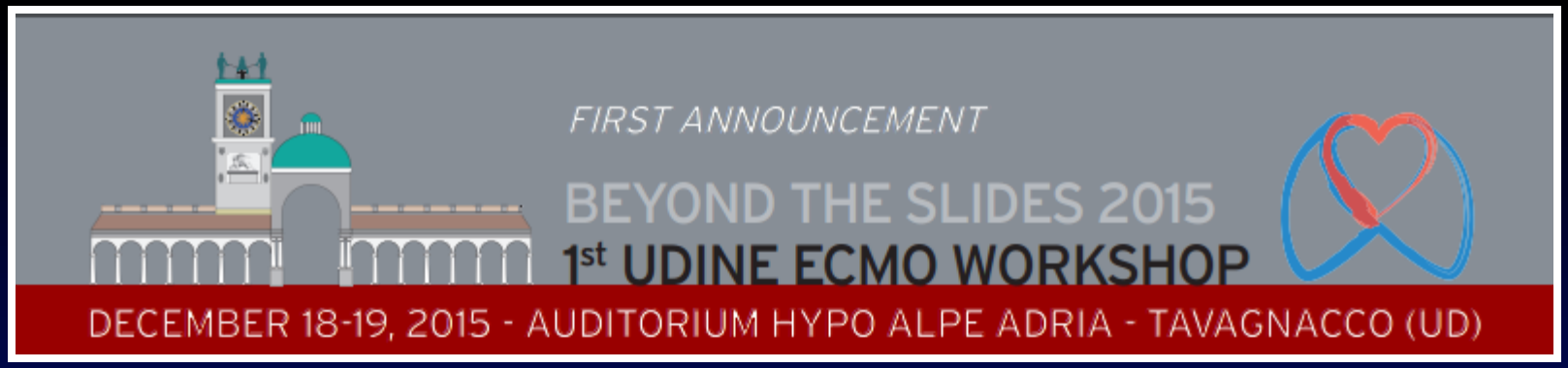

ECMO AND CTEPH

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INTRODUCTION

NICE 2013 – PH CLINICAL CLASSIFICATION

1. Pulmonary arterial hypertension

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2 mutation
  - 1.2.2 Other mutations
- 1.3 Drugs and toxins induced
- 1.4 Associated with:
  - 1.4.1 Connective tissue disease
  - 1.4.2 Human immunodeficiency virus (HIV) infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease (Table 6)
  - 1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

- 1'.1 Idiopathic
- 1'.2 Heritable
  - 1'.2.1 EIF2AK4 mutation
  - 1'.2.2 Other mutations
- 1'.3 Drugs, toxins and radiation induced
- 1'.4 Associated with:
  - 1'.4.1 Connective tissue disease
  - 1'.4.2 HIV infection

1''. Persistent pulmonary hypertension of the newborn

2. Pulmonary hypertension due to left heart disease

- 2.1 Left ventricular systolic dysfunction
- 2.2 Left ventricular diastolic dysfunction
- 2.3 Valvular disease
- 2.4 Congenital / acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies
- 2.5 Congenital /acquired pulmonary veins stenosis

3. Pulmonary hypertension due to lung diseases and/or hypoxia

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental lung diseases (Web Table III)

4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions

- 4.1 Chronic thromboembolic pulmonary hypertension
- 4.2 Other pulmonary artery obstructions
  - 4.2.1 Angiosarcoma
  - 4.2.2 Other intravascular tumors
  - 4.2.3 Arteritis
  - 4.2.4 Congenital pulmonary arteries stenoses
  - 4.2.5 Parasites (hydatidosis)

4%

5. Pulmonary hypertension with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
- 5.2 Systemic disorders, sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: pulmonary tumoral thrombotic microangiopathy, fibrosing mediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

INTRODUCTION

- Despite the powerful fibrinolytic capacity of the pulmonary circulation, *CTEPH may occur in 0.5% to 3.8% (150- 600 new cases/year in Italy)* of the patients who survived one or more episodes of diagnosed acute pulmonary embolism
- Moreover, even in adequately treated patients, *relapses of DVT and PE will occur*

- Jamieson SW, Kapelanski DP. Pulmonary endarterectomy. *Curr Probl Surg* 2000; 37:165-252
- Pengo V, Lensing AW, Prins MH, Marchiori A, Davidson BL, Tiozzo F et al. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. *N Engl J Med* 2004; 350:2257-64

- *Misdiagnosed disease* → true incidence in Italy of CTEPH may be up to *200-800 new cases / year*
- *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)*

NATURAL HISTORY

- Pulmonary embolism (symptomatic / asymptomatic)
- Possible "*honeymoon*" period: months / years
- Hypertensive remodeling of the patent pulmonary vascular bed *(Eisenmenger-like)*
- Onset and progressive worsening of pulmonary arterial hypertension
- Right ventricle hypertrophy with progressive right heart deterioration → right heart failure
- Left ventricle compression with left heart functional impairment → biventricular heart failure
- Multiorgan failure (end stage disease)

GENERAL CONDITIONS

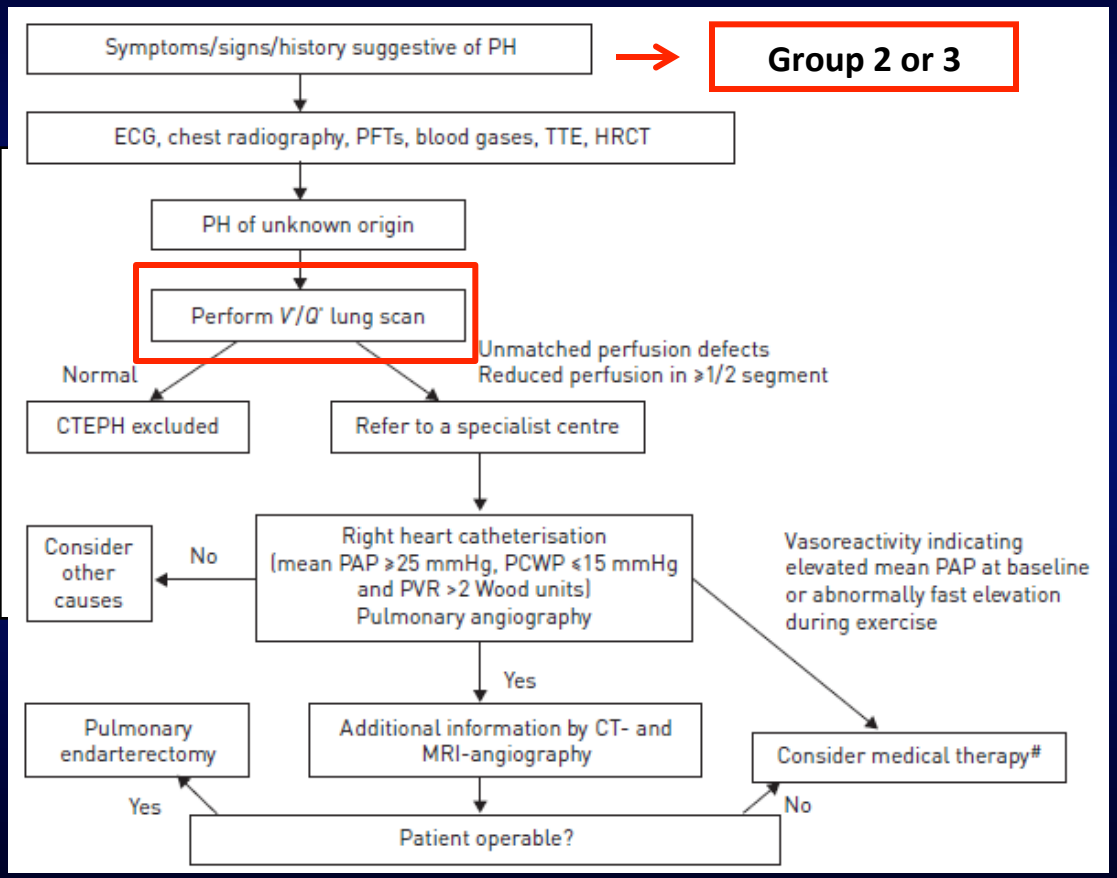
- Low cardiac output with dyspnea, cough, cyanosis, hepatomegaly, ascites, lower limb edema, syncope, *hemoptysis* and *interscapular olosystolic murmur*
- Chronic respiratory failure (oxygen-dependent)
- Frequent positive anamnesis for deep venous thrombosis and / or coagulative and immunologic disorders

