Building a Pulmonary Endarterectomy Program

Marc de Perrot, MD, MSc
Toronto Pulmonary Endarterectomy Program
Toronto General Hospital
Associate Professor of Surgery
University of Toronto
Conflict of Interest Disclosure

- Honorarium from Actelion and Bayer
Chronic thromboembolic pulmonary hypertension (CTEPH)

- CTEPH results from incomplete resolution of pulmonary emboli (PE)
- The incidence of CTEPH is about 10x higher than previously estimated and occurs in 1%-5% of the patients after acute PE
- The prevalence of CTEPH in the population is unknown
  - 10%-50% of the patients with CTEPH undergoing surgery do not have any documented history of acute PE
Epidemiology of Venous Thromboembolism (VTE)

- Annual incidence of VTE is ~1 case /1,000 inhabitants
- Incidence increases with age
  >60 years: 2 cases /1,000
  >70 years: 3 cases /1,000
  >80 years: 5 cases /1,000

Estimated incidence of acute PE in the US is about 600,000 cases per year

25-year data from Olmsted County, Minnesota, 1966 – 1990, 2218 Cases

Silverstein et al Arch of Intern Med. 1998
Resolution of pulmonary hypertension after first episode of acute PE

- 15 healthy patients with acute PE treated with heparin alone
- Normal RV can not generate
  - systolic PA pressure >50-70 mmHg
  - mean PA pressure >35-40 mmHg
- PA pressures improve over 10-21 days in most patients

Dalen et al *NEJM* 1969;280:1194-7
Resolution of pulmonary hypertension on echocardiogram after acute PE

- 78 patients followed by echocardiogram for 1 year after an episode of acute PE

- Systolic PA pressure improves during first 3-6 weeks after acute PE with minimal change thereafter
Incidence of residual pulmonary hypertension on echocardiogram after acute PE

- Of the 78 patients, 5% presented residual severe PH at 1 year after acute PE
  - 3 of the 4 patients with residual severe PH underwent pulmonary endarterectomy
- Risk factor for CTEPH: PAsP>50 mmHg at presentation
  - Patients developing CTEPH likely already had underlying chronic PE at the time of acute presentation

Acute massive PE treated with topical thrombolysis

Pulmonary angiogram before thrombolysis
Evidence of acute PE

Pulmonary angiogram after thrombolysis
Evidence of underlying chronic disease
Reassessment after 3-6 months

Reassessment shows persistence of chronic disease with PH on right heart cath

Pulmonary endarterectomy specimen
Incidence of CTEPH after acute symptomatic PE

- 223 consecutive patients treated for acute PE
- Prospective F/U of 1 to 10 years (mean 5 years)
- Cumulative incidence of CTEPH of 3.8% at 2 years

- Annual incidence of up to 25 cases per million inhabitants (incidence of idiopathic PAH is 2-3 cases per million)

Pengo et al NEJM 2004;350:2257
Autopsy series

- Large autopsy series of 263 cadavers from Oxford, UK
- Prevalence of fibrous bands in the pulmonary artery was 15%
- The prevalence increased with age

<table>
<thead>
<tr>
<th>Age (years)</th>
<th># of cases</th>
<th>% of total cases</th>
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<tbody>
<tr>
<td>40-59</td>
<td>1</td>
<td>7%</td>
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<tr>
<td>60-69</td>
<td>9</td>
<td>15%</td>
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<tr>
<td>70-79</td>
<td>13</td>
<td>20%</td>
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<tr>
<td>80+</td>
<td>15</td>
<td>25%</td>
</tr>
</tbody>
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- Clinical impact of these lesions is unknown

Tessa Morrell and Dunnill *J Clin Path* 1967;20:139
Pathological features of proximal pulmonary arteries (lobar, segmental, subsegmental) in CTEPH

- Mural thickening
- Webs and bands
- Stenosis
- Obstruction
- Localized thrombi
Pulmonary angiogram and angio CT

Webs and bands, Wall thickening and irregularities, Narrowed and truncated vessels, Usually no residual clot is visible in the lumen

de Perrot et al CMAJ 2006
Pathological features of distal pulmonary arteries (vessels <0.5-1 mm) in CTEPH

- Eccentric fibrosis (organized thrombi) are suggestive but not specific of CTEPH
- Medial hypertrophy
- Intimal thickening
- (Plexiform lesion)

