PULMONARY ENDARTERECTOMY IS THE GOLD-STANDARD THERAPY FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION
INTRODUCTION

• *Chronic thromboembolic pulmonary hypertension (CTEPH)* represents the *only* type of pulmonary hypertension surgically treatable, in the majority of cases, without transplant

• This life-saving conservative surgery is called *pulmonary endarterectomy (PEA)*
PULMONARY ENDOARTECTOMY: THE PAVIA EXPERIENCE

SURGICAL TREATMENT OF CTEPH

First HLTx for CTEPH

First PEA

First DLTx for CTEPH

First PEA in patient listed for DLTx

Reverse right ventricular remodeling after pulmonary endarterectomy

Andrea M. D’Ammini, MD, Giorgio Zucchi, MD, Stefano Ghio, MD, Giulia Magnini, MD, Matteo Puzzi, MD, Laura Scoleri, MD, Giulia Molini, MD, Catherine Kiersy, MD, and Mario Viganò, MD

J Thorac Cardiovasc Surg 2007;133:162-8

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PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

SURGICAL TREATMENT OF CTEPH

PAVIA EXPERIENCE

Tx for CTEPH

PATIENTS DIAGNOSED WITH CTEPH

PEAs PERFORMED

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PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

INTRODUCTION

PEA vs. LTx

• Elective surgery, non donor-dependent
• No “transplant window” to be considered
• Age is not a contraindication
• Lower post-operative complications
  – early (acute graft failure, acute rejection, infections)
  – late (BOS, neoplasms, infections)
• Outcome
  – post-operative long term survival
  – quality of life (back to normal)
  – steady functional improvement
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

ORGAN AVAILABILITY

• Lungs are delicate and susceptible of damage during IMV
  - only 28.5% of available lungs are transplanted

• Organ donation opposition is still too prevalent
  - 28.7% (Italy, 2011)
  - 27.6% (Italy, 30-06-2012)

• Donors are getting older

• Smoke is still common in Italy
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

THORACIC TRANSPLANTATION

1403 TRANSPLANTS (17/11/1985 – 14/05/2013)

- 1042 HEART TRANSPLANTS
- 322 LUNG TRANSPLANTS
- 39 HEART-LUNG TRANSPLANTS
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

THORACIC TRANSPLANTATION
1403 TRANSPLANTS (17/11/1985 – 14/05/2013)

- 361 VASCULAR LUNG DISEASES
- 80 LUNG AND HEART-LUNG TRANSPLANTS
- 281 PARENCHYMAL LUNG DISEASES
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

THORACIC TRANSPLANTATION

1403 TRANSPLANTS (17/11/1985 – 14/05/2013)

DLTx for PULMONARY ARTERIAL HYPERTENSION

U. G. PRE DLTx

U. G. 1° POST DLTx

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THORACIC TRANSPLANTATION
1403 TRANSPLANTS (17/11/1985 – 14/05/2013)

HLTx for EISENMENGER’S SYNDROME

M. P. PRE HLTx

M. P. 1° POST HLTx
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

LUNG TRANSPLANTATION
361 TRANSPLANTS (12/02/1992 – 14/05/2013)

HEART-LUNG TRANSPLANTS SURVIVAL

Kaplan-Meier survival estimate
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

LUNG TRANSPLANTATION

361 TRANSPLANTS (12/02/1992 – 14/05/2013)

ALL LUNG TRANSPLANTS SURVIVAL

Kaplan-Meier survival estimate

analysis time
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

EPIDEMIOLOGY

• Epidemiologic data: in Italy \( \approx 65,000 \) cases / year of acute symptomatic pulmonary embolism (PE)

• Prevalence of CTEPH in pts surviving an acute PE (\( \approx 80\% \)) is calculated between 0.5% – 3.8%
  → up to 2,000 new cases / year

• Considering asymptomatic pulmonary embolism and misdiagnosed pulmonary embolism, the true incidence of CTEPH may be even greater

• CTEPH is still *under-diagnosed* and nowadays only few physicians are aware of the *surgical procedure* called *PEA*