MARKED THROMBOPHILIA

- A *PERMANENT INFERIOR VENA CAVA FILTER* was placed before PEA in the majority (595/679) of patients

- Lifelong oral anticoagulation was prescribed after PEA

REFERENCE


Symptoms/signs/history suggestive of PH
Group 2 or 3
ECG, chest radiography, PFTs, blood gases, TTE, HRCT
PH of unknown origin
Perform V/Q' lung scan
Normal
Unmatched perfusion defects
Reduced perfusion in ≥1/2 segment
CTEPH excluded
Refer to a specialist centre
Consider other causes
No
Right heart catheterisation (mean PAP ≥25 mmHg, PCWP ≤15 mmHg and PVR >2 Wood units) Pulmonary angiography
Vasoreactivity indicating elevated mean PAP at baseline or abnormally fast elevation during exercise
Yes
Pulmonary endarterectomy
Additional information by CT- and MRI-angiography
Consider medical therapy#
Yes
No
Patient operable?

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 or WHO functional class III or IV*
- Full anticoagulation for at least 3 months (?)
- Since 2003 we have performed PEA in *NYHA or WHO functional class II* patients, given the natural history of the disease

HEMODYNAMIC

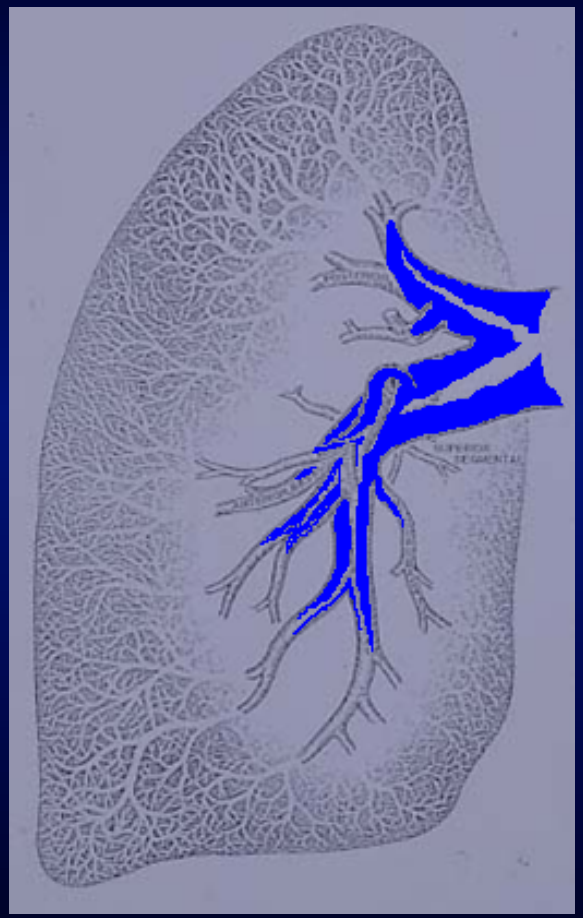
- Pulmonary hypertension (mPAP ≥ 25 mmHg)
- Causing low cardiac output

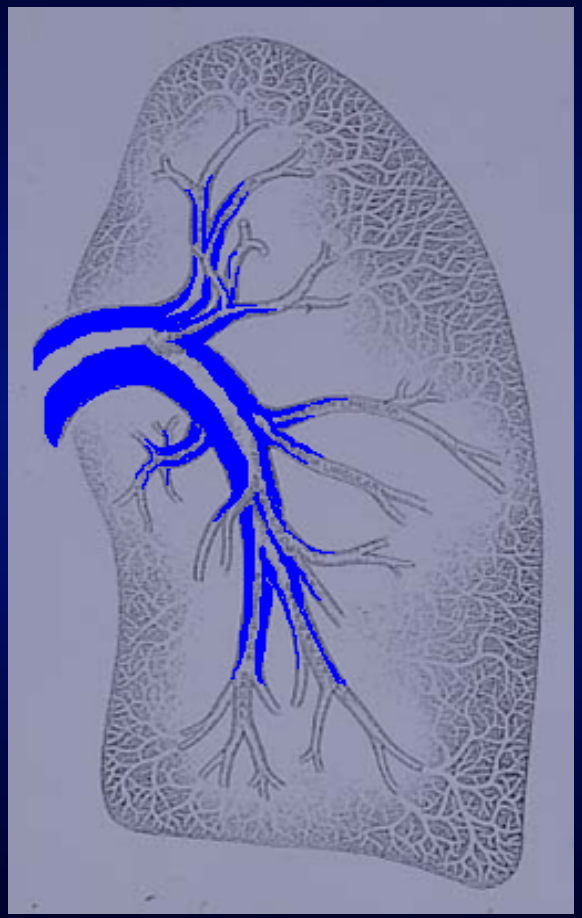
- Resulting in calculated pulmonary vascular resistances (PVR) > *300 dyne*sec*cm^{-5}*

