University of Pavia - School of Medicine
Foundation I.R.C.C.S. Policlinico "San Matteo"
Cardiac Surgery - Intrathoracic Transplantation - Pulmonary Hypertension
Pavia, Italy

Prof. Andrea M. D'Armini, M.D.

PULMONARY ENDARTERECTOMY (PEA) AND BALLOON PULMONARY ANGIOPLASTY (BPA): THE PRESENT AND THE FUTURE?

FINANCIAL DISCLOSURE

Last three years

Actelion Pharmaceuticals Ltd
Bayer HealthCare
Merk Sharp Dohme

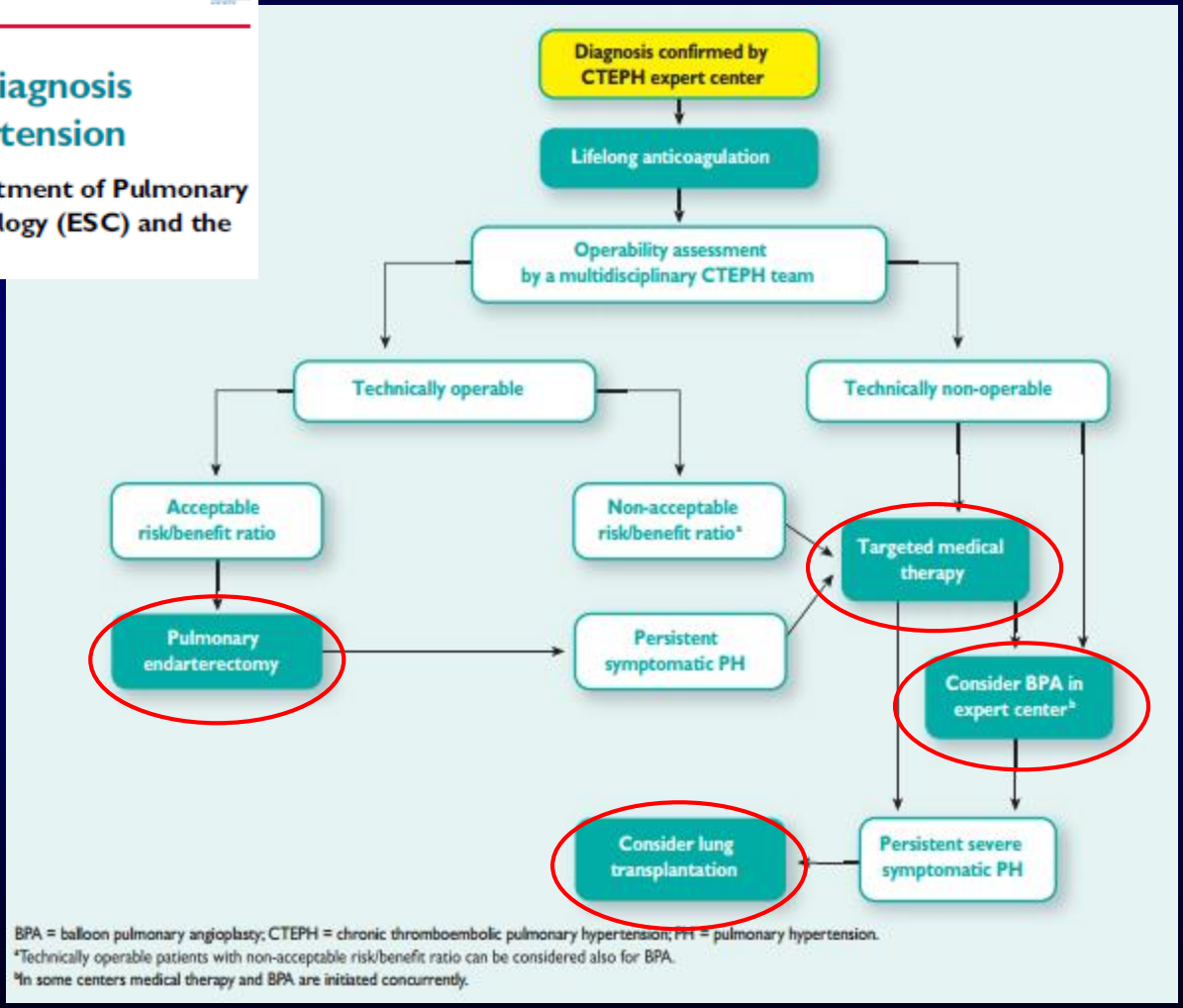
GUIDELINES FOR CTEPH

European Heart Journal
doi:10.1093/eurheartj/ehv317

ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)



BPA = balloon pulmonary angioplasty; CTEPH = chronic thromboembolic pulmonary hypertension; PH = pulmonary hypertension.
[a]Technically operable patients with non-acceptable risk/benefit ratio can be considered also for BPA.
[b]In some centers medical therapy and BPA are initiated concurrently.

SURGICAL TREATMENT OF CTEPH

PAVIA EXPERIENCE

First HLTx for CTEPH

First PEA

First DLTx for CTEPH

First PEA in patient listed for DLTx

First PEA in patient previously enrolled in RCT for inoperability

Reverse right ventricular remodeling after pulmonary endarterectomy

Andrea M. D'Armini, MD,[a] Giorgio Zanotti, MD,[a] Stefano Ghio, MD,[b] Giulia Magrini, MD,[b] Matteo Pozzi, MD,[a] Laura Scelsi, MD,[b] Giulia Meloni, MD,[c] Catherine Klersy, MD,[d] and Mario Viganò, MD[a]

J Thorac Cardiovasc Surg 2007;133:162-8

08-MAR-1991

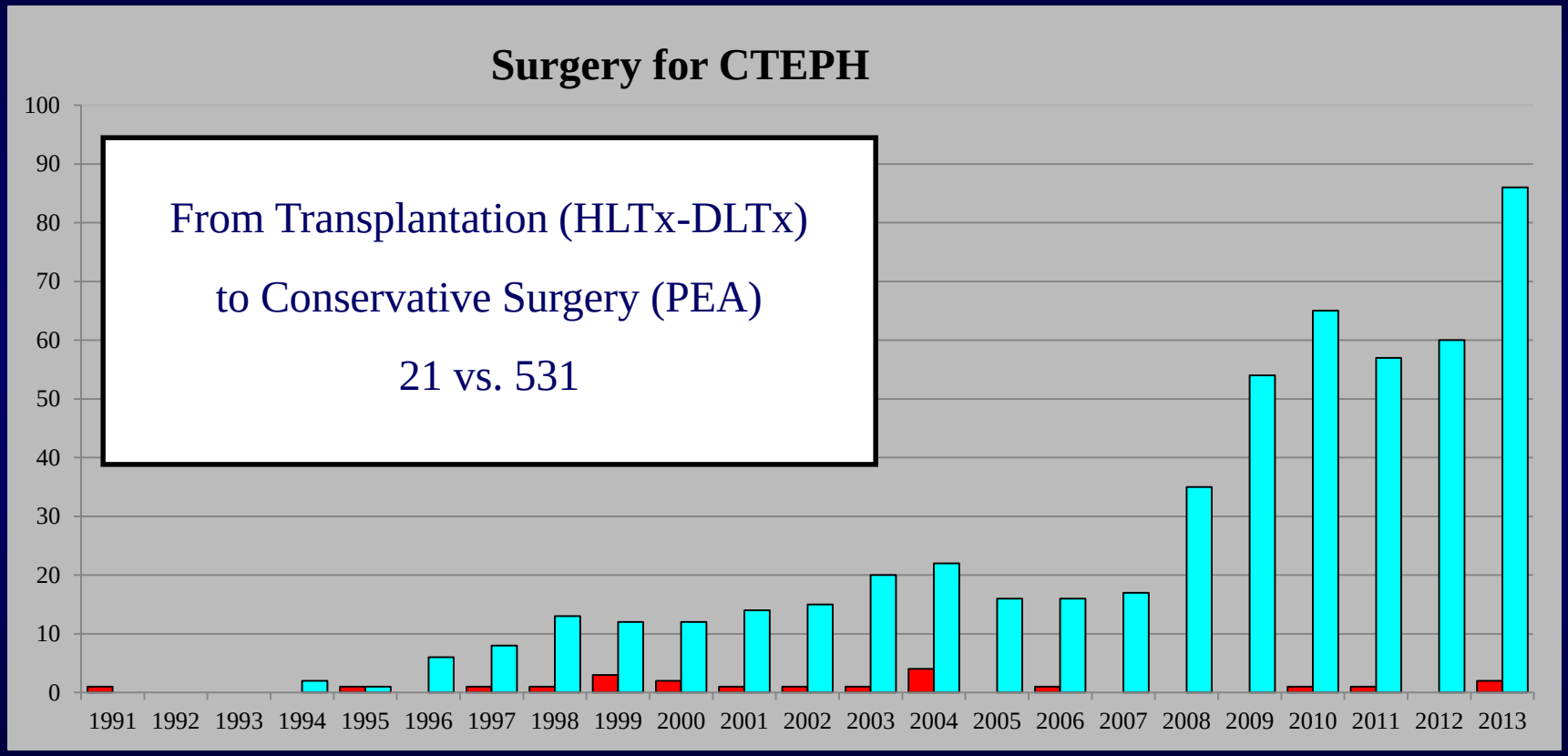
11-APR-1994

25-DEC-1995

28-JUL-2003

30-NOV-2009

SURGICAL TREATMENT OF CTEPH



1991 — 22 yrs — 2013

SURGICAL TREATMENT OF CTEPH

Chronic thromboembolic pulmonary hypertension: From transplantation to distal pulmonary endarterectomy

Andrea M. D'Armini, MD,[a]
Marco Morsolini, MD, PhD,[b]
Gabriella Mattiucci, MD,[b]
Valentina Grazioli, MD,[a]
Maurizio Pin, MD,[a] Antonio Sciortino, MD,[a]
Eloisa Arbustini, MD,[c] Claudio Goggi, MD,[a] and
Mario Viganò, MD[a]

The Journal of Heart and Lung Transplantation

J Heart Lung Transplant. 2016 Jan 6. pii: S1053-2498(16)00024-3

SURGICAL TREATMENT OF CTEPH

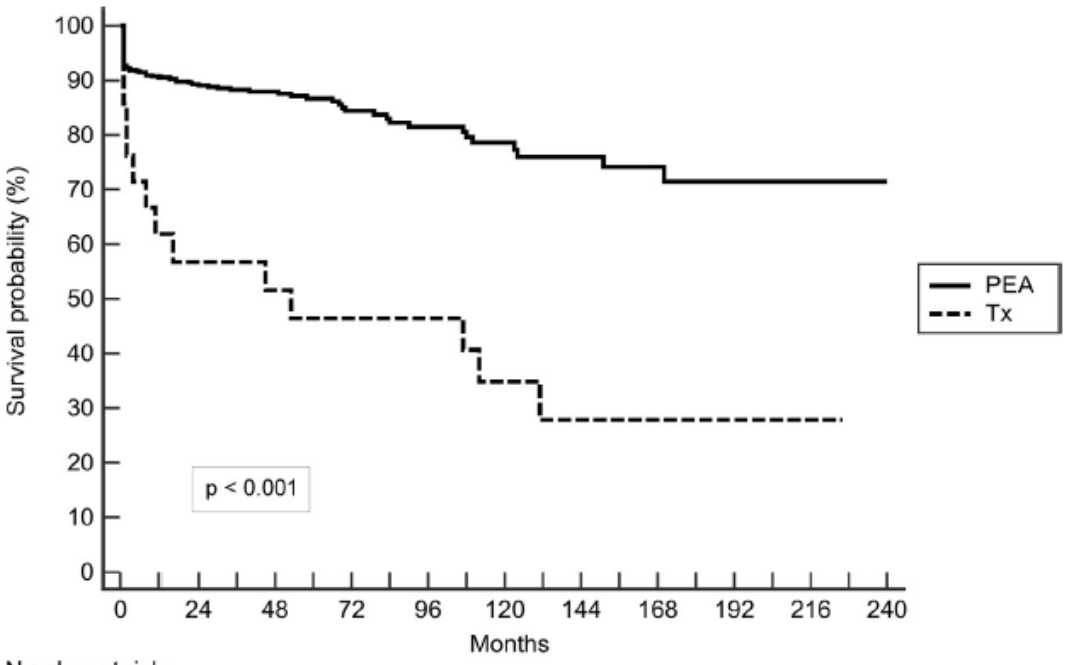


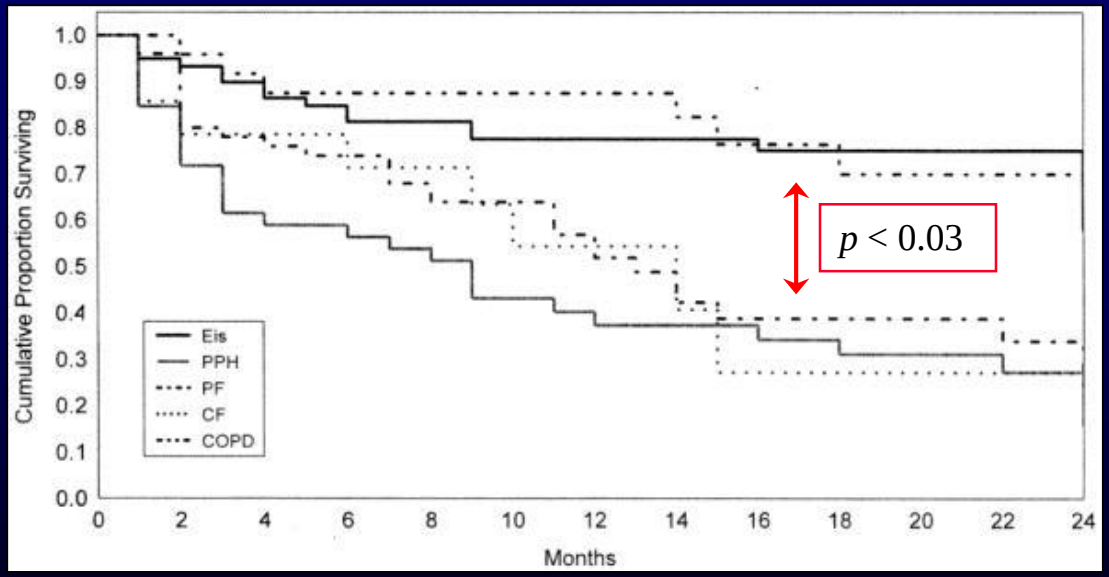
Figure 4. Survival after PEA and LTx.