CTEPH patients develop a distal vasculopathy that is similar to patients with PAH

Pietra et al *J Am Coll Cardiol* 2004;43;25-32
Moser et al *Chest* 1993;103:685-92
Mechanisms leading to pulmonary hypertension in CTEPH

Pulmonary hypertension is due to:

- Obstruction of PA bed by thrombo-embolic material
- Occurrence of \textit{in situ} thrombosis
- Development of microvascular disease
  - Overflow vasculopathy
  - Post-obstructive vasculopathy

\textbullet PH progresses despite adequate anticoagulation!!
Long-term outcome of patients with CTEPH treated with anticoagulation alone

Riedel et al  *Chest* 1982;81:151-8
Pulmonary endarterectomy (PEA)

- Therapy of choice for patients with CTEPH
- Curative treatment
- Excellent long term survival
- Treatment of coumadin only in the long-term
Pulmonary endarterectomy

Endarterectomy ≠ Embolectomy

1961: Right thoracotomy for possible tumor, but occluded pulmonary artery found and thrombectomized [JTCVS 1963;45:482]


1982: Importance of deep hypothermic circulatory arrest to stop the bronchial circulation is emphasized [Surgery 1982;92:1096]

1984: Large literature review reports 84 cases with an overall operative mortality of 22% [Chitwood et al Clin Chest Med 1984;5:507]
Milestones in pulmonary endarterectomy


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1984: Large literature review reports 84 cases with an overall operative mortality of 22% [Chitwood et al Clin Chest Med 1984;5:507]
Experience and results with 150 pulmonary thromboendarterectomy operations over a 29-month period

SW Jamieson, WR Auger, PF Fedullo, RN Channick, JM Kriett, RY Tarazi, KM Moser

• First large series with an operative mortality of 8.6%

• Using standardized surgical technique:
  – Bilateral approach with cardiopulmonary bypass
  – Intrapericardial dissection of the right and left pulmonary artery
  – Deep hypothermic circulatory arrest to stop the bronchial circulation
  – Endarterectomy of all involved vessels with specific dissectors

J Thorac Cardiovasc Surg 1993;106:116-126
Development of specific dissectors

Blunt dissecting tip with suction channel in the center
Operative mortality after pulmonary endarterectomy since 1994

AATS 2010
Abstract 28
Long-term survival after pulmonary endarterectomy
San Diego, CA

Archibald et al Am J Respir Crit Care Med 1999;160:523-8
Indications for pulmonary endarterectomy

- Diagnosis of CTEPH must be established
- Surgically accessible disease
- Symptoms related to CTEPH
- Absence of significant co-morbidities
Candidates for pulmonary endarterectomy

- Patients with stenosis and intra-luminal webs present in the segmental vessels can be candidates for PEA
Perspective

• Considering the potentially high prevalence of the disease and the current success of surgery, it is likely that the number of centers performing this procedure will keep increasing, particularly in institutions with large cardiothoracic programs and pulmonary hypertension clinics
Development of a successful new program

• New programs should be developed in collaboration with previously established programs
  – Learn the technique; avoid the learning curve

• Dedicated team should be put in place
  – PH physicians, intensivists, anesthesists, radiologists, and surgeons (2 surgeons if possible)

• Results depend as much on:
  ➢ Adequate patients’ selection
  ➢ Excellent quality of the surgery
  ➢ Optimal peri-operative management
Development of a new program at the Toronto General Hospital

- Program started in August 2005 in collaboration with Hospital Marie-Lannelongue in Paris
  - Philippe Dartevelle and Elie Fadel
- Dedicated team reviewed each potential candidate
- Specific OR nurses and perfusionists were involved
- Multiple in-service for all staff involved
- Education and information for referring physicians
  - Role of V/Q scan for diagnosis; Importance of early referral
Toronto General Hospital experience

- 59 patients evaluated up to March 2010
  - 41 patients underwent pulmonary endarterectomy
    - 38 patients underwent elective surgery
    - 3 patients underwent emergency surgery due to CV collapse
  - 18 patients did not have surgery because of:
    - Distal disease (n=8)
    - Lack of PH at rest (n=5)
    - Medical co-morbidities (n=3)
    - Patient’s refusal (n=1)
    - Death before surgery (n=1)
Profile of patients undergoing elective PEA