ANATOMY

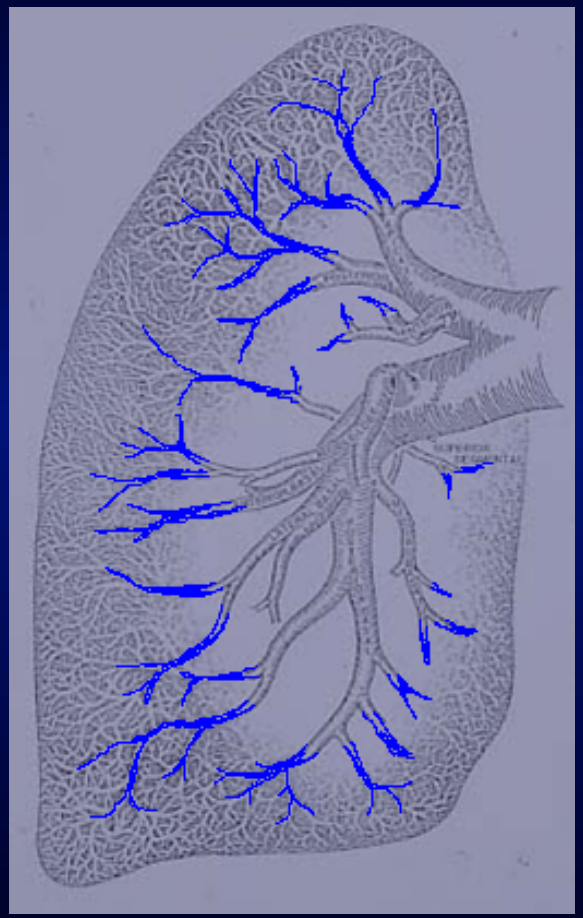
- The surgical treatment depends on the localization of the lesions in the pulmonary arterial branches
- Lesions can be classified as **PROXIMAL**
  DISTAL

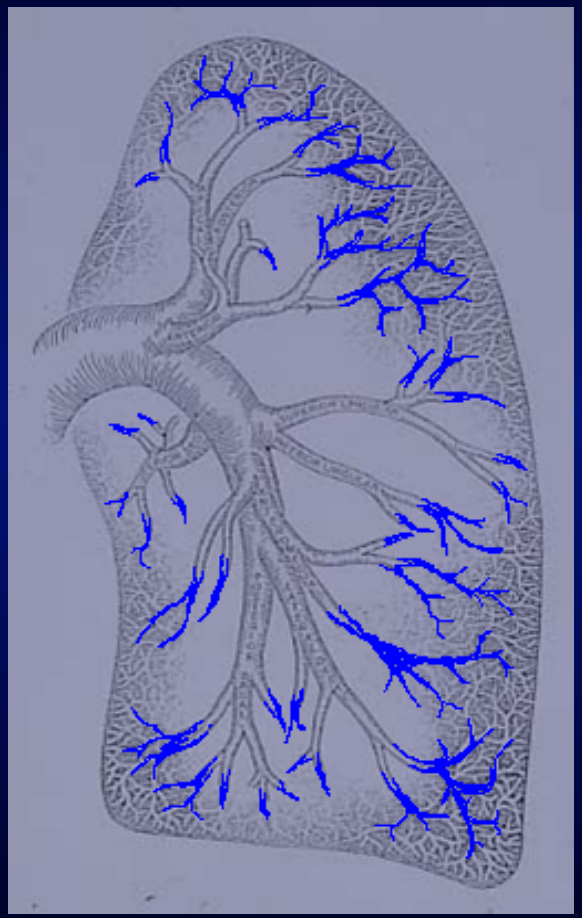
PROXIMAL LESIONS





DISTAL LESIONS



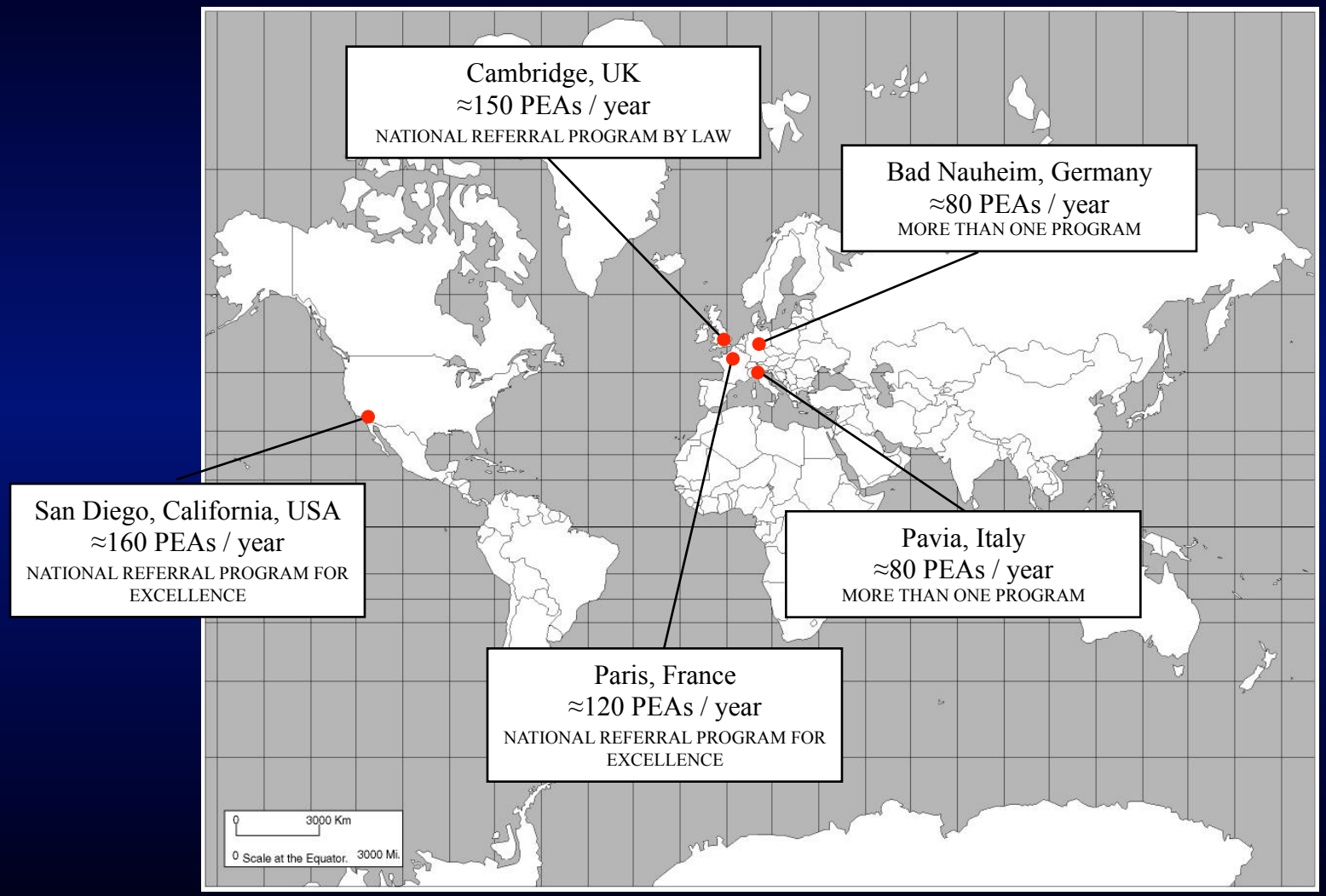


CONTRAINDICATION TO PEA

Concomitant severe parenchymal lung disease is the real absolute contraindication to PEA