LTx WAITING LIST SURVIVAL

Risk factors for early death in patients awaiting heart-lung or lung transplantation: experience at a single european center

D'Armini AM, Callegari G, Vitulo P, Klersy C, Rinaldi M, Pederzolli C, Grande A, Fracchia C, Viganò M

Transplantation 1998; 66(1):123-7



INTRODUCTION

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

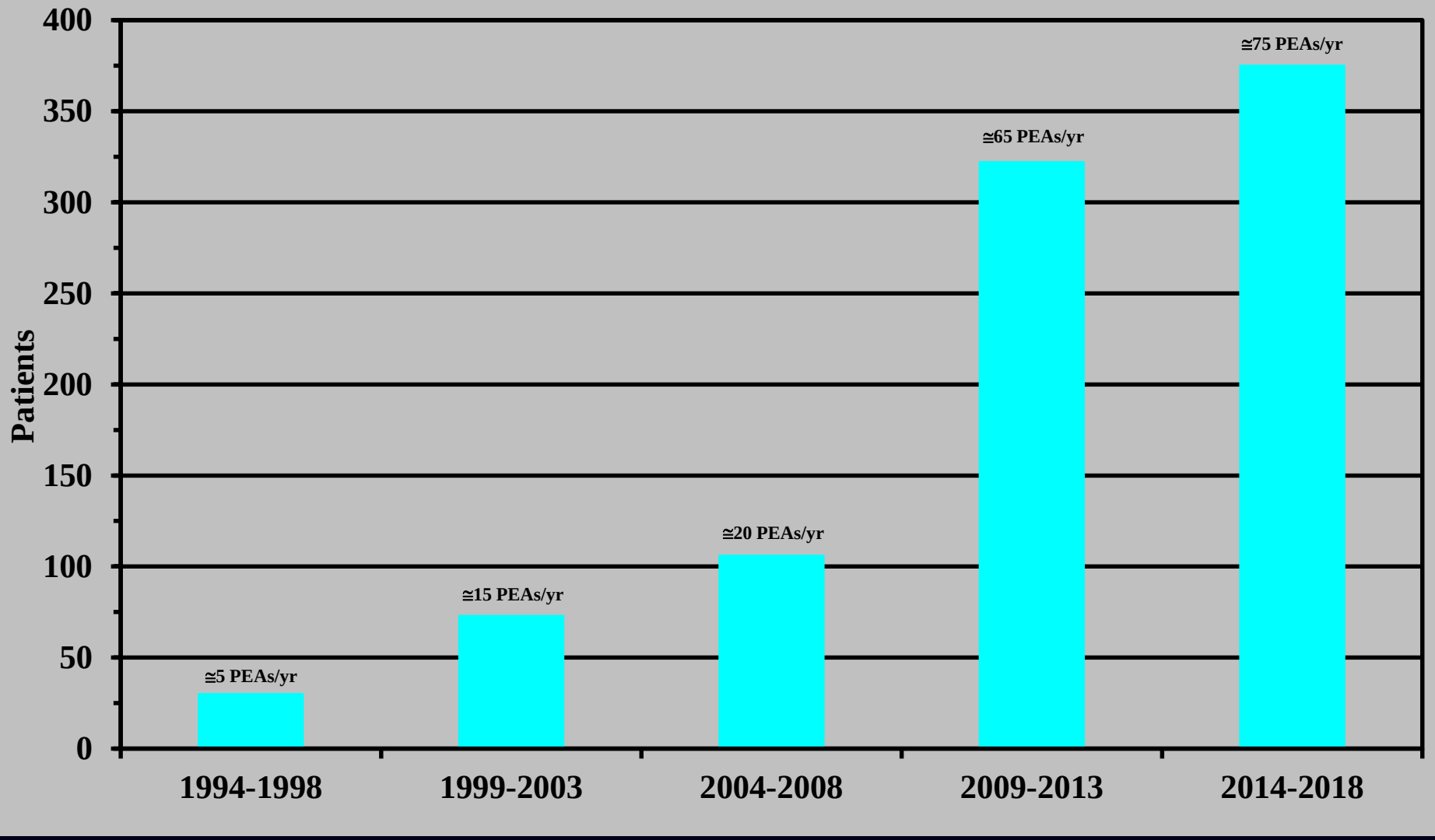
- This life-saving conservative surgery is called *pulmonary endarterectomy (PEA)*

OUR PROGRAM

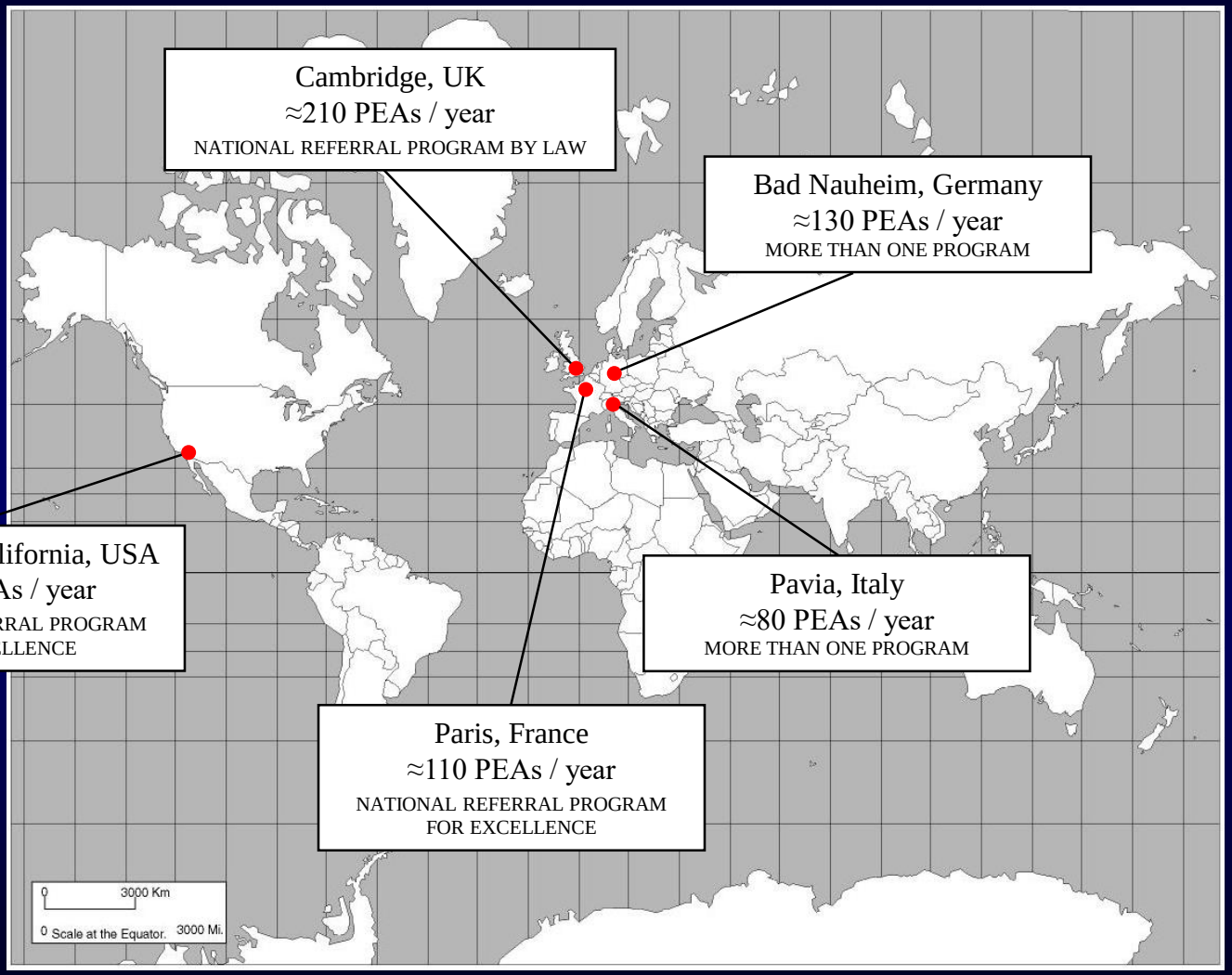
- National referral program
- Begin: April 1994
- October 2019: 975 PEAs performed

NUMBER OF PEAs IN 5-YEAR GROUPS

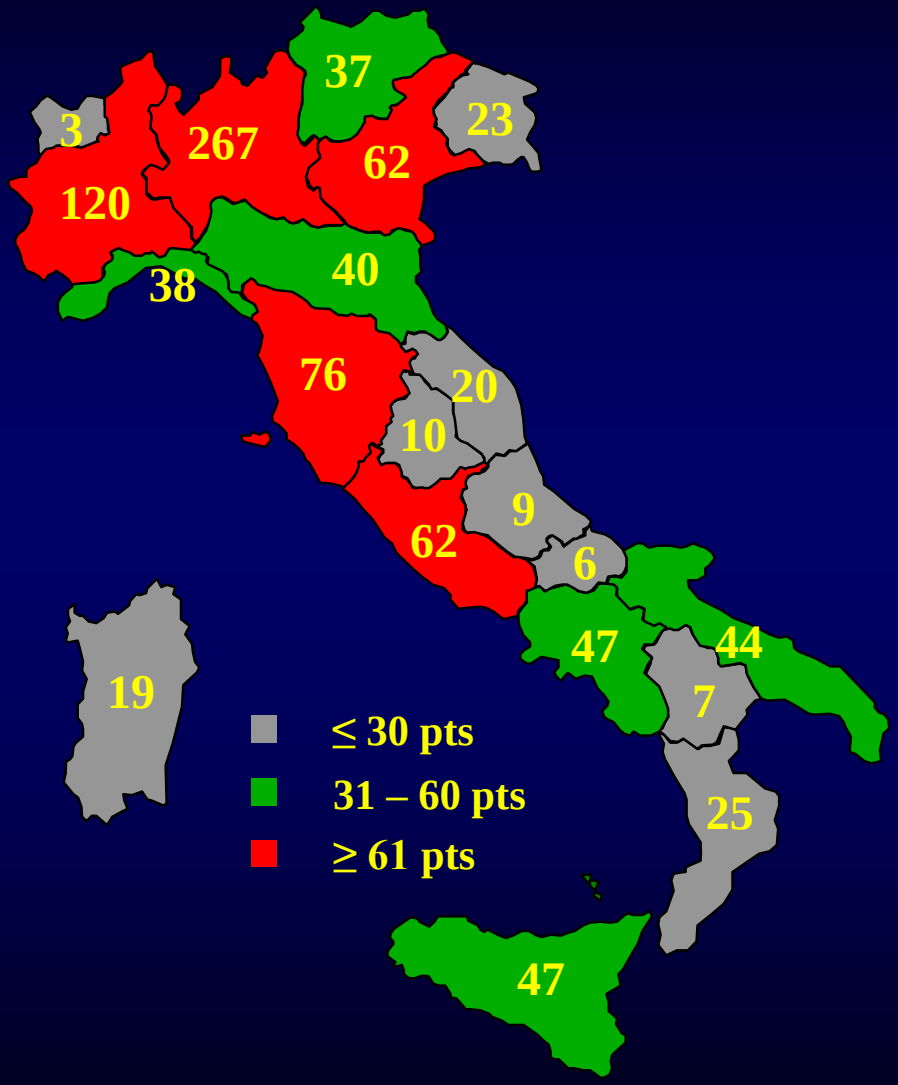
906 PEAs



MAIN WORLD PEA CENTERS



PATIENTS' REFERRAL



FROM 4/1994 TO 10/2019
975 PEAs

Pts coming from outside Italy: 13	
- Albania	3
- Greece	1
- Israel	1
- Kosovo	1
- Romania	2
- Russia	1
- Scotland	1
- Uganda	1
- USA	1
- Vatican City	1