• For all these reasons about *9000 PEA* have been performed worldwide so far with ≈ *30 %* of all cases carried out by the San Diego Group
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

NATURAL HISTORY

- Pulmonary embolism (symptomatic / asymptomatic)
- “Honeymoon” period: months / years
- Hypertensive remodeling of the patent pulmonary vascular bed (*Eisenmenger-like*)
- Right ventricle hypertrophy with progressive right heart deterioration $\rightarrow$ right failure
- Left ventricle compression with left heart functional impairment
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

GENERAL CONDITIONS

- Low cardiac output with dyspnea, cough, cyanosis, hepatomegaly, ascites, lower limb edema, syncope, hemoptysis and interscapular olosystolic murmur

- Hypoxemia with exercise, sometimes at rest also

- Frequent positive anamnesis for deep venous thrombosis and/or coagulative and immunologic disorders
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

COAGULATIVE DISORDERS

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>% PTS</th>
<th>MEAN ± SD</th>
<th>RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPERHOMOCYSTEINEMIA (µmol/L)</td>
<td>72.6 %</td>
<td>21.7 ± 8.3</td>
<td>14.1 – 63.2</td>
</tr>
<tr>
<td>EXCESS FACTOR VIII ANTIGEN (%)</td>
<td>78.2 %</td>
<td>206.7 ± 33.9</td>
<td>161.1 – 392.9</td>
</tr>
<tr>
<td>EXCESS FACTOR VIII RISTOCETIN (%)</td>
<td>47.6 %</td>
<td>182.1 ± 46.6</td>
<td>150.0 – 334.0</td>
</tr>
<tr>
<td>EXCESS FACTOR VIII (%)</td>
<td>27.4 %</td>
<td>179.3 ± 25.8</td>
<td>153.4 – 220.0</td>
</tr>
<tr>
<td>PAI EXCESS (U/ml)</td>
<td>53.2 %</td>
<td>5.1 ± 1.2</td>
<td>3.6 – 7.9</td>
</tr>
<tr>
<td>FACTOR V LEIDEN</td>
<td>15.3 %</td>
<td>1.34 ± 0.55</td>
<td>0.50 – 1.99</td>
</tr>
</tbody>
</table>
### IMMUNOLOGIC DISORDERS

<table>
<thead>
<tr>
<th>DISORDER</th>
<th>% PTS</th>
<th>MEAN ± SD</th>
<th>RANGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-Nuclear Antibodies (ANA)</td>
<td>23.4%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Lupus Anticoagulant (LAC)</td>
<td>19.4%</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Anti-Cardiolipin Antibodies (ACA) IgG</td>
<td>20.2%</td>
<td>56.3 ± 40.3</td>
<td>10.3 – 121.0</td>
</tr>
<tr>
<td>Anti-Cardiolipin Antibodies (ACA) IgM</td>
<td>13.7%</td>
<td>30.8 ± 30.5</td>
<td>7.3 – 101.0</td>
</tr>
<tr>
<td>Anti-Phospholipid Antibodies (APA) IgG</td>
<td>14.5%</td>
<td>63.2 ± 36.5</td>
<td>8.4 – 121.0</td>
</tr>
<tr>
<td>Anti-Phospholipid Antibodies (APA) IgM</td>
<td>12.9%</td>
<td>28.0 ± 23.5</td>
<td>10.1 – 91.3</td>
</tr>
<tr>
<td>Positive Direct Coombs’ Test</td>
<td>8.9%</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>
MARKED THROMBOPHILIA

• A \textit{PERMANENT INFERIOR VENA CAVA FILTER} was placed before PEA in the majority of patients

• Lifelong oral anticoagulation was prescribed after PEA
INDICATIONS FOR SURGERY

• The indications for the *surgical treatment* of these patients are based on

  CLINIC
  HEMODYNAMIC

• The indications for the *type of surgery* are based on

  ANATOMY
CLINIC

- Patients must be in *NYHA functional class III or IV*
- Full anticoagulation for at least 3 months
- Some Authors (we too) have performed PEA even in *NYHA class II* patients, given the natural history of the disease
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