Such patients are not suitable for PEA and must be *listed for DLTx* (if indicated)

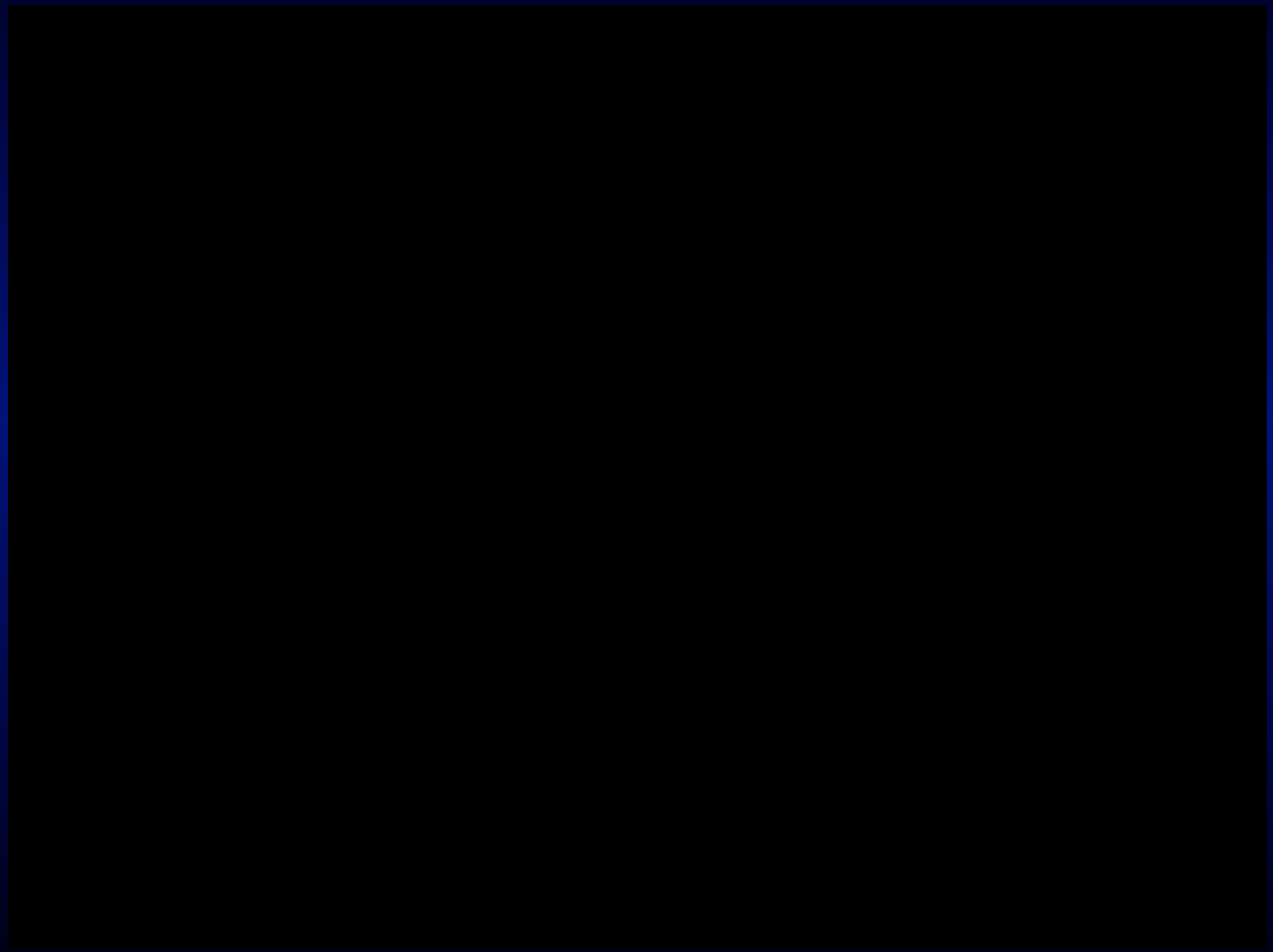
MAIN WORLD PEA CENTERS



OUR PROGRAM

- National referral program
- Begin: April 1994
- To date: 679 PEAs performed

PULMONARY ENDARTERECTOMY



CPB MANAGEMENT

- Original San Diego technique

  - a single (20 min) deep hypothermic (18° C) total circulatory arrest for each side

