Incidence

• Incidence of VTE in the general population 0.117%\(^1\):
  – 0.048% DVT
  – 0.069% PE

• Acute PE leads to haemodynamic failure and death within 1 hour in 20–40% of patients\(^2\)

• US figures:
  – ~600,000 cases of acute PE per year
  – 500–2,500 new CTEPH cases per year\(^3\)

• Estimated incidence of CTEPH historically given as 0.1–0.5% in patients surviving acute PE\(^2,3\)

• However, a recent study shows cumulative incidence of CTEPH is 3.8% at 2 years post-PE (overall incidence ~3%)\(^4\)

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Prognosis of CTEPH (untreated)


- mPAP < 30 mmHg
- mPAP > 30 mmHg

Survival over time shown with a Kaplan-Meier survival curve, with a statistically significant difference between the two groups (p = 0.04).
CTEPH following PE


Cumulative incidence of CTEPH

- 1.0% at 6 months
- 3.1% at 1 year
- 3.8% at 2 years
Natural history of PE (surviving patients)

ACUTE PE: symptomatic/asymptomatic

- Restoration of haemodynamics and exercise capacity\(^1,2,3\)
- Restoration of RHF\(^4\)
- Resolution of thromboemboli\(^1,2\)

Persisted PH/abnormal lung perfusion patterns\(^5,6,7\)

Risk of CTEPH\(^1\)

1–3%\(^7\)

CTEPH

Early natural history of CTEPH

• May be a long period (months–years) between initiating event (which may be silent) and symptoms of CTEPH (‘honeymoon period’)

• Usually present with late-stage disease
  – progressive dyspnoea on exertion
  – general clinical deterioration paralleling loss of right ventricular functional capacity

• Early natural history is therefore not fully characterised
  – non-specific symptoms
  – lack of previous history of VTE

{ UNDER-DIAGNOSIS }
Intravascular visualisation of CTEPH
Microscopic vascular features of CTEPH

- Photomicrograph of a muscular artery
- Shows eccentric intimal thickening (*) and organised thrombus (T)
- Thrombus contains recanalised vascular channels (arrows)

Original magnification x 40
Movat pentachrome elastic stain

Reproduced with permission from Frazier AA et al. Radiographics 2000; 20: 491–524.
Vascular features of CTEPH

Medial hypertrophy  Intimal proliferation  Plexiform lesion

Features of pulmonary hypertension

Reproduced with permission from Frazier AA et al. Radiographics 2000; 20: 491–524.
Aetiology: Embolic hypothesis

The initiating event in CTEPH is PE arising from a VTE.

- **VTE**
- **ACUTE PE**
- Incomplete resolution and organisation of thrombus
- Vascular occlusion/obliteration
- High pressure/shear stress in open areas
- Progressive pulmonary vascular resistance
- **CTEPH**
Clinical - Hemodynamic History
CTEPH

- Pre-clinical
- Symptomatic
- Decline

Initial Embolic Event

Time

PAP

C.O.
CTEPH: Diagnostic Evaluation

Ventilation / Perfusion scan

One - or more - segmental mismatched defects
Perfusion Scan: PAH
CT Scan Findings in CTEPH

• Mosaic pattern
  – May also be seen in parenchymal diseases such as hypersensitivity pneumonitis
UCSD Experience
1984 - 2006

Survivors
Deaths
Chronic Thromboembolic Pulmonary Hypertension

Surgical Selection

- Surgically accessible chronic thrombi
- Symptom - associated pulmonary hypertension
  (usually > 300 d-s-cm-5)
- Significant ventilatory impairment
- Other factors influencing operative risks:
  - Age
  - Obesity
  - Primary cardiac disease
Pulmonary Thromboendarterectomy

- Endarterectomy, not embolectomy
- Median sternotomy
- CPB with deep hypothermia
- Circulatory arrest periods
- Other procedures:
  - PFO closure
  - CABG
  - Valve replacement
Pulmonary Thromboendarterectomy

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Outcomes Post PTE

Removal of Chronic Thrombi

↓

RV Afterload Reduction

Decreased PVR

↓

Improved Cardiac Output
Preoperative

Postoperative
Perioperative hemodynamics in 250 PTE patients* who underwent surgery at UCSD, 1/00 to 1/02