HEMODYNAMIC

- Pulmonary hypertension (mPAP ≥ 25 mmHg)
- Causing low cardiac output
- Resulting in calculated pulmonary vascular resistances (PVR) > \(300 \text{ dyne*sec*cm}^{-5}\)
ANATOMY

• The surgical treatment depends on the localization of the lesions in the pulmonary arterial branches

• Lesions can be classified as **PROXIMAL** **DISTAL**
PULMONARY ENDOARTERECTOMY: THE PAVIA EXPERIENCE

PROXIMAL LESIONS
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

M.B. – 62 yrs M – Jul 2001 – PEA #64

Perfusion and ventilation scan

Pulmonary angiogram

<table>
<thead>
<tr>
<th>Hemodynamic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPAP</td>
<td>67</td>
</tr>
<tr>
<td>CI</td>
<td>1.6</td>
</tr>
<tr>
<td>PVR</td>
<td>1766</td>
</tr>
</tbody>
</table>
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

DISTAL LESIONS
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

S.S. – 31 yrs M – Sep 2002

Perfusion and ventilation scan

Pulmonary angiogram

<table>
<thead>
<tr>
<th>Hemodynamic</th>
</tr>
</thead>
<tbody>
<tr>
<td>mPAP</td>
</tr>
<tr>
<td>CI</td>
</tr>
<tr>
<td>PVR</td>
</tr>
</tbody>
</table>
Which lesions have to be considered as *inoperable*?

- *Different operability assessments* from different Centers

- Growing single surgeon’s experience due to *learning curve*
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

BACKGROUND

• **PEA** is the treatment of choice for patients with **CTEPH**
• About only **10-15 Centers** worldwide are performing PEA on a **routine basis**
• In expert hands, **mortality** ranges between 5% and 10% and technical failure is below 10%
• **Early hemodynamic results** are known to be excellent in case of successful operation
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

REFERENCE

CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

PETER F. FEDULLO, M.D., WILLIAM R. AUGER, M.D., KIM M. KERR, M.D., AND LEWIS J. RUBIN, M.D.


<table>
<thead>
<tr>
<th>YEAR</th>
<th>STUDY</th>
<th>LOCATION</th>
<th>NO. OF PATIENTS</th>
<th>PULMONARY VASCULAR RESISTANCE</th>
<th>PREOPERATIVE</th>
<th>POSTOPERATIVE</th>
<th>MORTALITY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>dyn-sec·cm⁻¹</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>Nakajima et al.⁹⁵</td>
<td>Japan</td>
<td>30</td>
<td>927±45</td>
<td>299±16</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>Mayer et al.⁹⁶</td>
<td>Germany</td>
<td>32</td>
<td>967±238</td>
<td>301±151</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>Gilbert et al.⁹⁷</td>
<td>Baltimore</td>
<td>17</td>
<td>760±200†</td>
<td>170±80†</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>1998</td>
<td>Miller et al.⁹⁸</td>
<td>Philadelphia</td>
<td>25</td>
<td>NA</td>
<td>NA</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>Dartevelle et al.⁹⁹</td>
<td>France</td>
<td>68</td>
<td>1174±416</td>
<td>519±250</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>1999</td>
<td>Ando et al.⁹⁰</td>
<td>Japan</td>
<td>24</td>
<td>1066±250</td>
<td>268±141†</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>Jamieson and Kapelanski³</td>
<td>San Diego, Calif.</td>
<td>457</td>
<td>877±452</td>
<td>267±192‡</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>Mares et al.⁹¹</td>
<td>Austria</td>
<td>33</td>
<td>1478±107‡</td>
<td>975±93‡</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>Mares et al.⁹²</td>
<td>Austria</td>
<td>14</td>
<td>1334±135‡</td>
<td>789±99‡</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>Rubens et al.⁹³</td>
<td>Canada</td>
<td>21</td>
<td>765±372</td>
<td>208±92</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>2000</td>
<td>D’Ammini et al.⁹⁴</td>
<td>Italy</td>
<td>33</td>
<td>1056±344</td>
<td>196±39§</td>
<td>9</td>
<td></td>
</tr>
</tbody>
</table>