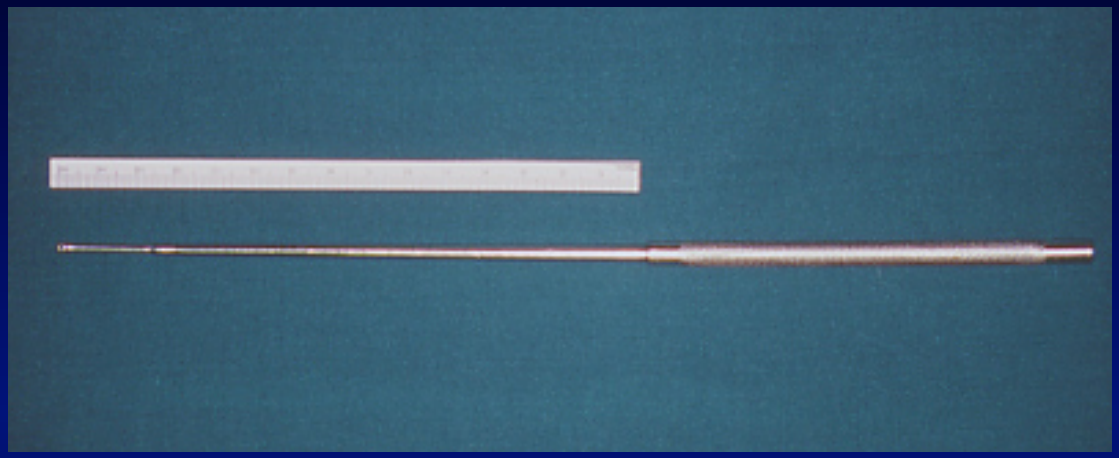
- Recent advances

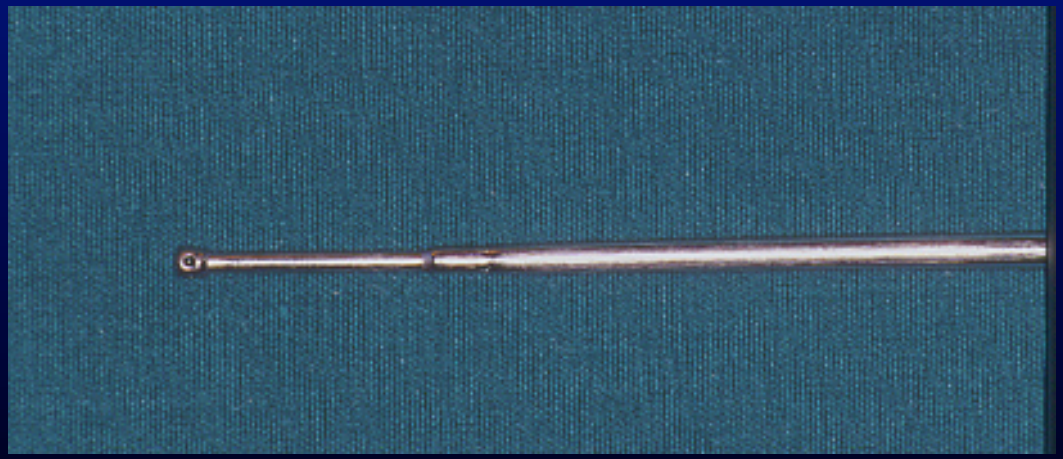
  - short periods (7 – 10 min) of intermittent moderate hypothermic (24 ° C) circulatory arrest

  - followed by short periods of reperfusion (≥ 5 min)