<table>
<thead>
<tr>
<th></th>
<th>Preoperative</th>
<th>Postoperative</th>
<th>Sig.**</th>
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</thead>
<tbody>
<tr>
<td>Mean PA Pressure (mmHg)</td>
<td>45.9 +/- 9.9</td>
<td>28.5 +/- 10.0</td>
<td>P&lt;.001</td>
</tr>
<tr>
<td>PA Systolic Pressure (mmHg)</td>
<td>75.8 +/- 16.6</td>
<td>47.5 +/- 16.8</td>
<td>P&lt;.001</td>
</tr>
<tr>
<td>Cardiac Output (L/min)</td>
<td>3.61 +/- 1.18</td>
<td>5.46 +/- 1.52</td>
<td>P&lt;.001</td>
</tr>
<tr>
<td>PVR (dyne-sec-cm-5)</td>
<td>942 +/- 422</td>
<td>316 +/- 236</td>
<td>P&lt;.001</td>
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</tbody>
</table>

*Complete pre- and postoperative hemodynamic numbers available in 242 patients; postoperative values within 72 hours following surgery

**Significance: two-tailed Student T-test

Abbreviations: PA, pulmonary artery; PVR, pulmonary vascular resistance
### Postoperative Complications in 250 PTE Patients Who Underwent Surgery at UCSD, 1/00 to 1/02

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of Patients</th>
<th>%</th>
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<tbody>
<tr>
<td>Reperfusion Lung Injury</td>
<td>76</td>
<td>30.4</td>
</tr>
<tr>
<td>Persistent Pulmonary HTN</td>
<td>34</td>
<td>14.0</td>
</tr>
<tr>
<td>Atrial Fibrillation-Flutter</td>
<td>30</td>
<td>12.0</td>
</tr>
<tr>
<td>Delirium</td>
<td>26</td>
<td>10.4</td>
</tr>
<tr>
<td>Nosocomial Lung Infection</td>
<td>23</td>
<td>9.2</td>
</tr>
<tr>
<td>Wound Infection</td>
<td>7</td>
<td>2.8</td>
</tr>
</tbody>
</table>

*Postoperative Pulmonary Vascular Resistance >500 d-s-cm-5; complete perioperative hemodynamic values available in 242 patients*
Pulmonary Thromboendarterectomy

Perioperative Mortality Rates
Perioperative Mortality Rates
UCSD

%
PTE: Perioperative Mortality

113 / 1877 Patients Undergoing PTE, 1990 - 2006 (6.0%)

31 Persistent pulmonary hypertension, RV Failure
23 Reperfusion pulmonary edema (RPE)
20 Persistent pulmonary hypertension + RPE
 8 Intraoperative arrest (5); Postop Arrest (3)
 5 Perioperative CVA
 4 Mediastinal hemorrhage (one post V.Fib arrest)
15 Multiorgan Failure, Sepsis
 1 Aortic dissection, arrhythmia (presumed), pericardial tamponade, myocardial infarction, failure to wean (COPD), pancreatitis / ARDS, massive lower GI bleed, pneumothorax + RPE,
Outcomes Post-PTE
Long-Term Survival

Survival

Years

<20 mm Hg (N=64)
21-30 mm Hg (N=19)
31-40 mm Hg (N=10)
41-50 mm Hg (N=19)
>50 mm Hg (N=35)

Survival probability

Years

Outcomes Post-PTE

Functional Status

- Improved Quality of life
- Return to Work
- Reduced Health Care Utilization
Chronic Thromboembolic Pulmonary Hypertension

Referral Requests (UCSD center):
1. Recent Medical Summary
2. Demographics
3. Pulmonary Angiogram report and film (CD)
4. Right & Left Heart Catheterizations within last 12 months
5. Echocardiogram report and CD/tape
6. PFT’s with ABG’s within the last 6 months
7. VQ scan report and film (CD)
8. Chest CT report and film (CD)
9. CXR report and film (CD) within last 6 months
10. Recent pertinent labs including ANA & Hepatitis screen
Chronic Thromboembolic Pulmonary Hypertension

Important Reminders:

“Be advised that the record review process cannot begin until films/CD’s have arrived at UCSD.”

“Please keep a record of the overnight tracking number.”
Pertinent Patient Issues

- Early diagnosis and referral
- Adequate diagnostic testing
- Insurance barriers
- Diligent patient follow-up and care until referral process is complete