*Plus–minus values are means ±SD. NA denotes not available.
†The value, derived from a graph, is approximate.
‡The value is the pulmonary-vascular-resistance index (pulmonary vascular resistance divided by body-surface area).
§The value is for 23 patients at three months of follow-up.
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

OUR PROGRAM

• National referral program
• Begin: April 1994
• To date: 471 PEAs performed
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

PATIENTS’ REFERRAL

OF 471 PEAs

Pts coming from outside Italy
- Greece  1
- Kosovo  1
- U.S.A.   1
- Uganda  1

- ≤ 15 pts
- 16 – 30 pts
- ≥ 31 pts
PULMONARY ENDARTECTOMY: THE PAVIA EXPERIENCE

AMOUNT OF PATIENTS
OF 471 PEAs

1994-2008 (15 yrs): 209 PEAs

2009-2012 (4 yrs): 236 PEAs
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

AMOUNT OF PATIENTS

NEW EVALUATIONS

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PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

AMOUNT OF PATIENTS

DIAGNOSTIC ACCURACY

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PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

AMOUNT OF PATIENTS
OPERABILITY RATE

2004: 25 patients, 74%
2010: 73 patients, 89%

+15% increase
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

PAVIA CTEPH PROGRAM
January, 1st – December, 31st 2012 → 334 pts

New Evaluations (130 pts) Postop FUP (210 pts) Clinical Trials (14 pts) DLTx (1 pt)

CONFIRMED (69 pts - 63%)
• PROXIMAL LESIONS (65 pts)
  - 60 PEAs (6 pts evaluated in 2011)
  - 3 waiting for PEA
  - 4 refused PEA
  - 2 with severe co-morbidities
  - 1 with “too old” lesions (PA retraction + ↑↑ collaterals)
  - 1 died before arrival

OPERABILITY RATE 94 %
• DISTAL LESIONS (4 pts)
  - 4 too old for DLTx

OTHER DIAGNOSIS (41 pts - 37%)
• RECENT EMBOLIZATION (22 pts)
  - 22 medical therapy
• MINIMAL CTE LESIONS WITHOUT PH (1 pt)
  - 1 medical therapy
• PULMONARY ARTERY MALIGNANCY (3 pts)
  - 3 PEAs
• PULMONARY ARTERY ANEURYSM (2 pts)
  - 1 medical therapy
  - 1 Pulmonary artery reduction
• PULMONARY ARTERY & VALVE STENOSIS (2 pts)
  - 1 Pulmonary valve replacement
• MISCELLANEOUS (11 pts)
  - 3 Eisenmenger
  - 6 PPH
  - 1 Mediastinal fibrosis
  - 1 Rosai Dorfman syndrome → 1 PEA
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

PEA EXPERT CENTER

Guidelines for the diagnosis and treatment of pulmonary hypertension

The Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT)

A centre can be considered to have sufficient expertise in this field if it performs at least 20 PEA operations per year with a mortality rate <10%.
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

PEA EXPERT CENTER

Surgical management and outcome of patients with chronic thromboembolic pulmonary hypertension: Results from an international prospective registry

Eckhard Mayer, MD,a David Jenkins, FRCS,b Jaroslav Lindner, MD,c Andrea D’Armini, MD,d Jaap Klokke, MD,e Bart Meyns, MD,f Lars Bo Ilkjaer, MD,g Walter Klepetko, MD,h Marion Delcroix, MD,f Irene Lang, MD,h Joanna Pepke-Zaba, MD,b Gerald Simonneau, MD,i and Philippe Dartevelle, MDj

(J Thorac Cardiovasc Surg 2011;141:702-10)

TABLE 4. Center expertise and surgical management

<table>
<thead>
<tr>
<th></th>
<th>Average no. of PEA s per year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-10</td>
</tr>
<tr>
<td>No. of centers performing PEA, n (%)</td>
<td>6 (35.3%)</td>
</tr>
<tr>
<td>No. of patients, n (%)</td>
<td>54 (14.0%)</td>
</tr>
<tr>
<td>Change in PVR from diagnosis to end of intensive care, dyn.s.cm⁻⁵, median (range), n</td>
<td>-476 NS</td>
</tr>
<tr>
<td></td>
<td>(-1760 to 80)</td>
</tr>
<tr>
<td>n</td>
<td>43</td>
</tr>
<tr>
<td>Death, n (%),§</td>
<td>4 (7.4%) NS</td>
</tr>
<tr>
<td>In-hospital</td>
<td>6 (11.1%) NS</td>
</tr>
</tbody>
</table>