  - with cerebral near-infrared spectroscopy (NIRS) monitoring

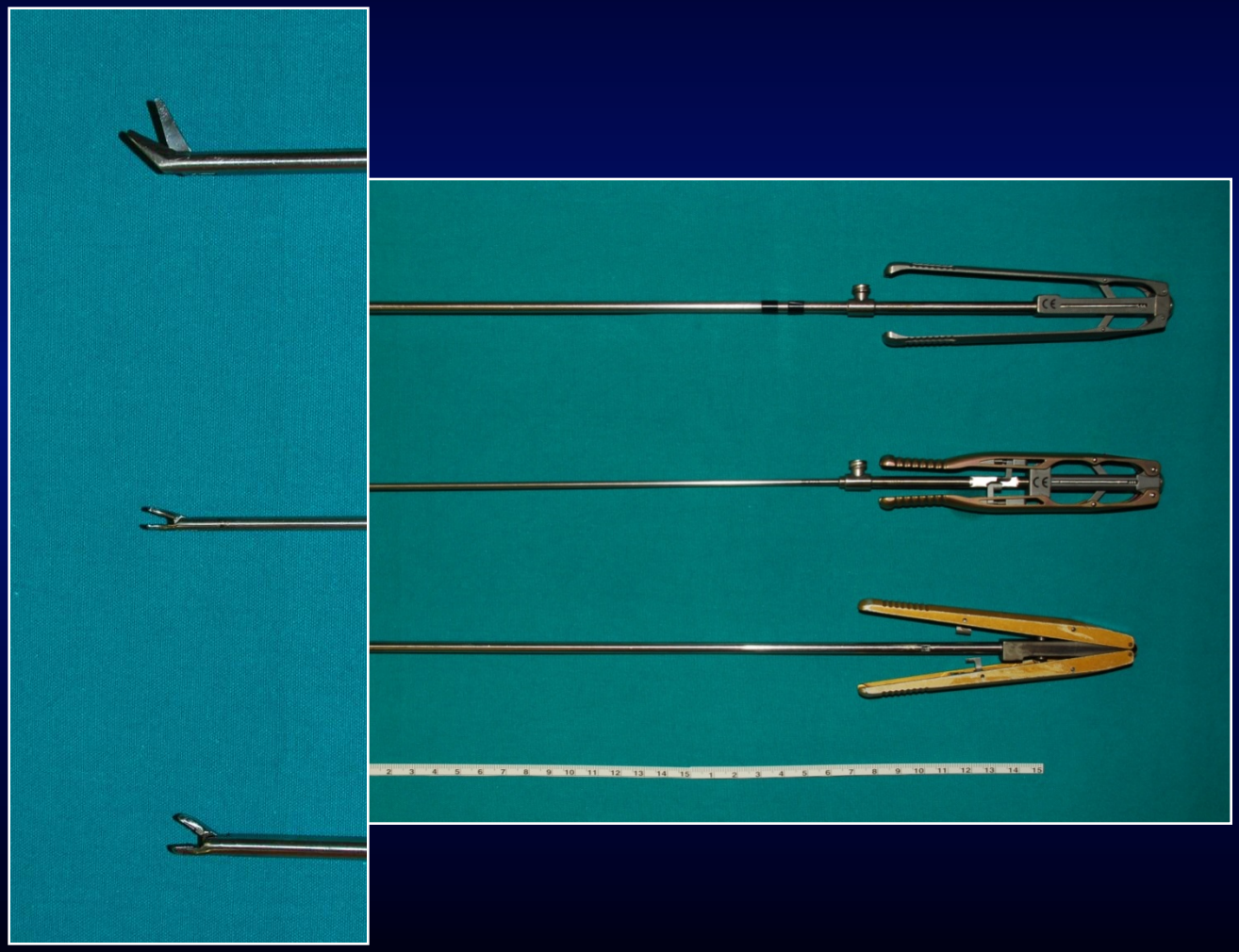
SURGICAL INSTRUMENT





SURGICAL INSTRUMENTS

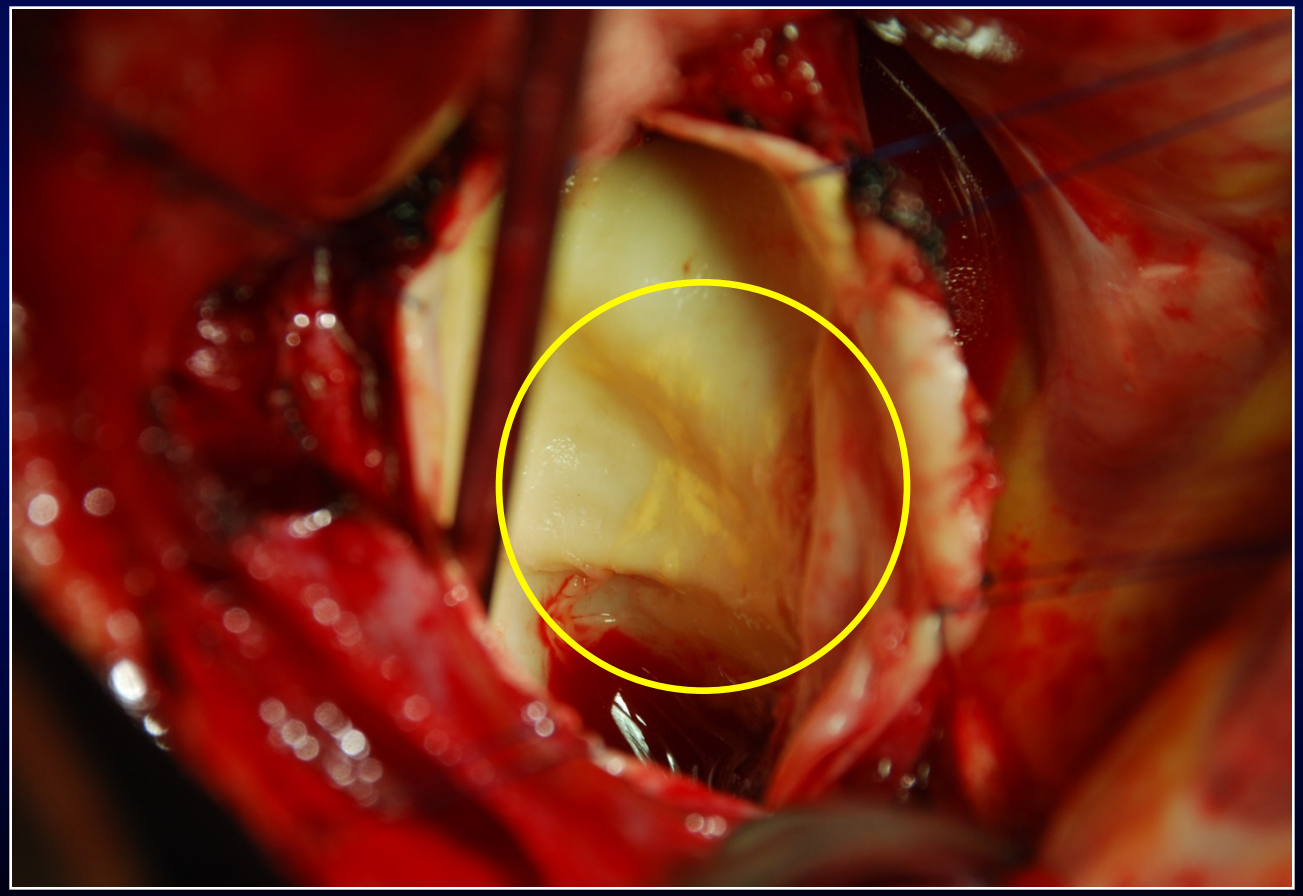
Derived from minimally-invasive cardiac surgery



TRICKS AND TIPS

The correct arterial dissection plane

Yellow-fibro-lipid plaques included into the removed cast



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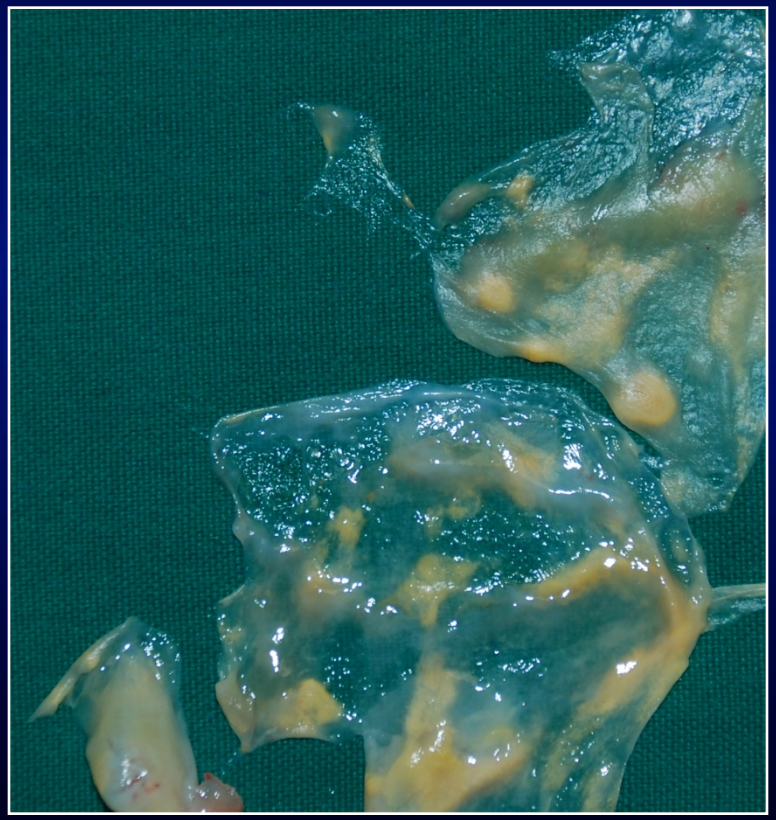
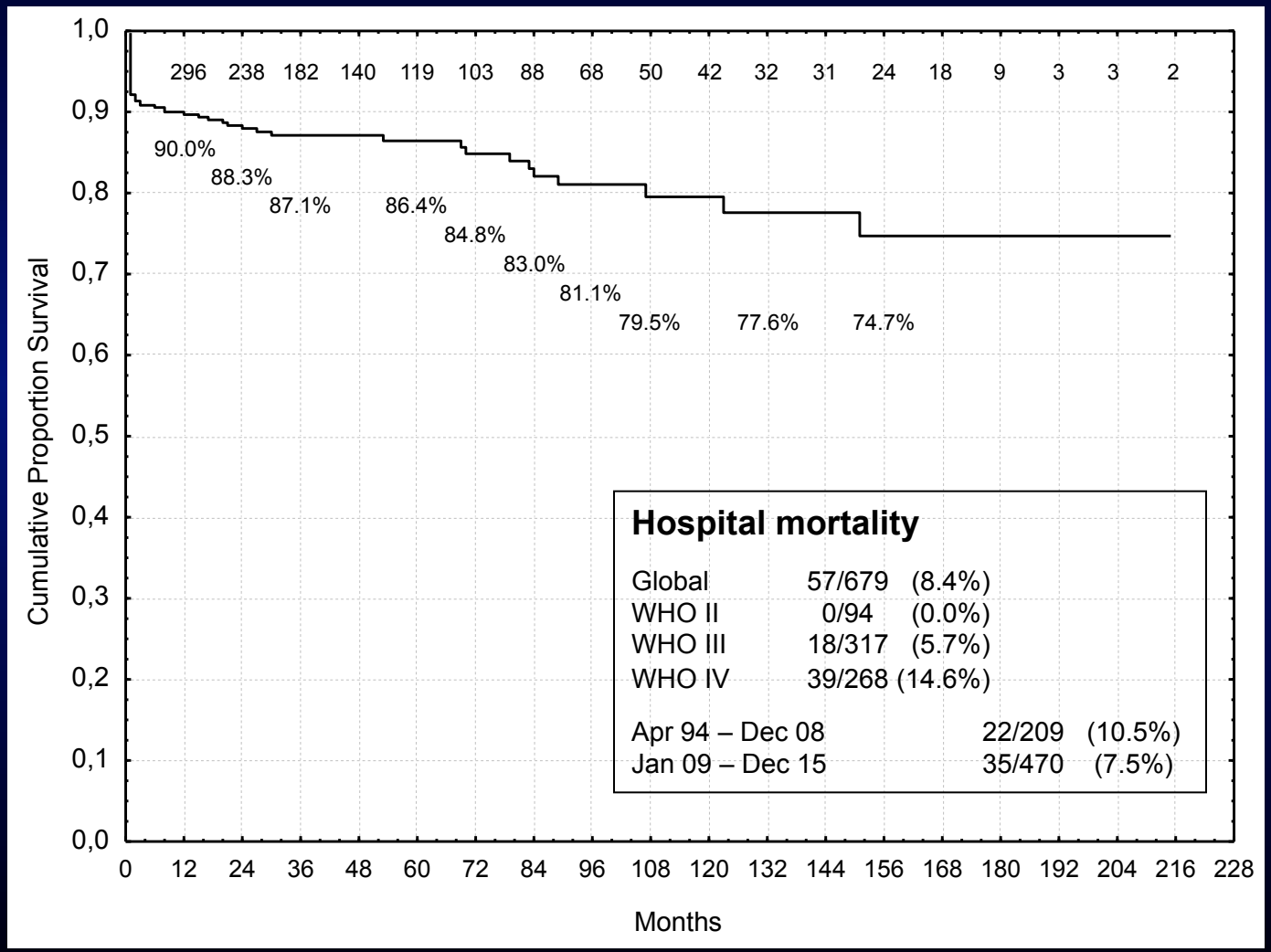