PATIENTS' REFERRAL

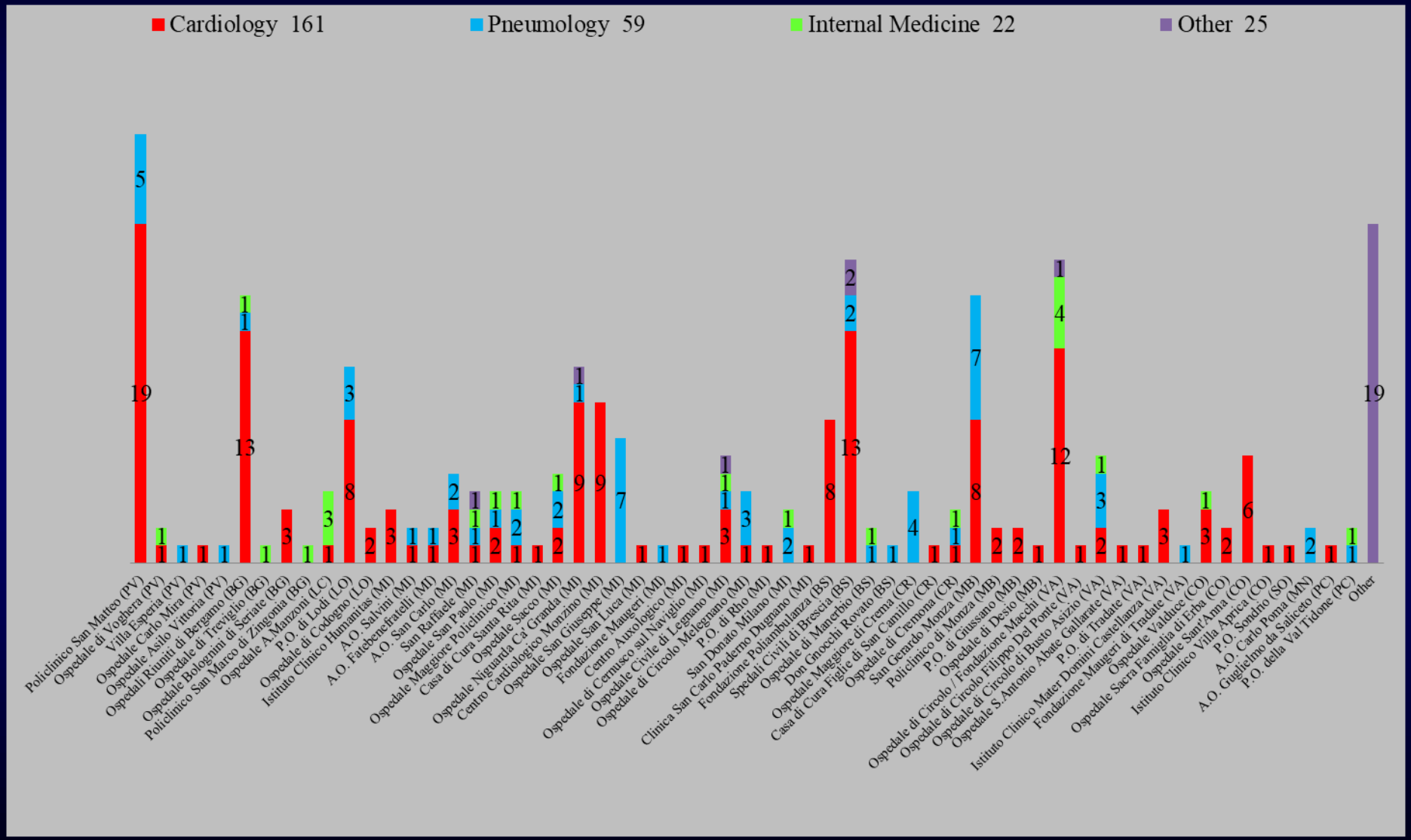
FROM 2014 TO 2018 → 375 PEAs
PTS / 10^6 / Year POPULATION

- ≤ 1 pt / 10^6 / Year
- 1 – 3 pts / 10^6 / Year
- ≥ 3 pts / 10^6 / Year

Update date population at 01/01/2019 (ISTAT)

PATIENTS' REFERRAL FROM LOMBARDIA

FROM 4/1994 TO 10/2019 - 267 PEAs



CLINIC

- *CTEPH* patients *must be* in *NYHA functional class III or IV* before being *evaluated for PEA!*

- *Since 2003* we have performed *PEA* in *NYHA functional class II* patients, given the *natural history of CTEPH* …and the *good results of PEA…*

INDICATIONS FOR SURGERY

NYHA FUNCTIONAL CLASS

ACQUIRED CARDIOVASCULAR DISEASE

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

Surgical management and outcome of patients with chronic thromboembolic pulmonary hyperte… international prospective registry

Eckhard Mayer, MD,[a] David Jenkins, FRCS,[b] Jaroslav …
Jaap Kloek, MD,[e] Bart Meyns, MD,[f] Lars Bo Ilkjaer, MI…
Irene Lang, MD,[h] Joanna Pepke-Zaba, MD,[b] Gerald Sir…

Study Design

This prospective registry was designed to include newly diagnosed (≤6 months) consecutive patients with CTEPH in participating centers in Europe and Canada, from February 2007 to January 2009. The registry proto-

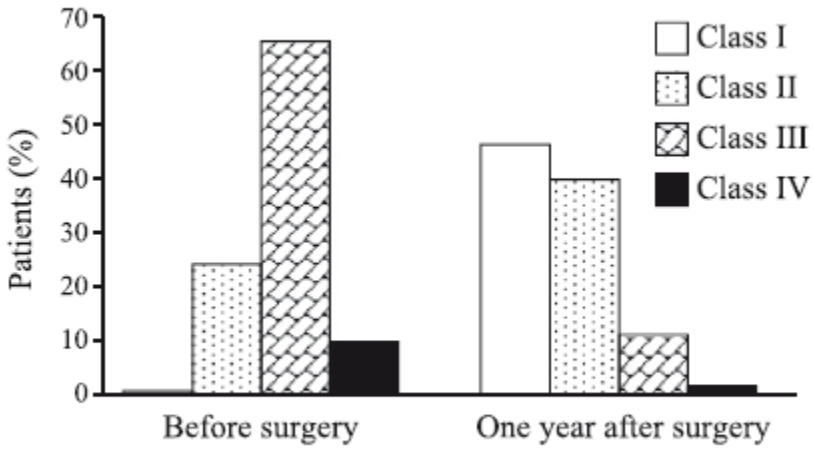
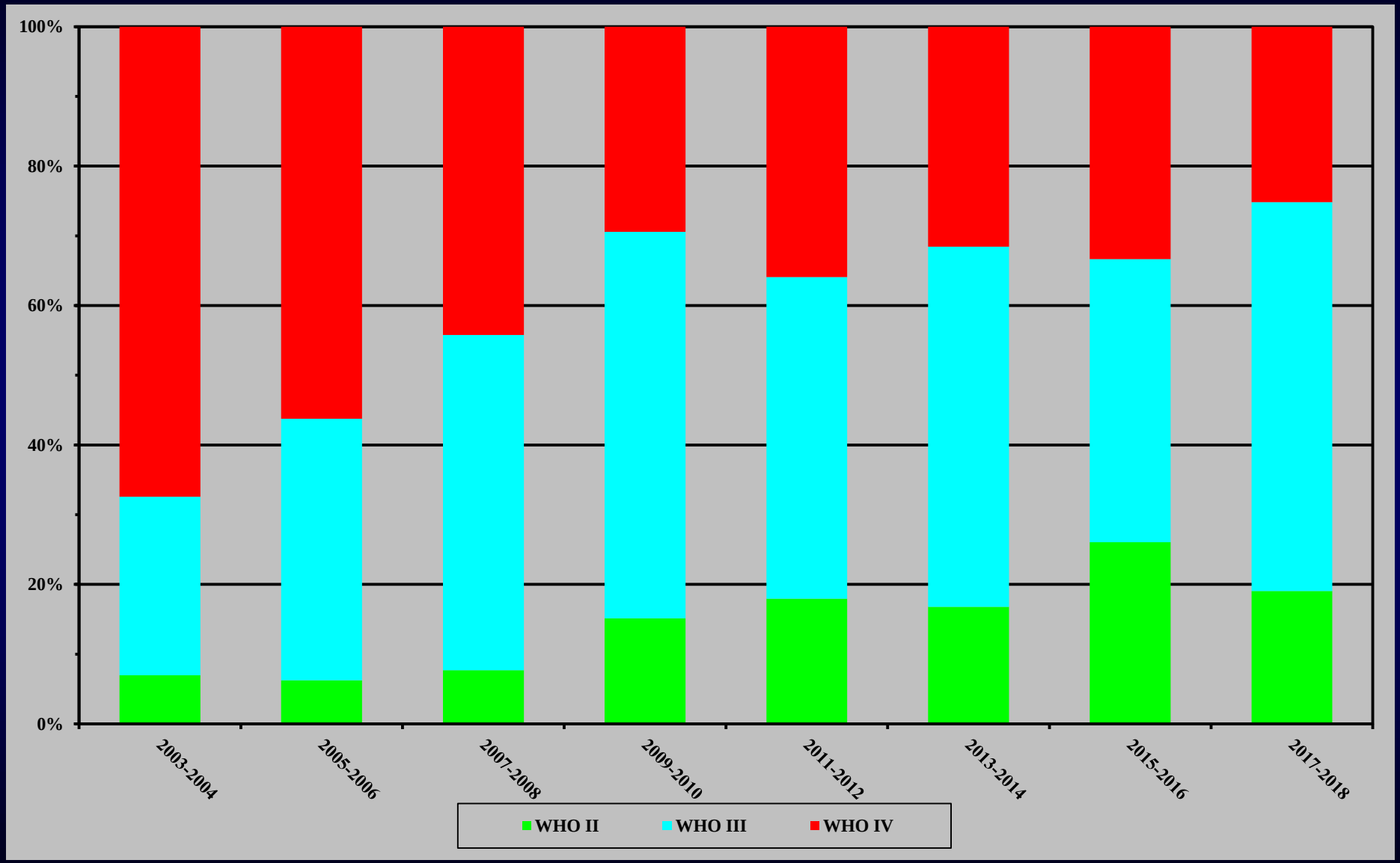


FIGURE 1. NYHA functional class before surgery and within 1 year after surgery (n = 221).

NYHA FUNCTIONAL CLASS

	INTERNATIONAL REGISTRY 2007-2008	PAVIA 2007-2008
II	25%	5%
III	65%	50%
IV	10%	45%

NYHA CLASS DISTRIBUTION 2003-2018



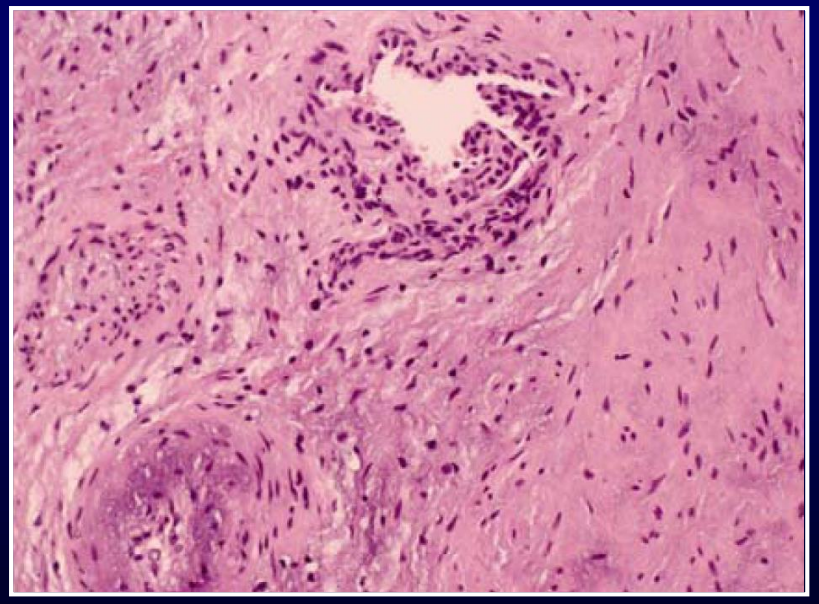
NYHA FUNCTIONAL CLASS

	INTERNATIONAL REGISTRY 2007-2008	PAVIA 2007-2008	PAVIA 2017-2018
II	25%	5%	19%
III	65%	50%	56%
IV	10%	45%	25%

PATHOPHYSIOLOGY

ACCORDING TO THE LENGTH OF THE DISEASE

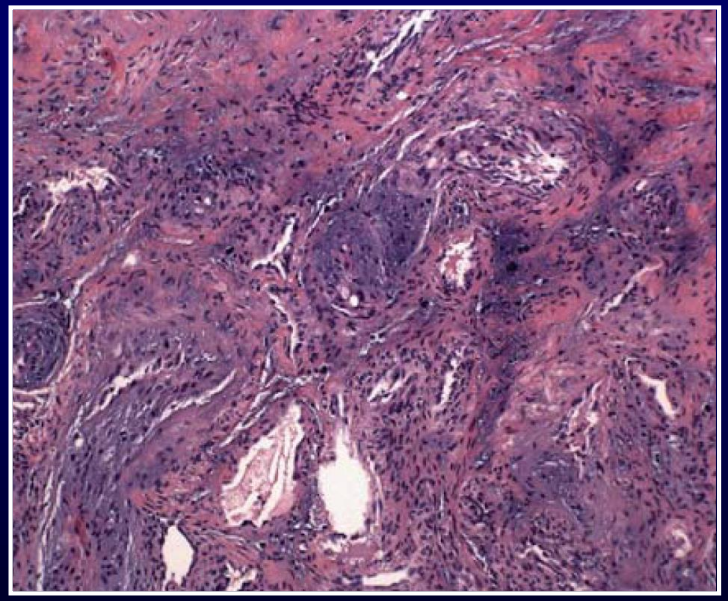
1. Hypertensive remodeling of the patent pulmonary vascular bed *(Eisenmenger-like)* due to volume and pressure overload