NS, Not significant; PEA, pulmonary endarterectomy; PVR, pulmonary vascular resistance. *Two patients underwent operations in 2 nonparticipating centers performing > 50 PEA s per year and < 10 PEA s per year, respectively. NS compared with † (Wilcoxon 2-sample test) or ‡ (Fisher’s exact test), †P < .05 compared with ‡ (Wilcoxon 2-sample test).
PULMONARY ENDOARTECTOMY: THE PAVIA EXPERIENCE

MAIN WORLD PEA CENTERS

Cambridge, UK
≈150 PEA s / year
NATIONAL REFERRAL PROGRAM BY LAW

Bad Nauheim, Germany
≈80 PEA s / year
MORE THAN ONE PROGRAM

San Diego, California, USA
≈160 PEA s / year
NATIONAL REFERRAL PROGRAM FOR EXCELLENCE

Pavia, Italy
≈60 PEA s / year
MORE THAN ONE PROGRAM

Paris, France
≈120 PEA s / year
NATIONAL REFERRAL PROGRAM FOR EXCELLENCE
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

AMOUNT OF PATIENTS

OF 471 PEAs

- 5 PEAs / yr
- 15 PEAs / yr
- 20 PEAs / yr
- 60 PEAs / yr

1994-1998
1999-2003
2004-2008
2009-2013

PATIENTS

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## PEA Population

Of 471 PEAs

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58 ± 16 (11 – 84) years</td>
</tr>
<tr>
<td>Gender</td>
<td>221 M – 250 F</td>
</tr>
<tr>
<td>WHO class</td>
<td>54 II – 221 III – 196 IV</td>
</tr>
<tr>
<td>Length III / IV</td>
<td>19 ± 23 months</td>
</tr>
<tr>
<td>Urgent / Emergent</td>
<td>86 / 471</td>
</tr>
<tr>
<td>Oxygen therapy</td>
<td>217 / 471</td>
</tr>
</tbody>
</table>
### Arterial Blood Gases

**Of 471 PEs**

<table>
<thead>
<tr>
<th></th>
<th>Mean ± SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pa O(_2)</td>
<td>66 ± 10</td>
<td>36 – 97 mmHg</td>
</tr>
<tr>
<td>Pa CO(_2)</td>
<td>31 ± 7</td>
<td>21 – 50 mmHg</td>
</tr>
<tr>
<td>O(_2)-sat</td>
<td>93 ± 3</td>
<td>66 – 98 %</td>
</tr>
</tbody>
</table>
### MODIFIED BRUCE TEST
OF 471 PEAs

<table>
<thead>
<tr>
<th>Steps</th>
<th>Walking distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (Pa O$_2$ &lt; 60)</td>
<td>42.6% 183 ± 160 (8 – 852) meters</td>
</tr>
<tr>
<td>Step 0 - ½</td>
<td>47.5%</td>
</tr>
<tr>
<td>Step 1 - 2</td>
<td>8.2%</td>
</tr>
<tr>
<td>Step 3 - 4</td>
<td>1.6%</td>
</tr>
</tbody>
</table>
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

PULMONARY ENDARTERECTOMY

- Median sternotomy
- Cardio Pulmonary Bypass
- Moderate hypothermia (24 °C)
- Circulatory arrest (7 min)
- Reperfusion period (5 min)
- Bilateral

PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

PULMONARY ENDARTERECTOMY

- Intra-wall dissection
- Peripheral extension
- Explore all branches

PULMONARY ENDARTELECTOMY: THE PAVIA EXPERIENCE

SURGICAL INSTRUMENT
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

TYPICAL SURGICAL SPECIMENS

E.L. – 38 yrs M – Dec 1999 – PEA #42
mPAP  43 →  20  (-53%)
CO    3.3 →  6.9  (+109%)
PVR   994 →  220  (-78%)