CUMULATIVE PROPORTION SURVIVING

OF 679 PEAs



FOLLOWING PULMONARY ENDARTERECTOMY

COMPLICATIONS

COMPLICATIONS

FOLLOWING PULMONARY ENDARTERECTOMY

- Persistent severe pulmonary hypertension
- Airways bleeding
- Lung reperfusion edema
- Right ventricular failure

COMPLICATIONS
FOLLOWING PULMONARY ENDARTERECTOMY

Persistent severe pulmonary hypertension

When only a small amount of thromboembolic material is removed from the pulmonary arteries, the hemodynamic improvement is expected to be very poor, and right ventricular failure has to be deemed as irreversible

In case of hemodynamic impairment despite full medical therapy, ECMO should be considered only as *bridge to transplant*, given the irreversibility of such condition

COMPLICATIONS
FOLLOWING PULMONARY ENDARTERECTOMY

Airways bleeding

Some unsuccessful attempts of stopping airways bleeding with ECMO have been performed in the past

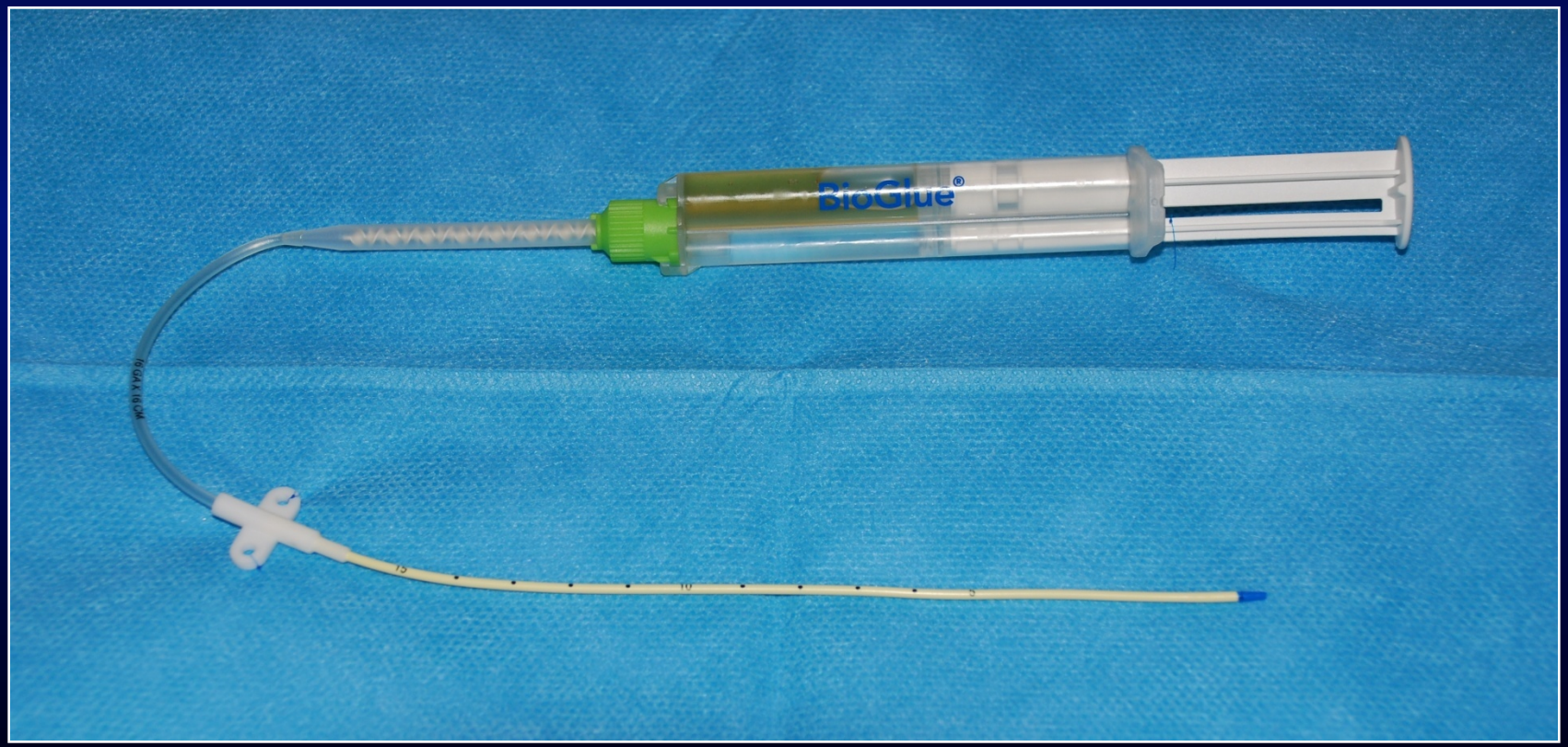
The need for systemic anticoagulation thwarts the hemostasis attempt of bypassing the pulmonary circulation

Moreover, sometimes the bleeding is not due to arterial wall injuries but arises from pathological systemic-to-pulmonary arterial shunts, which develops during long-lasting disease

COMPLICATIONS

FOLLOWING PULMONARY ENDARTERECTOMY

Airways bleeding



COMPLICATIONS

FOLLOWING PULMONARY ENDARTERECTOMY

Bridge to recovery

The sudden reperfusion of many segmental and subsegmental arterial branches may lead to regional lung edema, particularly when an extensive PEA is performed