- Median age (years): 57 (range 25 – 82)
- Body mass index (kg/m$^2$): 28 (range 23 – 45)
- Mean PA pressure (mmHg): 46 (range 23 – 74)
- Cardiac Index (L/min/m$^2$): 1.9 (range 1.1 – 3.8)
- TPR (Dynes.s.cm$^{-5}$): 879 (range 380 – 2540)
Principles of pulmonary endarterectomy

– Bilateral procedure
  • To achieve complete relief of obstruction

– Intrapericardial surgery
  • To avoid pleural adhesions
  • To have bilateral access
  • To use cardiopulmonary bypass

– Circulatory arrest (18 -20 C)
  • To stop the bronchial back bleeding and obtain good visualization of the distal vessels

– Video-assistance
  • To provide light and visualization of distal vessels
Peri-operative management

• Specific therapy: Solumedrol (1g), Thiopental (10 mg/kg), tranexamic acid

• Oxymetric swan for optimal fluid balance

• Lung protective ventilation
  – Pressure control ventilation, PEEP ≥ 5 cmH₂O
  – Maintain PaCO₂ in normal range (35-45 mmHg)

• Extubation on POD1 or POD2

• Anticoagulation with iv heparin resumed after a few hours, therapeutic levels achieved within 12-24 hours
Endarterectomy specimen
Combined elective procedures

- Mitral valve replacement n=1
- Tricuspid valve replacement n=1 (septic emboli with endocarditis of tricuspid valve)
- PFO closure n=3
- Exchange transfusion for sickle cell disease (n=1)
- Tricuspid valve annuloplasty n=0
Duration of the procedure

- **Cardiopulmonary bypass:** 4h 13’ (range 2h 41’ - 6h 05’)
- **Aortic X-clamp:** 2h 15’ (range 1h 08’ - 3h 22’)
- **Circulatory arrest:**
  - **Total** 33’ (from 12’ to 67’)
    - **Right side** 19’ (from 9’ to 39’)
    - **Left side** 15’ (from 0’ to 28’)

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Postoperative course

- Median extubation time: 1 day (1-32)
  - 76% extubated on POD1 or POD2
- Median ICU stay: 3 days (2-35)
- Median length of hospital stay: 13 days (7-150)
- 30-day mortality after elective PEA: 2.6% (n=1)
- 30-day mortality, incl. emerg cases: 7.3% (n=3)

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Main causes for delayed extubation (n=9, 24%)

- Right ventricular dysfunction (n=3)
- Pulmonary edema (n=2)
- Pneumonia (n=2)
- Agitation/ somnolence (n=2)
Blood transfusion requirements

- **Red blood cells**
  - No transfusion: 60%
  - 1-2 units: 20%
  - >=3 units: 20%

- **Fresh frozen plasma**
  - No transfusion: 70%
  - 1-2 units: 10%
  - >=3 units: 20%

- **Platelets**
  - No transfusion: 90%
  - 1-2 units: 5%
  - >=3 units: 5%
Improvement in pulmonary vascular resistance

![Graph showing improvement in pulmonary vascular resistance.]

Total pulmonary resistance (Dynes.sec.cm-5)

- **Preop**
- **Postop**
- **Follow-up**

$\text{p}<0.0001$
Improvement in NYHA dyspnea score

NYHA dyspnea class

Preop  Follow-up
0   1   2   3   4

$p<0.0001$

NYHA class

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Improvement in 6’ walk distance

Pre-op                  3-6 months post-op

6’ walk distance (m)

$p<0.0001$

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Survival after elective pulmonary endarterectomy 2005 - 2010 (March)

Cumulative survival

Months after elective PEA

Overall survival
Survival without progression of pre-capillary PH

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Conclusions

• The prevalence of CTEPH is potentially much higher than previously estimated. The disease is still largely underdiagnosed.

• Elective pulmonary endarterectomy can be done safely in experienced centers with an operative mortality of 5% or less.

• The number of centers performing this procedure will keep increasing, particularly in institutions with large cardiothoracic programs and PH clinics.

• Collaboration with previously established programs and a dedicated team are important for the success of a new program.
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- OR nurses
- Thoracic nurses

Hospital Marie-Lannelongue

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- Elie Fadel

- D.O.T.S.