PATHOPHYSIOLOGY

ACCORDING TO THE LENGTH OF THE DISEASE

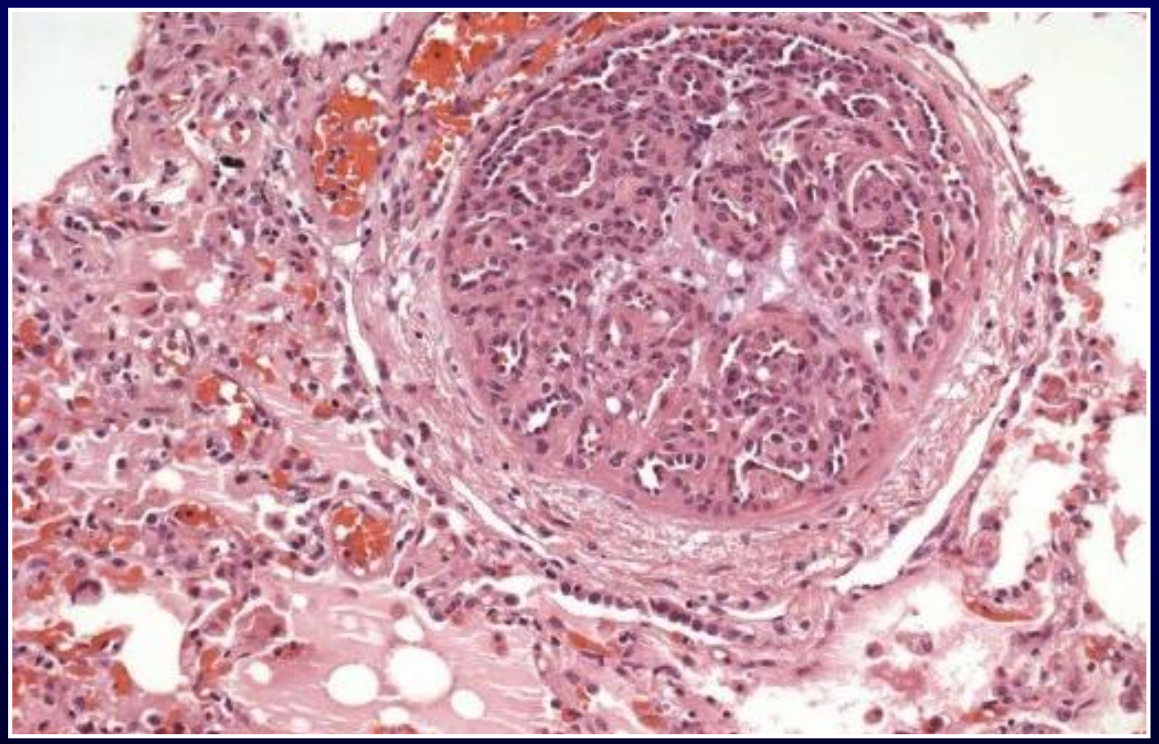
2. Chronic arteriopathy of the obstructed branches with *calcifications* and possible *retraction* of the distal vessels



PATHOPHYSIOLOGY

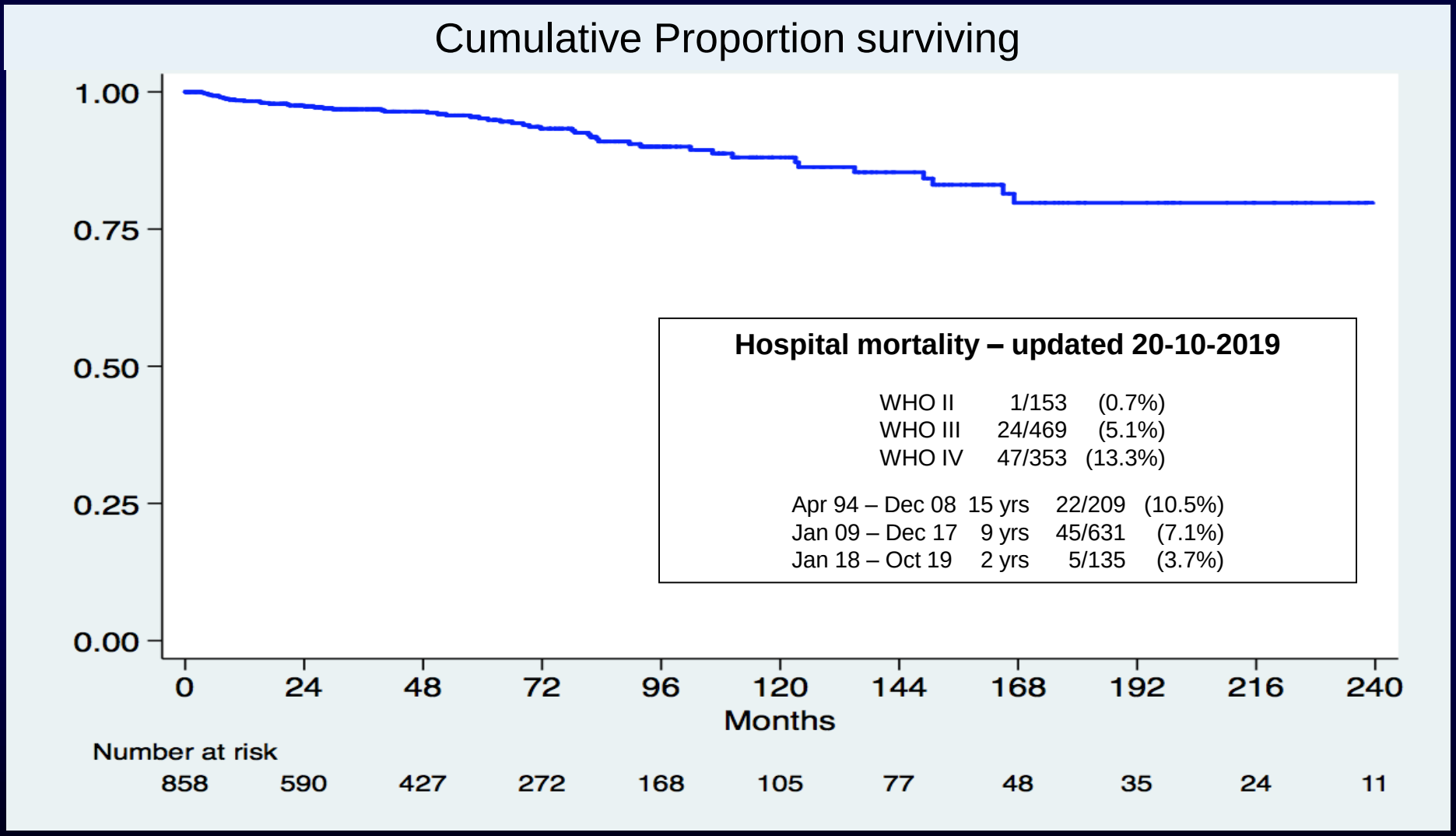
ACCORDING TO THE LENGTH OF THE DISEASE

3. *Plexiform lesions* stemming from the capillary bed



CUMULATIVE PROPORTION SURVIVING

OF 975 PEAs



HEMODYNAMIC

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

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

PVR

ACQUIRED CARDIOVASCULAR DISEASE

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 Kloek, 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, MD[j]

J Thorac Cardiovasc Surg. 2011 Mar;141(3):702-10

PVR

TABLE 3. Impact of specific parameters on in-hospital death and death at 1 year

		In-hospital deaths n (%)	Deaths at 1 year n (%)
PVR (dyn.s.cm^{-5}), n = 340			
<400	n = 48	0 (0%)*	1 (2.1%) NS
400–800	n = 141	4 (2.8%)*	8 (5.7%) NS
800–1200	n = 104	6 (5.8%) NS	9 (8.7%) NS
> 1200	n = 47	5 (10.6%)†	6 (12. 8%)†
NYHA functional class, n = 386			
I and II	n = 75	0‡	NS
III	n = 262	12 (4.6%)*	
IV	n = 49	6 (12.2%)†	6 (1
History of confirmed pulmonary embolism, n = 386			
Yes	n = 308	12 (3.9%) NS	19 (6.2%) NS
No	n = 78	6 (7.7%)†	
Presence of an inferior vena cava filter, n = 298			
Yes	n = 42	—	
No	n = 256	—	
Circulatory arrest duration, n = 378			
≤ 20 min	n = 52	2 (3.8%) NS	
21–40 min	n = 185	5 (2.7%) NS	
1–60 min	n = 103	8 (7.8%) NS	
> 60 min	n = 38	3 (7.9%)†	
Presence of coronary disease or myocardial infarction, n = 276			
Yes	n = 40	4 (10.0%)*	
No	n = 236	5 (2.1%)†	
Presence of thrombophilic disorder, n = 254			
Yes	n = 141	7 (5.0%) NS	
No	n = 113	2 (1.8%)†	

PVR, Pulmonary vascular resistance; *NS*, not significant; *NYHA*, New York Heart Association. Values are presented as numbers of patients (percen
compared with †. ‡P < .005 compared with †. NS compared with ‡ (Fisher's exact test)

PVR (dyn.s.cm^{-5}), n = 340

<400	n = 48	0 (0%)*
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J Thorac Cardiovasc Surg. 2011 Mar;141(3):702-10

PVR

The changing landscape of chronic thromboembolic pulmonary hypertension management

Michael Madani1, Takeshi Ogo2 and Gérald Simonneau3,4,5

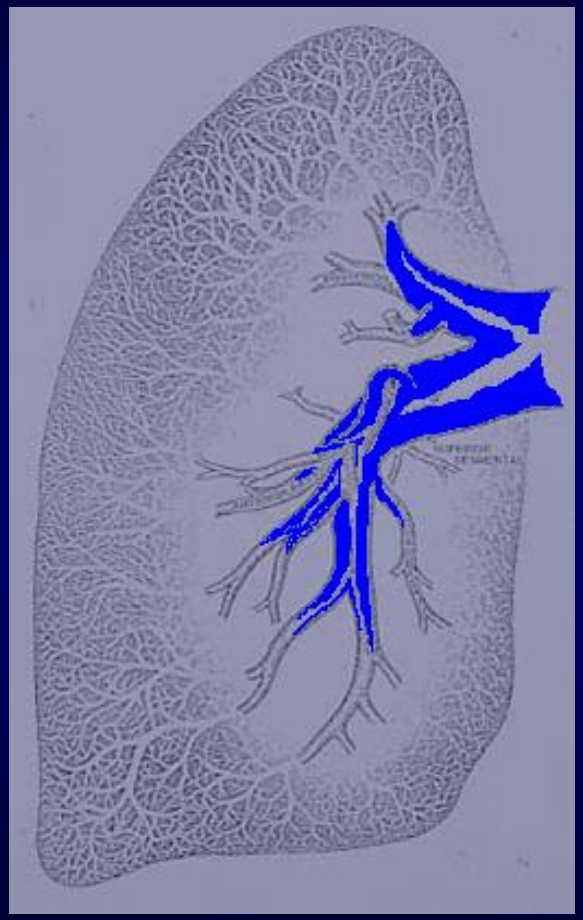
Eur Respir Rev. 2017 Dec 20;26(146)

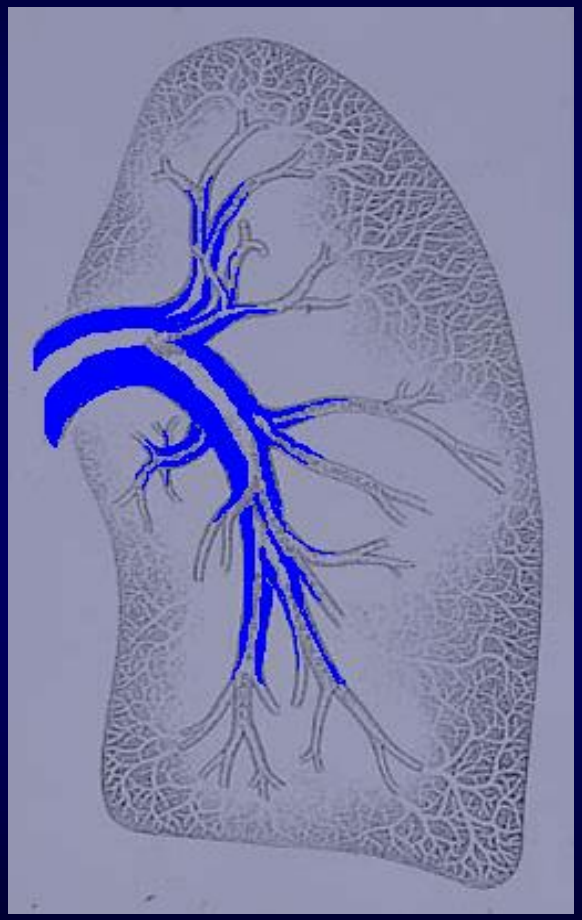
PVR

Measurement of a patient's haemodynamic status by right heart catheterisation is also an important part of risk assessment [1, 2]. Although high pre-operative PVR (>1000–1200 dyn·s·cm^{-5}) is correlated with an increased risk of post-operative mortality [13, 14, 35, 36], patients with a high PVR are in a position to gain the most benefit from surgery, as they often show the greatest relative improvement in PVR after the procedure [13, 14]. Therefore, high PVR should not necessarily be considered a contraindication for pulmonary endarterectomy [14, 37]. High pre-operative PVR in conjunction with comparatively low levels of surgically accessible thrombotic material is indicative of significant microvascular disease [36, 38].