P.A. – 66 yrs M – Jun 2001 – PEA #60
mPAP  50 →  25  (-50%)
CO    2.6 →  4.4  (+69%)
PVR   1385 →  364  (-74%)

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LEARNING CURVE
JAMIESON TYPE III
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

JAMIESON TYPE I vs. TYPE II vs. TYPE III

L.M.E.L. - 65 yrs M - Oct 2004 - PEA #119
mPAP  39 → 19  (-51%)
CO    4.4 → 5.4  (+23%)
PVR   665 → 222 (-66%)

G.A.C. - 52 yrs F - Jul 2003 - PEA #96
mPAP  48 → 27  (-44%)
CO    2.1 → 4.2  (+100%)
PVR   1638 → 381 (-77%)

B.A. - 43 yrs F - May 2009 - PEA #233
mPAP  49 → 19  (-61%)
CO    3.3 → 5.0  (+52%)
PVR   1067 → 224 (-79%)
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

JAMIESON TYPE III

A peculiar case: a “seasoned veteran” in CTEPH

- Name: XX-XX-1949
- Date of birth: XX-XX-1949
- Height: 150 cm
- Weight: 48 Kg
- Italian
- Varese
- House Painter

Systemic arterial hypertension
Gastroesophageal reflux disease
A peculiar case: a “seasoned veteran” in CTEPH

JUNE 2004
Onset of mild dyspnea (WHO II)

JUNE 2005
Worsening of dyspnea (WHO III)

JULY 2005
Admission to the Cardiology ward of a local hospital

- ECG: right ventricle overload
- Echocardiogram: dilation and hypokinesia of the right chambers
  - severe tricuspid regurgitation
  - severe pulmonary hypertension (sPAP 85 mmHg)
- Lung V/Q scan: bilateral mismatches with multiple perfusion defects
- HRCT scan: multiple bilateral segmental perfusion defects
- Venous echocolor Doppler of lower limbs: negative

CTEPH
A peculiar case: a “seasoned veteran” in CTEPH

SEPTEMBER 2005
Admission to our Division for operability assessment

• COMPLETE DIAGNOSTIC WORKUP: CTEPH CONFIRMED
  • Right Heart Catheterization:
    - RA 1 mmHg
    - RV 82 / 0 mmHg
    - PA 82 / 39 / 13 mmHg
    - PCWP 3 mmHg
    - CO 3.3 L/min
    - CI 2.2 L/min
    - RVEF 25 %
    - PVRP 873 dyn*s*cm⁻⁵

• OPERABILITY: INOPERABLE FOR EXCLUSIVELY DISTAL DISEASE

DOUBLE LUNG TRANSPLANT WAITING LIST
A peculiar case: a “seasoned veteran” in CTEPH

LUNG V/Q SCAN

VENTILATION

PERFUSION
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

JAMIESON TYPE III

A peculiar case: a “seasoned veteran” in CTEPH

PULMONARY ANGIOGRAM
A peculiar case: a “seasoned veteran” in CTEPH

HRCT SCAN
JAMIESON TYPE III

A peculiar case: a “seasoned veteran” in CTEPH

DECEMBER 2005

Enrollment in the BENEFIT study
(bosentan vs. placebo in inoperable forms of CTEPH)

INOPERABILITY CONFIRMED BY THE INTERNATIONAL COMMITTEE

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
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<tbody>
<tr>
<td>RA</td>
<td>4</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>RV</td>
<td>82/2</td>
<td>82/0</td>
<td>85/3</td>
</tr>
<tr>
<td>PA</td>
<td>82/46/24</td>
<td>82/45/22</td>
<td>85/49/28</td>
</tr>
<tr>
<td>PCWP</td>
<td>5</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>CO</td>
<td>3.1</td>
<td>2.4</td>
<td>3.0</td>
</tr>
<tr>
<td>CI</td>
<td>2.1</td>
<td>1.6</td>
<td>2.0</td>
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<tr>
<td>RVEF</td>
<td>34</td>
<td>11</td>
<td>12</td>
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<td>PVR</td>
<td>1057</td>
<td>1343</td>
<td>1164</td>
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<tr>
<td>Serum-BNP</td>
<td>360</td>
<td>324</td>
<td>151</td>
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<tr>
<td>WHO</td>
<td>III</td>
<td>III</td>
<td>II</td>
</tr>
</tbody>
</table>
A peculiar case: a “seasoned veteran” in CTEPH