When ventilation with high PEEP is not enough to counteract this occurrence, veno-arterial ECMO is useful to protect the lung parenchyma from alveolar breakdown

COMPLICATIONS

FOLLOWING PULMONARY ENDARTERECTOMY

Bridge to recovery

Long-lasting diseases lead to advanced right heart failure

Sometimes, despite the prompt relief from the high afterload after PEA, the pre-operative myocardial impairment is so advanced that the right ventricle may take a few days before improving the systolic function

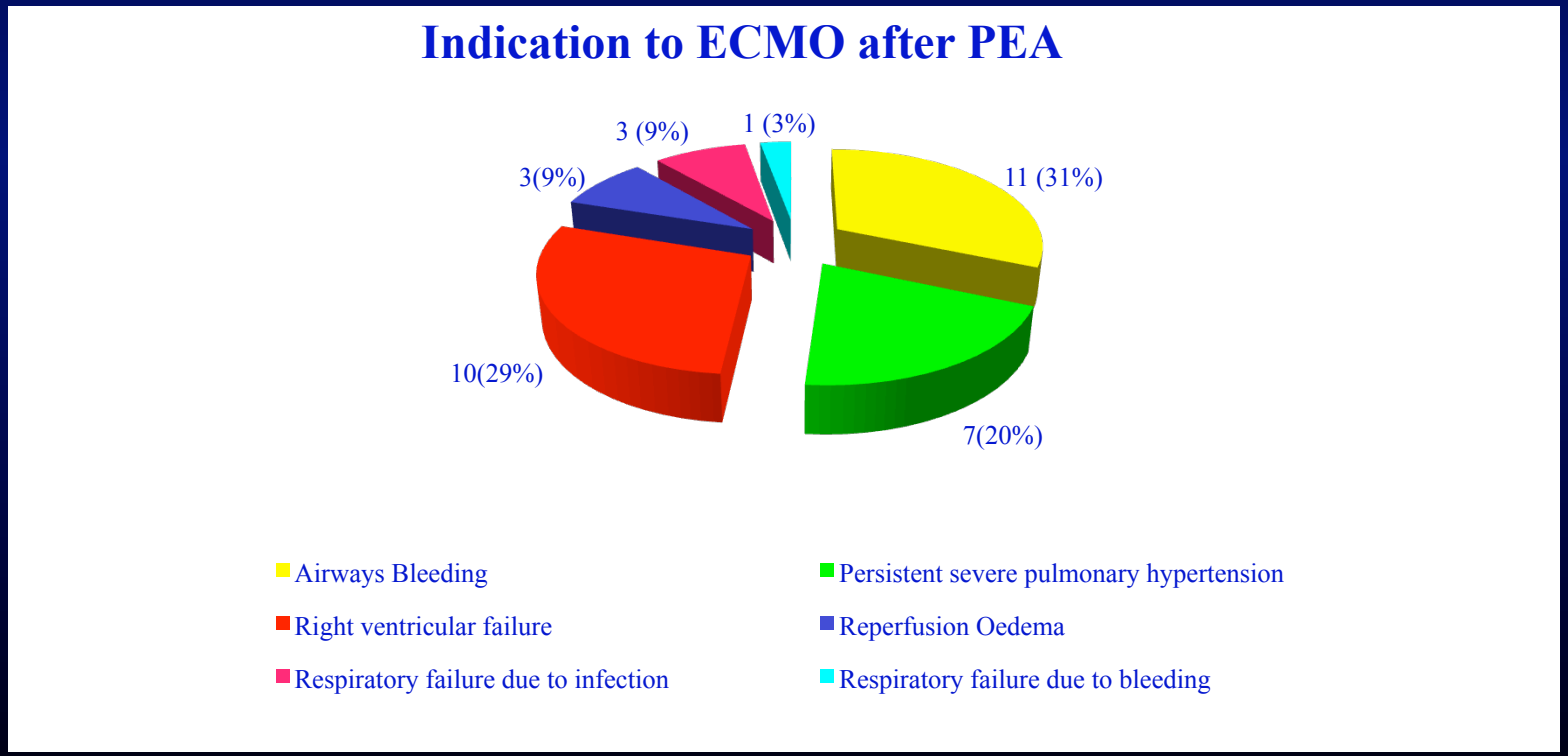
Veno-arterial ECMO is effective in assisting hemodynamic during the progressive myocardial recovery

ECMO AFTER PEA

April 11th, 1994 – December 7th, 2015

37 ECMO in 35 patients over 679 PEAs (5%)

Mean age 57 ± 16 yrs (20 – 80)



ECMO AFTER PEA

Airways bleeding

April 11th, 1994 – August 30th, 2015

11 patients assisted with ECMO

Duration	5 ± 6 days
Survival	18 %

Given the clear failure

alternative strategies were developed

ECMO AFTER PEA

Airways bleeding

May 19th, 2005 – August 30th, 2015

42 patients

Multiple strategies sometimes combined each other:

Bronchoscopy/Drugs/Bronchial Blocker ± Bioglue

±

Lobectomy

±

Pneumonectomy

±

Transplant

ECMO AFTER PEA

Airways bleeding

May 19th, 2005 – August 30th, 2015

42 patients (1 with incoercible bleeding)

Final strategy:		Stop Bleeding
• Pneumonectomy	5 pts	2 pts
• Lung lobectomy	5 pts	4 pts
• Bronchial blocker	7 pts	4 pts
• BioGlue®	13 pts	12 pts
• Percutaneous embolization	2 pts	2 pts
• Drugs/Bronchoscopy	9 pts	7 pts

ECMO AFTER PEA

Right ventricular failure

April 11th, 1994 – December 7th, 2015

10 patients assisted with ECMO

Duration	5 ± 3 days
Survival	40 %

Successful bridge to recovery

ECMO AFTER PEA

Persistent severe pulmonary hypertension

April 11th, 1994 – December 7th, 2015

7 patients

4 pts eligible for Tx
(1 DLTx and 3 HLTx)

Duration	4 ± 1 days
Survival	100 %

Successful bridge to transplant

3 pts non eligible for Tx (2 age, 1 tumor)

Duration	8 ± 3 days
Survival	0 %

Unsuccessful treatment

ECMO AFTER PEA

Lung reperfusion edema

April 11th, 1994 – December 7th, 2015

3 patients assisted with ECMO

Duration	6 ± 3 days
Survival	67 %

Successful bridge to recovery

ECMO AFTER PEA

CONCLUSIONS

- Indications for ECMO after PEA
  - Lung reperfusion edema (BTR)
  - Right ventricular failure (BTR)
  - Persistent severe pulmonary hypertension (only BTT)

- Unsuccessful ECMO after PEA
  - Airways bleeding
  - Persistent severe pulmonary hypertension in patients non eligible for transplantation