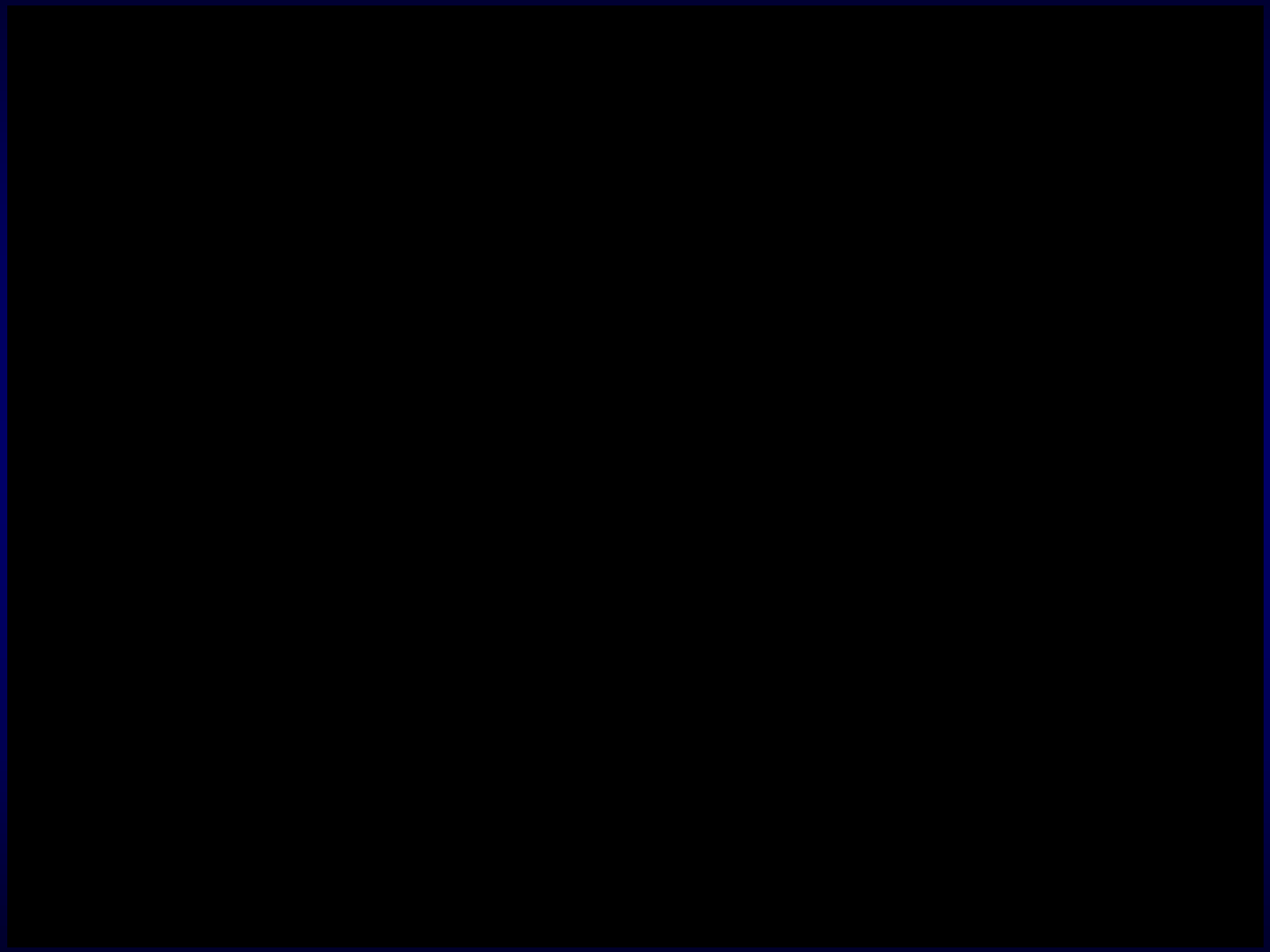
Eur Respir Rev. 2017 Dec 20;26(146)

PROXIMAL LESIONS

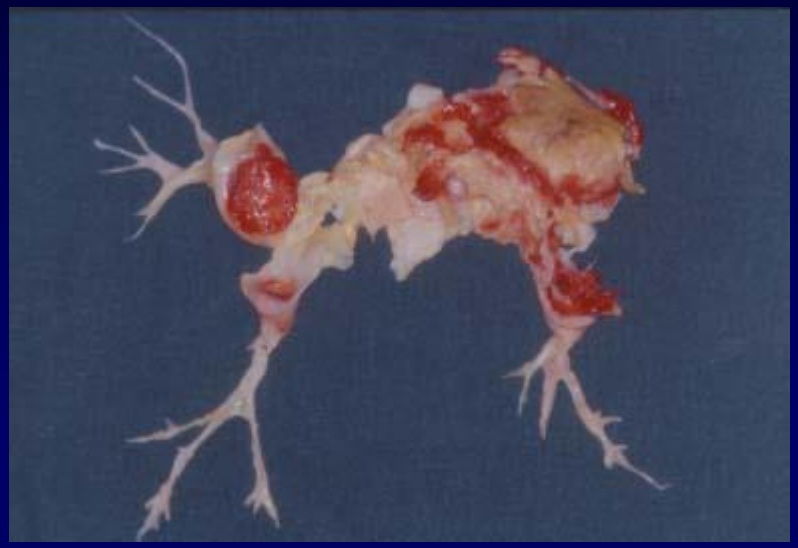




SURGICAL TECHNIQUE – J1

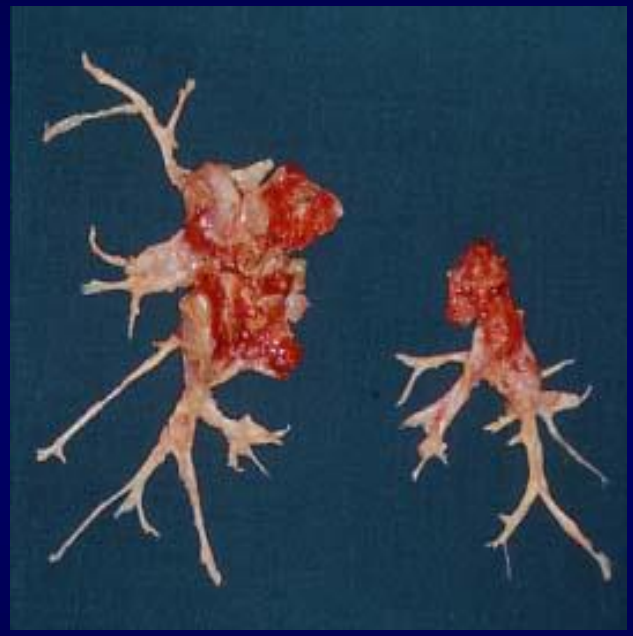


TYPICAL "OLD" SURGICAL SPECIMENS (JAMIESON 1)



E.L. – 38 yrs M – Dec 1999 – PEA #42

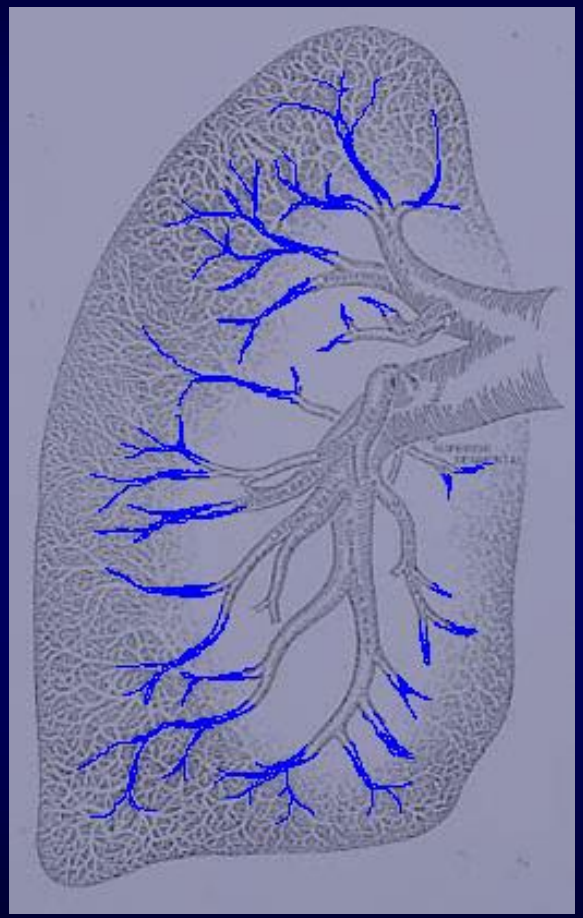
mPAP	**43**	**→**	**20**	**(-53%)**
CO	**3.3**	**→**	**6.9**	**(+109%)**
PVR	**994**	**→**	**220**	**(-78%)**

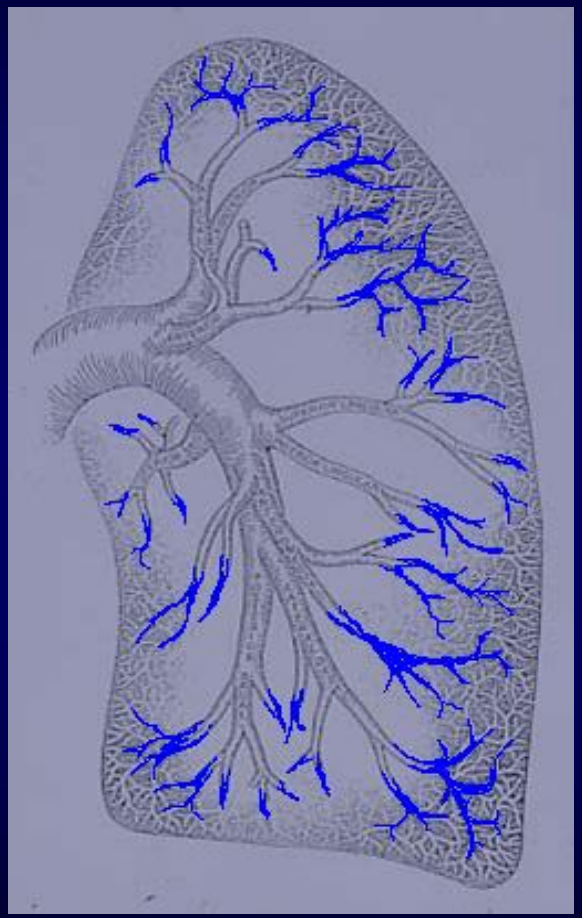


P.A. – 66 yrs M – Jun 2001 – PEA #60

mPAP	**50**	**→**	**25**	**(-50%)**
CO	**2.6**	**→**	**4.4**	**(+69%)**
PVR	**1385**	**→**	**364**	**(-74%)**

DISTAL LESIONS





EVOLVING SURGICAL TECHIQUE

Evolving surgical techniques for pulmonary endarterectomy according to the changing features of chronic thromboembolic pulmonary hypertension patients during 17-year single-center experience

Marco Morsolini, MD,[a,b] Salvatore Nicolardi, MD,[a,b] Elisa Milanesi, MD,[c] Eleonora Sarchi, MD,[d] Gabriella Mattiucci, MD,[a] Catherine Klersy, MD, MSc,[e] and Andrea Maria D'Armini, MD[a]

(J Thorac Cardiovasc Surg 2012;144:100-7)

SURGICAL PROTOCOL

	Original San Diego protocol	Actual Pavia protocol
Aortic clamp	Yes	No
Cardioplegia	Yes	No
Hypothermia	Deep (18°C)	Moderate (24°C)
Circulatory arrest	A single (20 minutes) period of circulatory arrest for each side (with a maximum of a third)	Intermittent short periods of circulatory arrest (≈7-10 minutes) followed by short re-perfusion periods (≈5-7 minutes)
Total arrest time	Maximum 60 minutes	Maximum 180 minutes

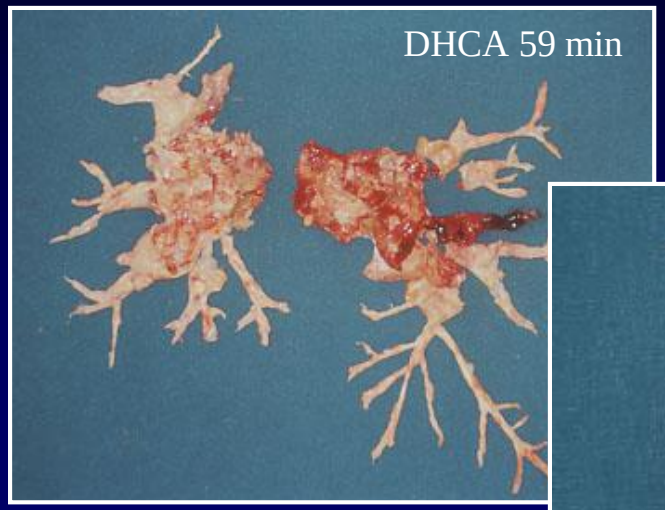
Since 15-10-2009 (#245)