BENEFIT and BENEFIT-OPEN LABEL EXTENSION

Clinical course

6mWT

Follow-up

UNIVERSITY OF PAVIA SCHOOL OF MEDICINE - SAN MATTEO HOSPITAL - PAVIA - ITALY
A peculiar case: a “seasoned veteran” in CTEPH

OCTOBER 2009
Worsening of dyspnea (back to WHO III)

NOVEMBER 2009
Admission to our Division for therapy update

NEW OPERABILITY ASSESSMENT → NOW TECHNICALLY OPERABLE
(JUST ALIKE THE PREVIOUS FINDINGS)

BILATERAL PULMONARY ENDARTERECTOMY
Right: upper, middle and lower lobe
Left: upper lobe, lingula and lower lobe
Moderate hypothermia (23° C)
Intermittent circulatory arrests
right side: 91 min
left side: 47 min
total time: 138 min
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

JAMIESON TYPE III

A peculiar case: a “seasoned veteran” in CTEPH

BILATERAL PEA – SURGICAL SPECIMEN

UNIVERSITY OF PAVIA SCHOOL OF MEDICINE - SAN MATTEO HOSPITAL - PAVIA - ITALY
**A peculiar case: a “seasoned veteran” in CTEPH**

**BILATERAL PEA**

Hemodynamic results

<table>
<thead>
<tr>
<th></th>
<th>Preoperative 27-NOV-2009</th>
<th>At discharge 15-DEC-2009</th>
<th>3 months FUP 26-FEB-2010</th>
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<tbody>
<tr>
<td>RA</td>
<td>7</td>
<td>3</td>
<td>3 (mmHg)</td>
</tr>
<tr>
<td>RV</td>
<td>120/0</td>
<td>53/0</td>
<td>35/0 (mmHg)</td>
</tr>
<tr>
<td>PA</td>
<td>120/65/36</td>
<td>53/22/8</td>
<td>35/19/12 (mmHg)</td>
</tr>
<tr>
<td>PCWP</td>
<td>5</td>
<td>5</td>
<td>5 (mmHg)</td>
</tr>
<tr>
<td>CO</td>
<td>3.5</td>
<td>3.9</td>
<td>4.2 (L/min)</td>
</tr>
<tr>
<td>CI</td>
<td>2.4</td>
<td>2.7</td>
<td>2.9 (L/min/m²)</td>
</tr>
<tr>
<td>RVEF</td>
<td>6</td>
<td>18</td>
<td>21 (%)</td>
</tr>
<tr>
<td>PVR</td>
<td>1371</td>
<td>308</td>
<td>267 −81 % (dyn<em>s</em>cm⁻¹)</td>
</tr>
<tr>
<td>Serum-BNP</td>
<td>996</td>
<td>742</td>
<td>106 (pg/ml)</td>
</tr>
<tr>
<td>WHO</td>
<td>III</td>
<td>I</td>
<td>I</td>
</tr>
</tbody>
</table>
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

JAMIESON TYPE III
The “seasoned veteran”

DIAGNOSIS

TRANSPLANT WAITING LIST

SPECIFIC MEDICAL THERAPY

PULMONARY ENDARTERECTOMY (Gold Standard)

SPECIFIC PAH-DRUG DISCONTINUATION

UNIVERSITY OF PAVIA SCHOOL OF MEDICINE - SAN MATTEO HOSPITAL - PAVIA - ITALY
CUMULATIVE PROPORTION SURVIVING
OF 471 PEAs

Hospital mortality
- Global: 42/471 (8.9%)
- WHO II: 0/54 (0.0%)
- WHO III: 14/221 (6.3%)
- WHO IV: 28/196 (14.3%)

Apr 94 – Dec 08: 22/209 (10.5%)
Jan 09 – May 13: 20/262 (7.6%)
FOLLOW-UP

In literature few data are reported on mid- and long-term cardiopulmonary function, particularly on exertion, and on clinical outcomes after PEA.