TAILORED AND LESS INVASIVE SURGERY

SURGICAL PROTOCOL

More than 730 PEAs with this technique

JAMIESON TYPE1 vs. TYPE2 vs. TYPE3

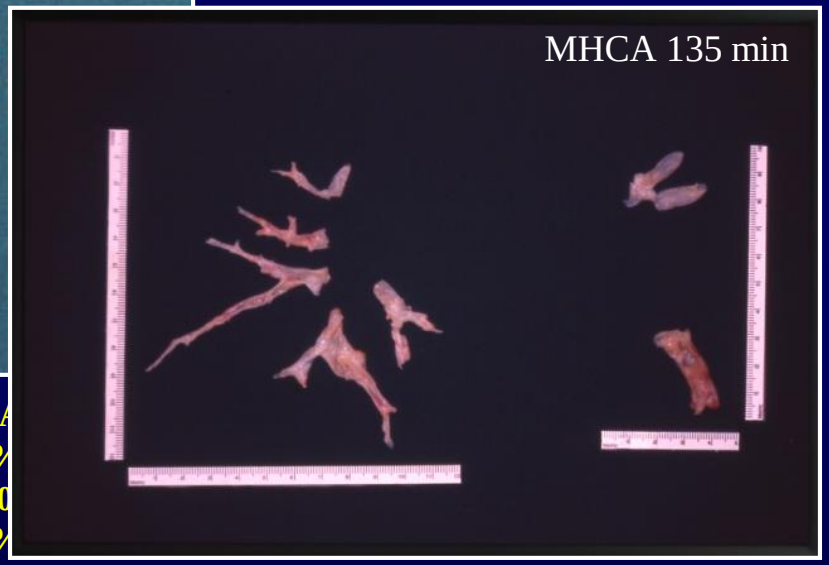


L.M.E.L. - 65 yrs M - Oct 2004 - PE

mPAP	**39**	→	**19**	**(-51%)**
CO	**4.4**	→	**5.4**	**(+23%)**
PVR	**665**	→	**222**	**(-66%)**

G.A.C. - 52 yrs F - Jul 2003 - PE

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%)**

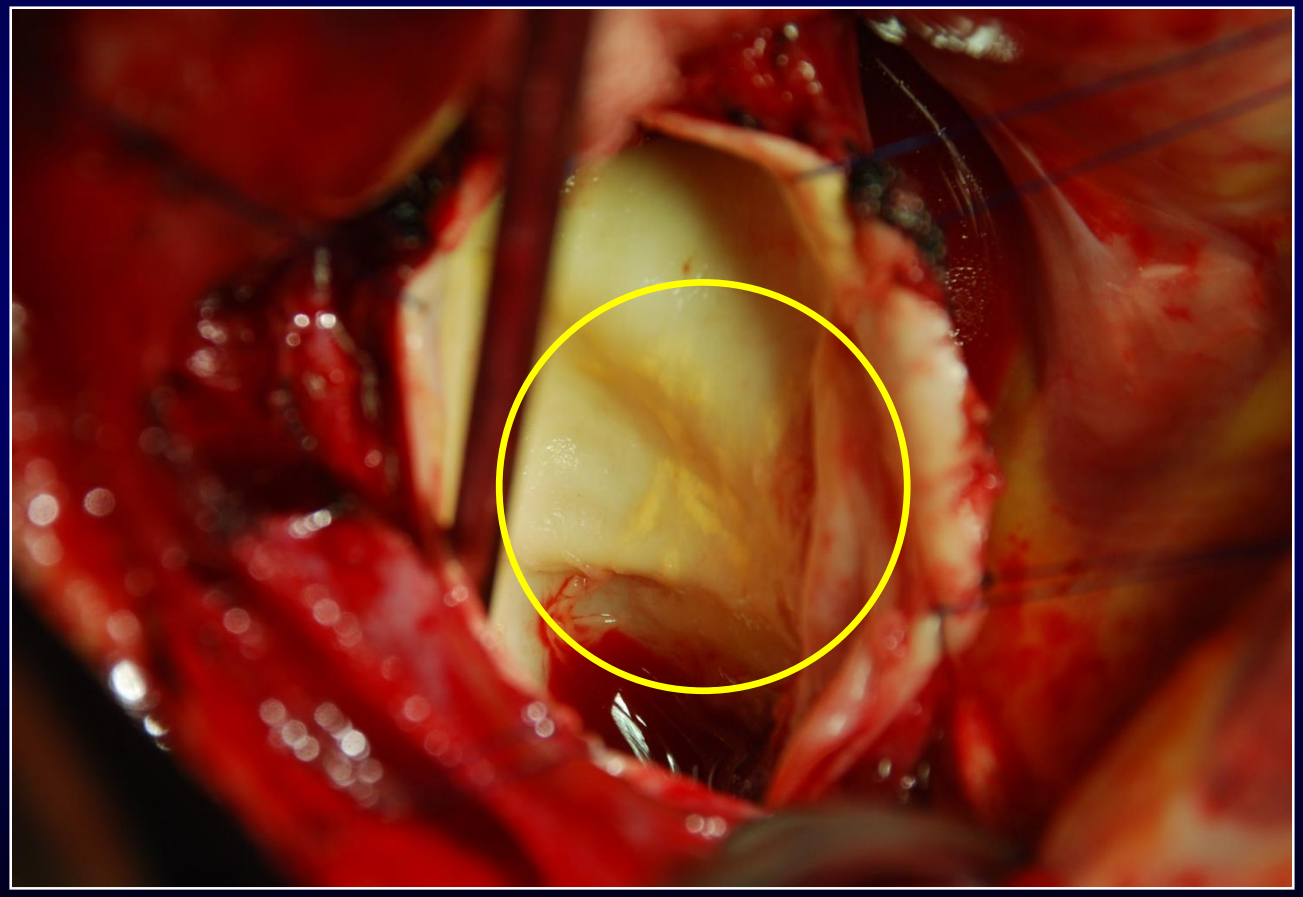
DHCA, deep hypothermic circulatory arrest;

MHCA, moderate hypothermic circulatory arrest.

TRICKS AND TIPS

The correct arterial dissection plane

Yellow-fibro-lipid plaques included into the removed cast



REVERSE ARIADNE'S THREAD

The correct arterial dissection plane

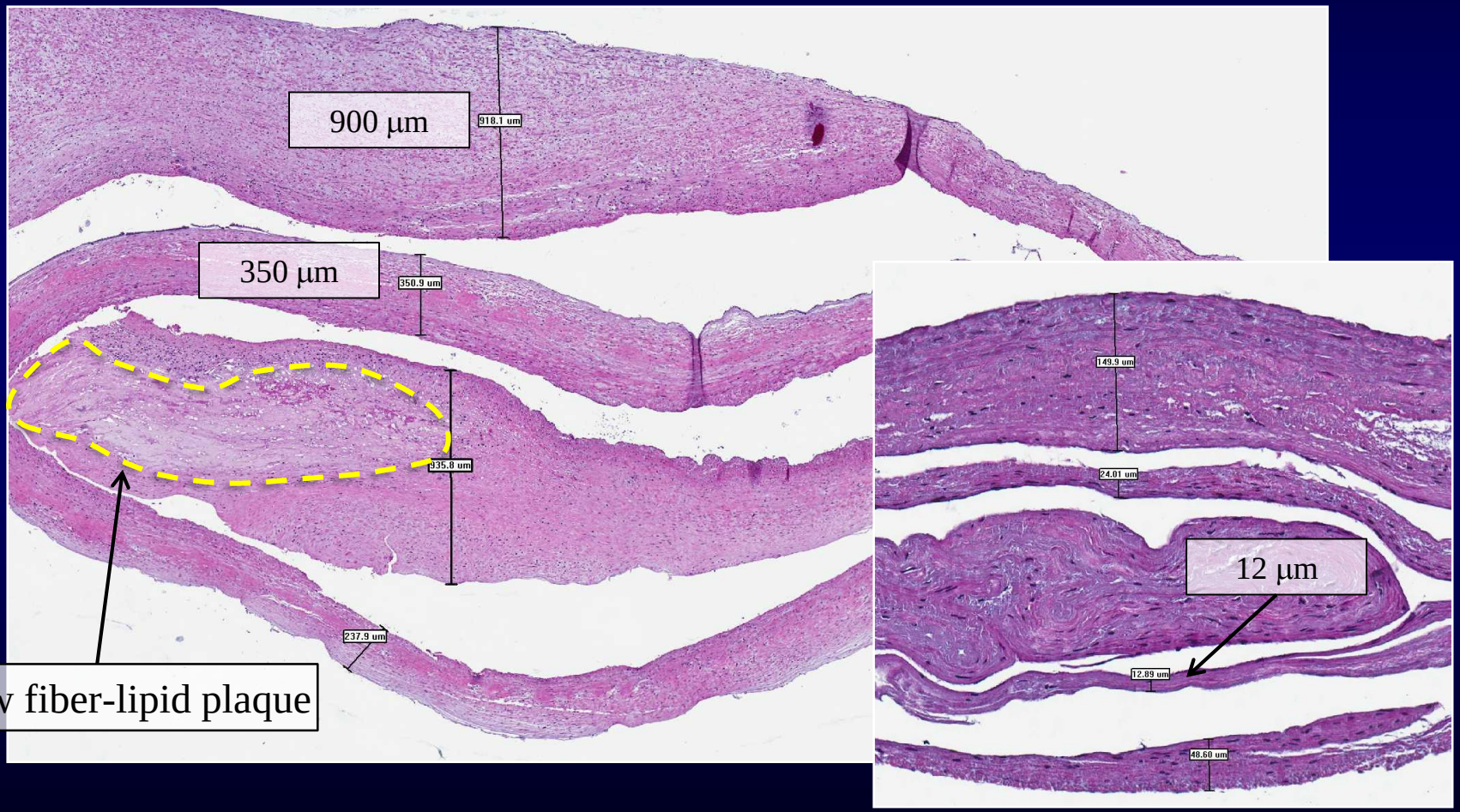
Yellow-fibro-lipid plaques included into the removed cast

TRICKS AND TIPS

Proximal dissection for the clearance of distal obstructions

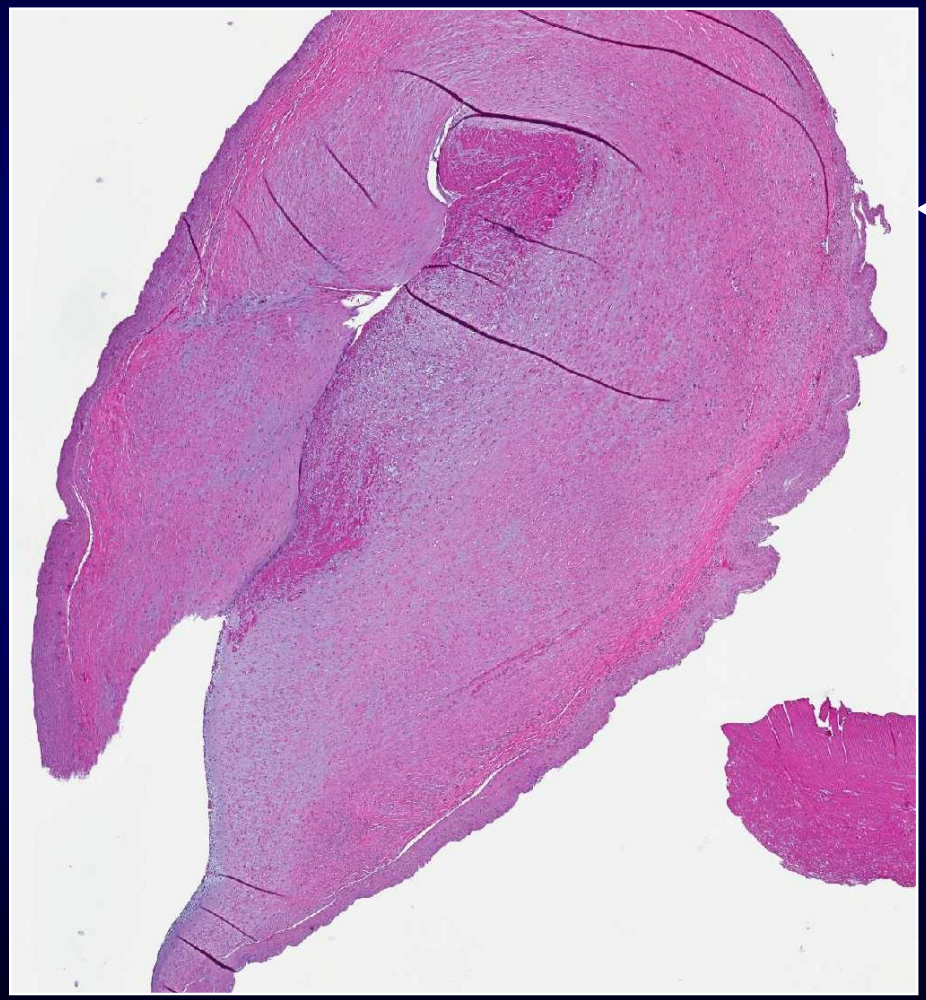
TRICKS AND TIPS

Proximal dissection for the clearance of distal obstructions

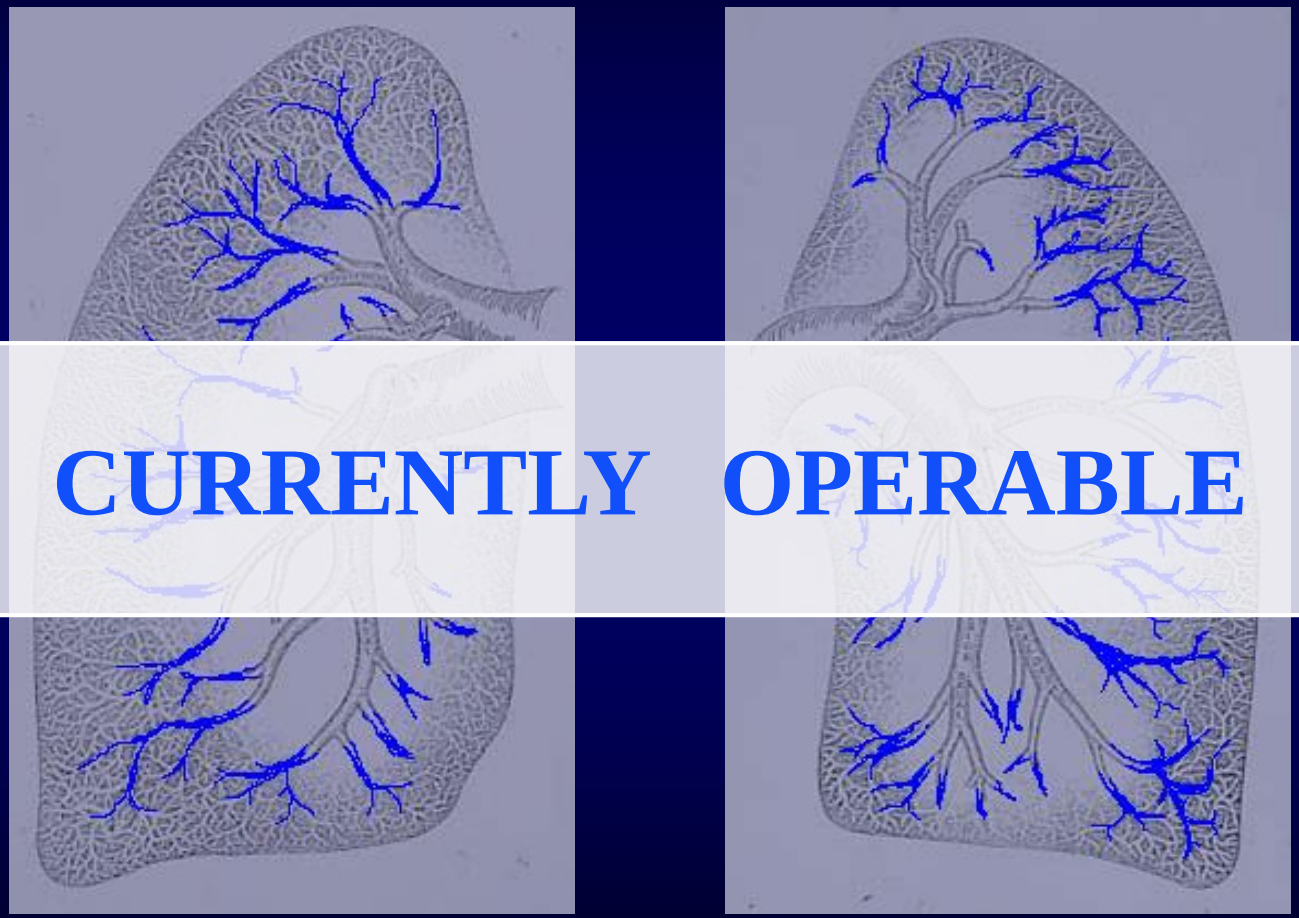


TRICKS AND TIPS

Proximal dissection for the clearance of distal obstructions

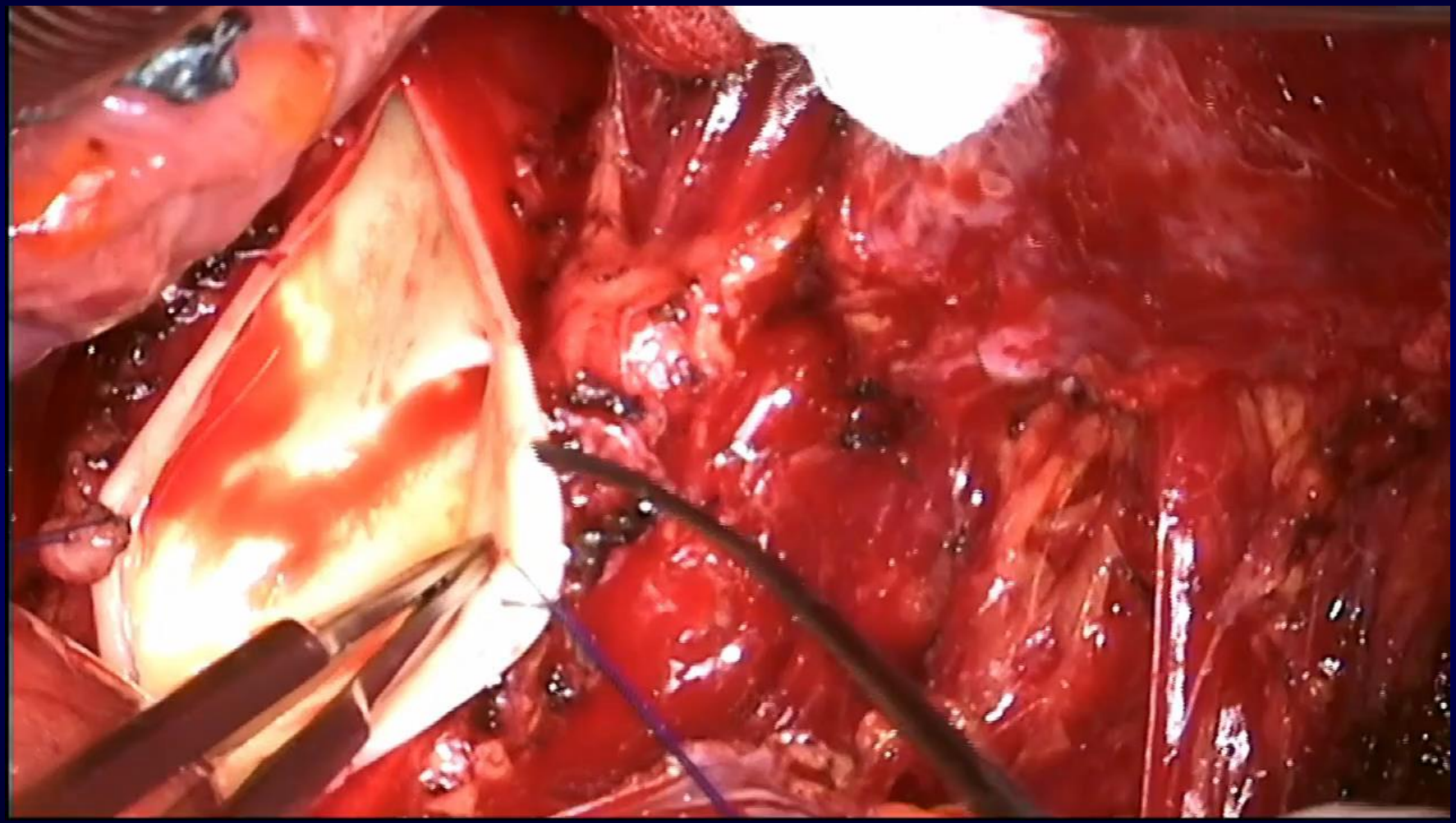


DISTAL LESIONS



CURRENTLY OPERABLE

EVOLVING SURGICAL TECHNIQUE – J3



DISTAL LESIONS

Pulmonary endarterectomy for distal chronic thromboembolic pulmonary hypertension

Andrea M. D'Armini, MD,[a,b] Marco Morsolini, MD, PhD,[a] Gabriella Mattiucci, MD,[a,b] Valentina Grazioli, MD,[a,b] Maurizio Pin, MD,[b] Adele Valentini, MD,[c] Giuseppe Silvaggio, MD,[b] Catherine Klersy, MD, MSc,[d] and Roberto Dore, MD[c]

(J Thorac Cardiovasc Surg 2014;148:1005-12)

DISTAL LESIONS

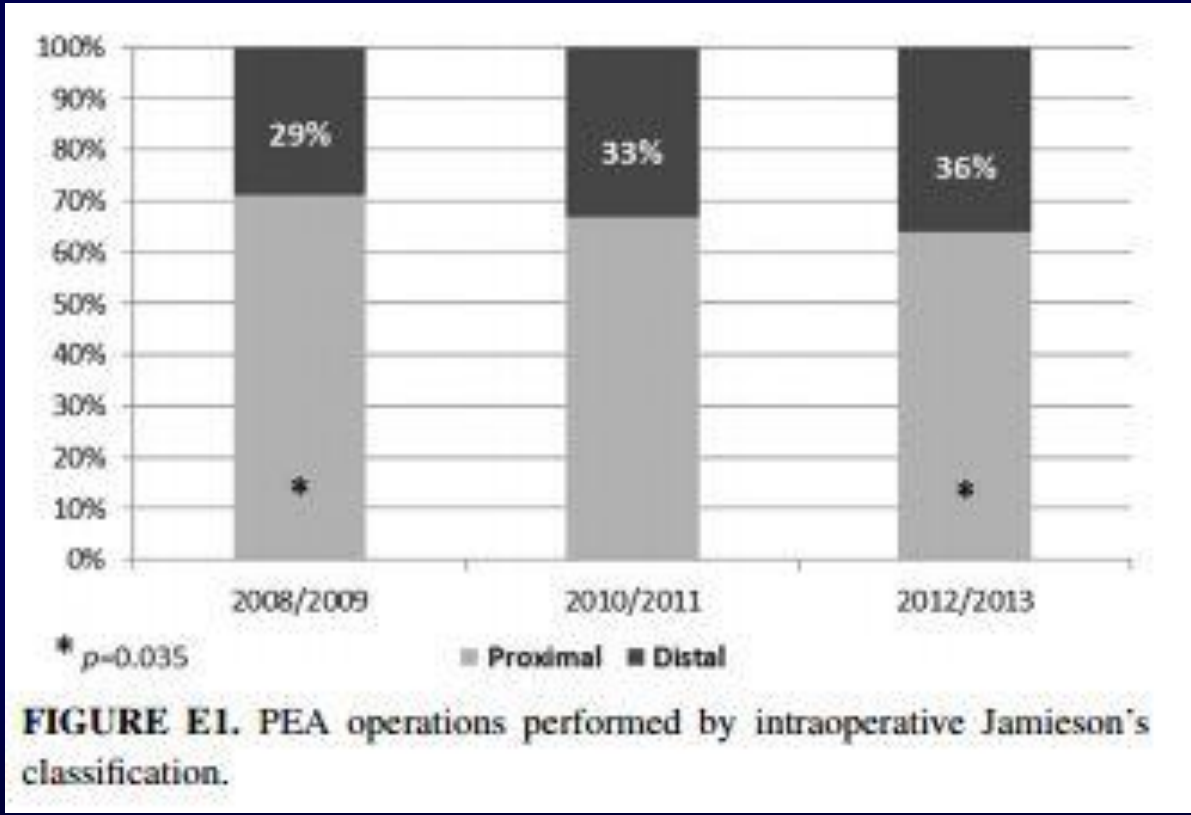


FIGURE E1. PEA operations performed by intraoperative Jamieson's classification.

DISTAL LESIONS

TABLE 2. Intraoperative comparison and early postoperative outcome

	Proximal	Distal	*P* value
Bilateral PEA (n)	192 (86.9)	95 (86.4)	1.000
Associated procedures (n)	38 (17.2)	19 (17.3)	1.000
Total CPB time (min)	338 ± 81 (327-348)	361 ± 64 (349-373)	**.005**
Hypothermia (°C)	24.0 ± 0.9 (23.9-24.1)	23.7 ± 1.0 (23.5-23.8)	**.003**
Total HCA time (min)	84 ± 32 (80-89)	102 ± 28 (97-107)	**<.001**
P_{AO_2}/F_{IO_2} 6 h	284 ± 91 (271-296)	280 ± 112 (259-301)	.758
MV duration (d)	2 (1-3)	2 (1-4)	.565
ICU stay (d)	4 (3-7)	4 (3-8)	.962
Postoperative hospital stay (d)	13 (10-16)	13 (11-17)	.541

	Risk	Risk difference (95% CI)	*P* value
Univariate analysis			
Hospital mortality		1.8 (−4.2 to 7.9)	.647
Proximal	6.3%		
Distal	8.1%		
Lung reperfusion edema		−0.5 (−4.4 to 3.4)	1.000
Proximal	3.2%		
Distal	2.7%		
Tracheostomy		−1.9 (−7.8 to 3.9)	.662
Proximal	8.3%		
Distal	6.4%		
Neurologic event		−4.7 (−10.6 to 1.1)	.209
Proximal	10.2%		
transient 13/22			
permanent 9/22			
Distal	5.5%		
transient 5/6			
permanent 1/6			

Bold values indicate significance ($P < .05$). *CI*, Confidence interval; *CPB*, cardiopulmonary bypass; *HCA*, hypothermic circulatory arrest; *ICU*, intensive care unit; *MV*, mechanical ventilation; P_{AO_2}/F_{IO_2} *6 h*, partial pressure of oxygen in arterial blood/fraction of inspired oxygen ratio 6 hours after admission to ICU; *PEA*, pulmonary endarterectomy.

DISTAL LESIONS

TABLE 3. Hemodynamic time course after pulmonary endarterectomy

	Proximal	Distal
Mean pulmonary arterial pressure (mm Hg)		
Preoperative	44 ± 10	46 ± 11
At discharge	22 ± 7	24 ± 6
3-mo follow-up	24 ± 9	25 ± 7
12-mo follow-up	23 ± 7	24 ± 8
P value*	<.001	<.001
PVR (dyne·s·cm^{-5})		
Preoperative	876 ± 392	926 ± 337
At discharge	251 ± 146	295 ± 161
3-mo follow-up	270 ± 175	300 ± 139
12-mo follow-up	243 ± 115	300 ± 224
P value*	<.001	<.001
Cardiac output (L/min)		
Preoperative	3.9 ± 1.3	3.7 ± 1.2
At discharge	5.0 ± 1.2	4.7 ± 1.2
3-mo follow-up	5.2 ± 1.1	5.0 ± 1.2
12-mo follow-up	5.0 ± 1.1	4.7 ± 1.0
P value*	<.001	<.001

PVR, Pulmonary vascular resistance. *Each time point versus preoperative. Test of interaction: $P = .975$ (mean pulmonary arterial pressure); $P = .777$ (PVR); $P = .825$ (cardiac output).

DISTAL LESIONS

TABLE 4. Partial pressure of oxygen in arterial blood, modified Bruce exercise test, and 6-minute walking distance time course after pulmonary endarterectomy

	Proximal	Distal
Arterial partial pressure of oxygen (mm Hg)		
Preoperative	65 ± 12	66 ± 11
3-mo follow-up	82 ± 13	80 ± 11
12-mo follow-up	80 ± 11	80 ± 11
P value*	<.001	<.001
Modified Bruce exercise test (m)		
Preoperative	51 (0-143)	52 (0-102)
3-mo follow-up	495 (182-658)	435 (143-586)
12-mo follow-up	520 (261-709)	474 (225-620)
P value*	<.001	<.001
6-min walking distance (m)		
Preoperative	277 ± 118	289 ± 112
3-mo follow-up	391 ± 118	398 ± 107
12-mo follow-up	389 ± 118	396 ± 112
P value*	<.001	<.001

*Each time point versus preoperative. Test of interaction: $P = .317$ (partial pressure of oxygen in arterial blood); $P = .205$ (modified Bruce exercise test); $P = .962$ (6-min walking distance).