**Reverse right ventricular remodeling after pulmonary endarterectomy**

Andrea M. D’Armini, MD, Giorgio Zanotti, MD, Stefano Ghio, MD, Giulia Magrini, MD, Matteo Pozzi, MD, Laura Scelsi, MD, Giulia Meloni, MD, Catherine Klersy, MD, and Mario Viganò, MD

*J Thorac Cardiovasc Surg 2007;133:162-8*

**Long-term Outcome after Pulmonary Endarterectomy**

Angelo G. Corsico, Andrea M. D’Armini, Isa Cerveri, Catherine Klersy, Elena Ansaldi, Rosanna Niniano, Elena Gatto, Cristian Monterosso, Marco Morsolini, Salvatore Nicolardi, Corrado Tramontin, Ernesto Pozzi, and Mario Viganò

FOLLOW-UP TIMING

- All pts underwent follow-up evaluation at:
  - discharge (at this interval NYHA class, lung function, and exercise tolerance are excluded because pts are to close to the surgical procedure)
  - 3rd month
  - yearly for 5 years
  - 7th, 10th and 15th year (10 controls)
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

WHO FUNCTIONAL CLASS

<table>
<thead>
<tr>
<th>Preop</th>
<th>3m</th>
<th>1y</th>
<th>2y</th>
<th>3y</th>
<th>4y</th>
<th>5y</th>
<th>7y</th>
<th>10y</th>
<th>15y</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

I-II I-IV

p < 0.01
mean PULMONARY ARTERY PRESSURE

The graph shows the mean pulmonary artery pressure (mPAP) over time postoperatively. The pressure decreases significantly postoperatively and remains stable for the follow-up period. The statistical significance is indicated with $p < 0.01$. 

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PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

PULMONARY VASCULAR RESISTANCES

![Graph showing changes in pulmonary vascular resistances over time.](image)

- Preop to Postop
- 3m, 1y, 2y, 3y, 4y, 5y, 7y, 10y, 15y

**PVR**

$p < 0.01$
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

ECHOCARDIOGRAPHY

Before PEA
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

ECHOCARDIOGRAPHY

First echo after PEA – POD #9
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

ECHOCARDIOGRAPHY

3-months FUP after PEA
PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

BRAIN-TYPE NATRIURETIC PEPTIDE

![Graph showing the time course of BNP (Brain-Type Natriuretic Peptide) levels post-Pulmonary Endarterectomy. The graph indicates a significant decrease in BNP levels from Preop to Postop, with a gradual increase in the subsequent years.](graph.png)

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PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

ARTERIAL OXYGEN PARTIAL PRESSURE

\[ p < 0.01 \]

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PULMONARY ENDARTERECTOMY: THE PAVIA EXPERIENCE

MODIFIED BRUCE TEST

MODIFIED BRUCE EXERCISE TOLERANCE TEST

$p < 0.01$
RESULTS

• The majority of pts experienced dramatic improvement in pulmonary hemodynamics after PEA

• After PEA the decrease in pulmonary artery pressure is immediate (in O.R.) and associated with complete recovery of RV morphology (at discharge)

• The functional results also show a progressive good recovery over a longer time (about years)
RESULTS

• About 5% of our pts failed to showed a decrease > 20% in PVR compared to pre-operative value

• About 8-10% of our pts showed a new increase in pulmonary pressure after PEA over time

• The reason could be a secondary small vessel arteriopathy (*Eisenmenger-type syndrome*) in the non-obstructed segments of the lungs already present at the time of PEA
CONCLUSION

- Poor survival rate of untreated pts (10% 5-yrs survival if mPAP ≥ 50 mmHg), low mortality rate after PEA and good mid- and long- term results confirm PEA as the procedure of choice for operable CTEPH pts

- The improvement of functional capacity strictly depends on the hemodynamic changes after PEA

- When CTEPH is diagnosed, given the natural history of the disease, patients should be referred for surgery even when in NYHA functional class II