DISTAL LESIONS

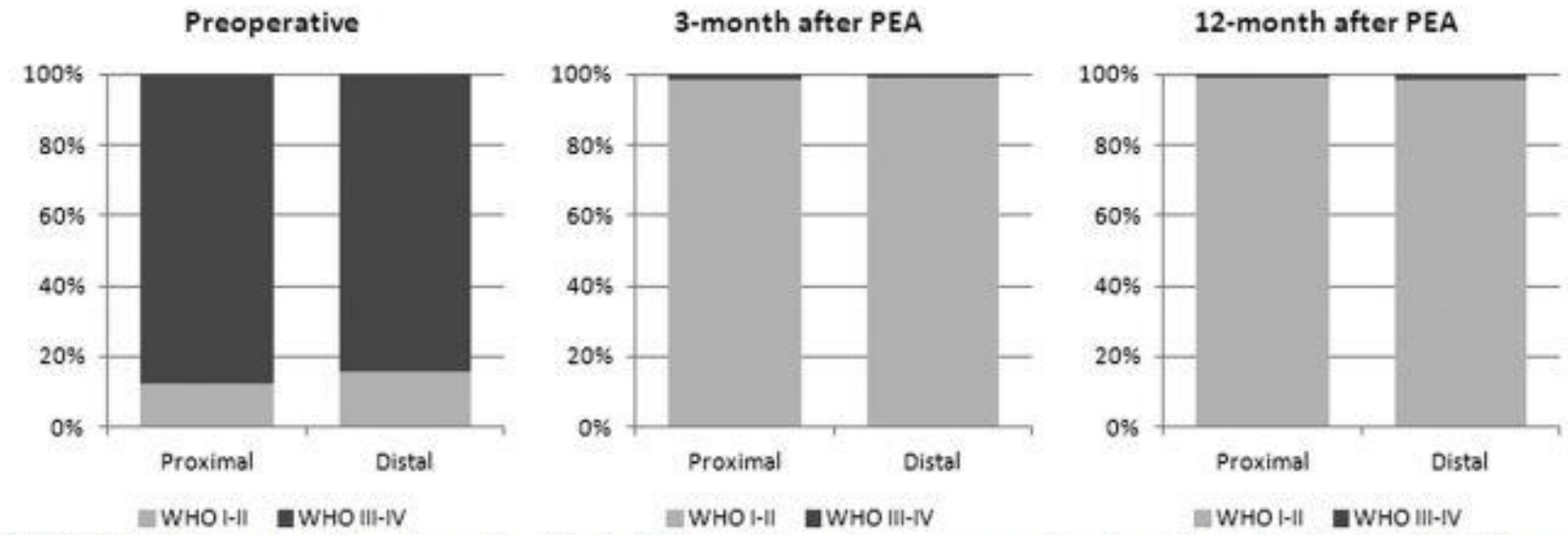


FIGURE E2. WHO functional class changes after PEA. $P < .001$ at each time point versus preoperative. Test of interaction: $P = .327$. *PEA*, Pulmonary endarterectomy; *WHO*, World Health Organization.

DISTAL LESIONS

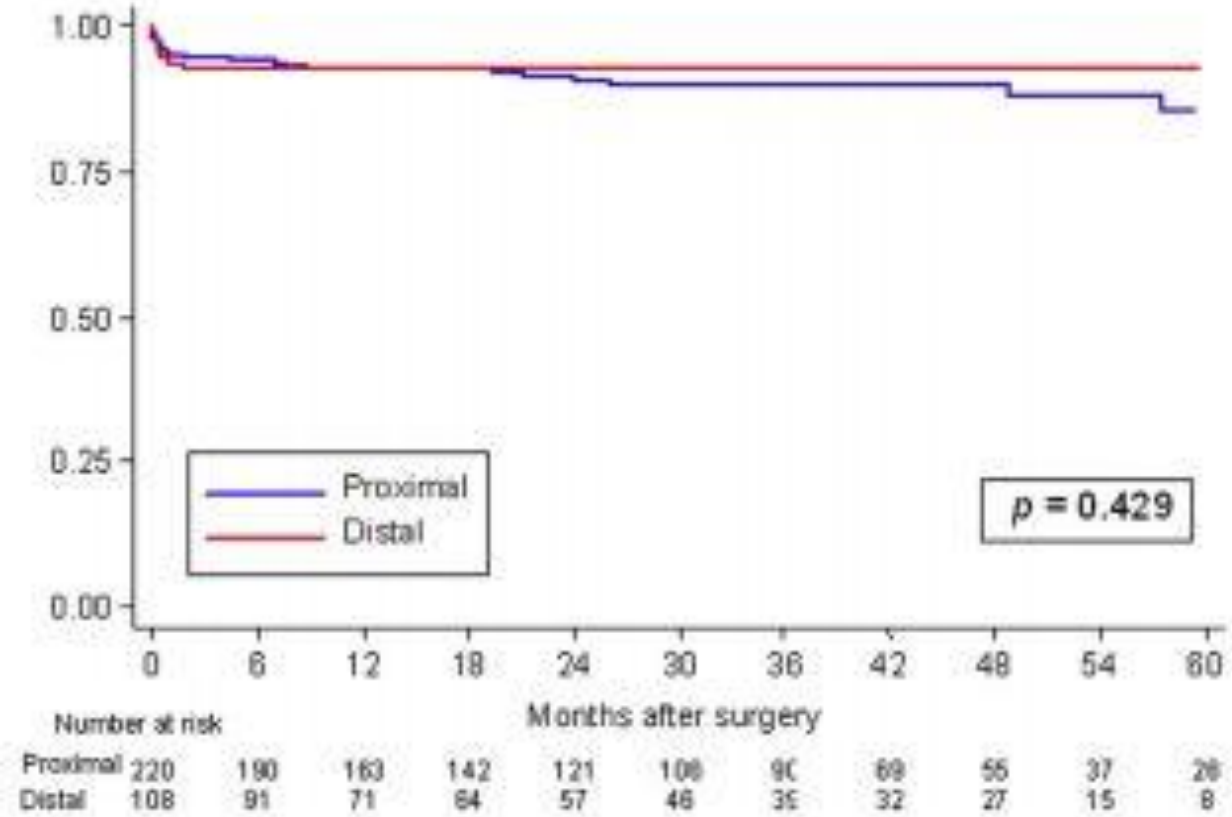
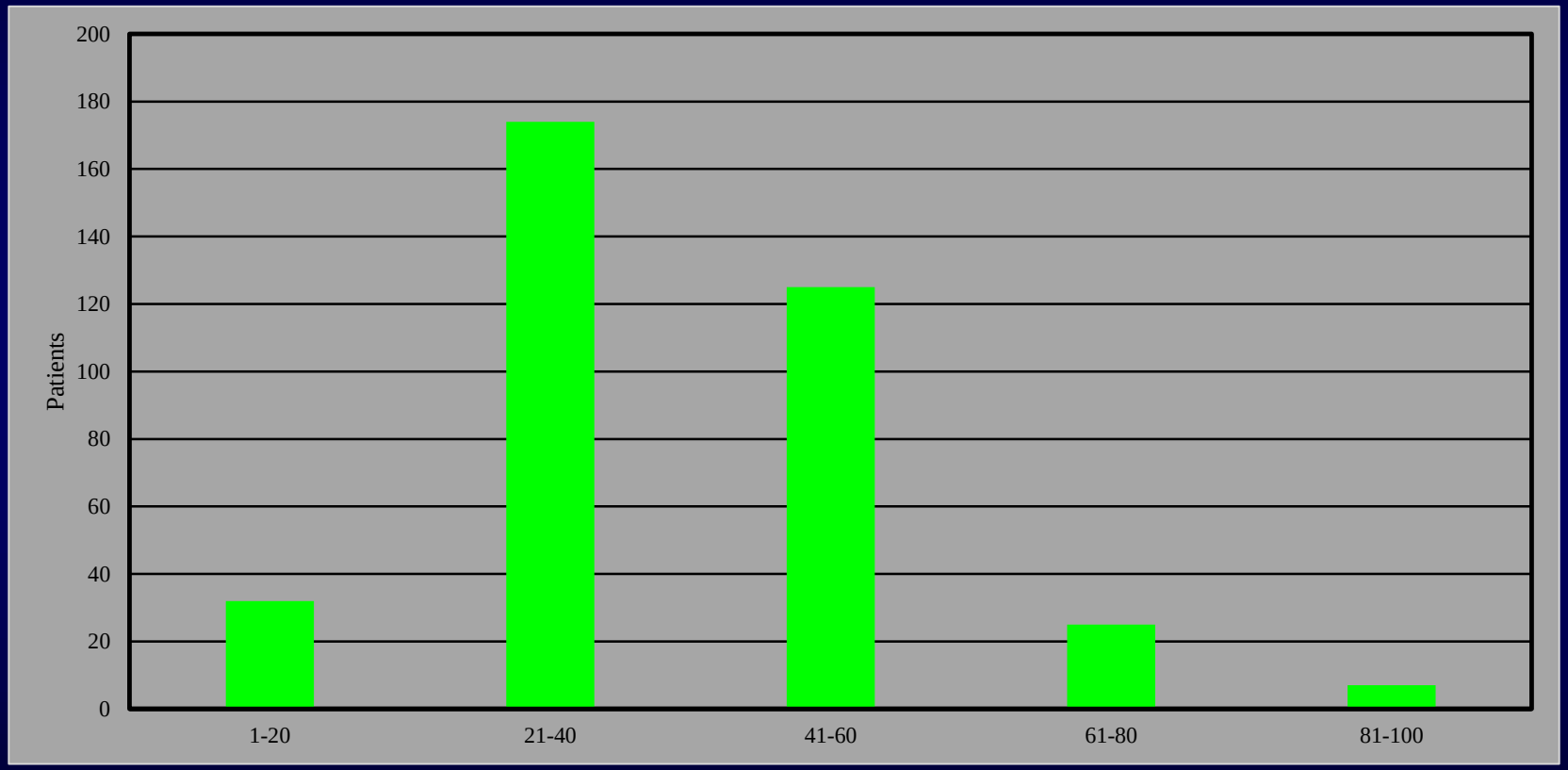


FIGURE 1. Survival after PEA.

PLANTY vs. SCARSE CTE OCCLUSIONS

GROUPED BY REOPENED BRANCHES

344 PEA



REOPENED BRANCHES AND TCA

	N°	Mean	SD	Min	P25	P50	P75	Max
Reopened Branches	344	38.7	± 15.7	7	28	37	48	100
TCA (min)	344	93.5	± 26.9	0	77	93	113	162

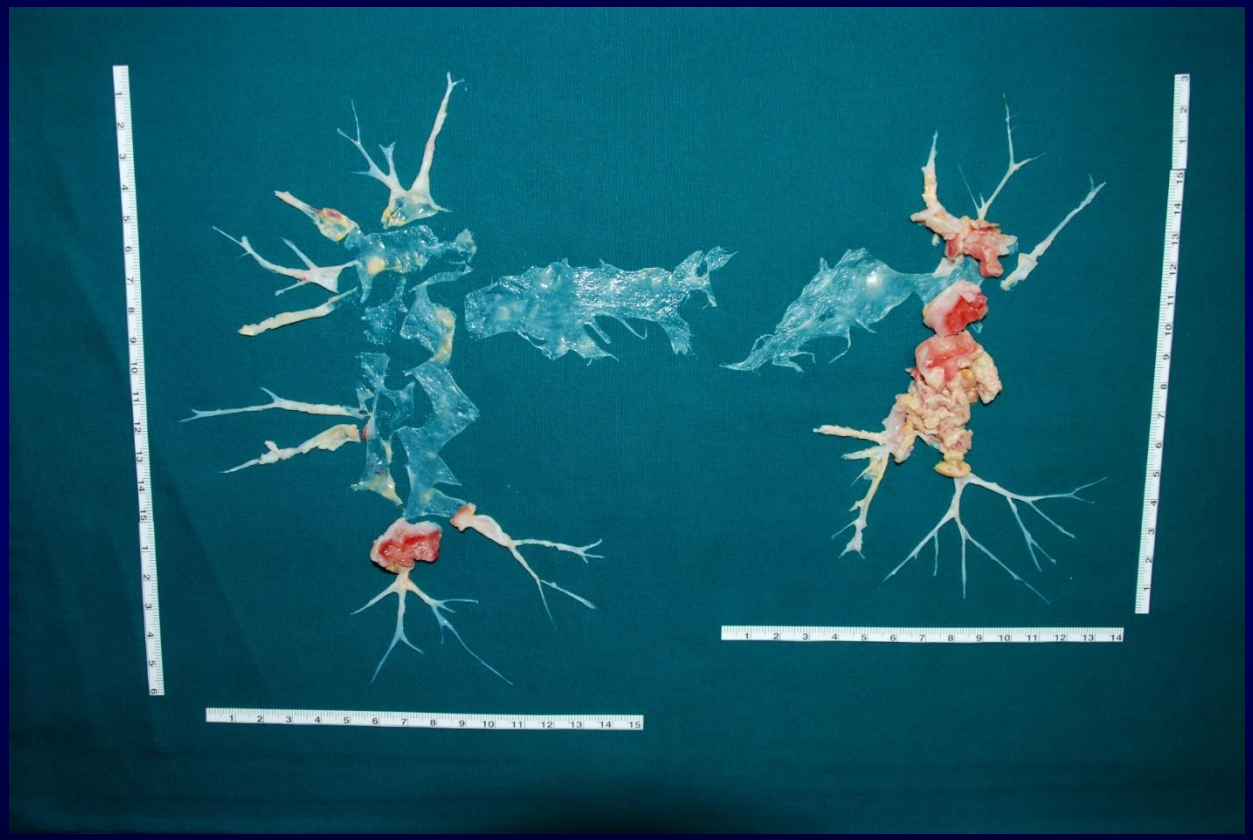
ASSOCIATION OF HEMODYNAMIC AND PAO2 DATA AT 3 MONTHS AND THE NUMBER OF REOPENED BRANCHES

	Number of Reopened branches subgroups (tertiles)						Number of Reopened branches (continuous)		
Outcome measure at 3 months	(a) Branches reopened 7-26	(b) Branches reopened 27-41	(c) Branches reopened 42-100	Univariable Model P value*	Multivariable Model P value**		Sperman's rho	Univariable Model P value	Multivariable Model P value**
PVR (dyne/sec/cm^{-5})	315 ± 163	277 ± 148	232 ± 105	< 0.001 a vs b 0.35 a vs c 0.001 b vs c 0.06	0.045 a vs b 0.41 a vs c 0.040 b vs c 0.64		- 0.25	< 0.001	< 0.001
CO (l/min)	5.1 ± 1.1	5.0 ± 1.2	5.2 ± 1.1	0.31	0.33		0.07	0.37	0.83
CI (l/min/m^2)	2.8 ± 0.5	2.7 ± 0.5	2.8 ± 0.5	0.34	0.29		0.05	0.43	0.92
mPAP (mmHg)	26 ± 9	24 ± 8	22 ± 6	0.009 a vs b 0.25 a vs c 0.007 b vs c 0.46	0.027 a vs b 0.15 a vs c 0.022 b vs c 1.00		- 0.18	<0.001	<0.001
PAO2 (mmHg)	77.4 ± 13.1	79.7± 12.3	82.2 ± 11.3	0.06	0.35		0.17	0.003	0.05

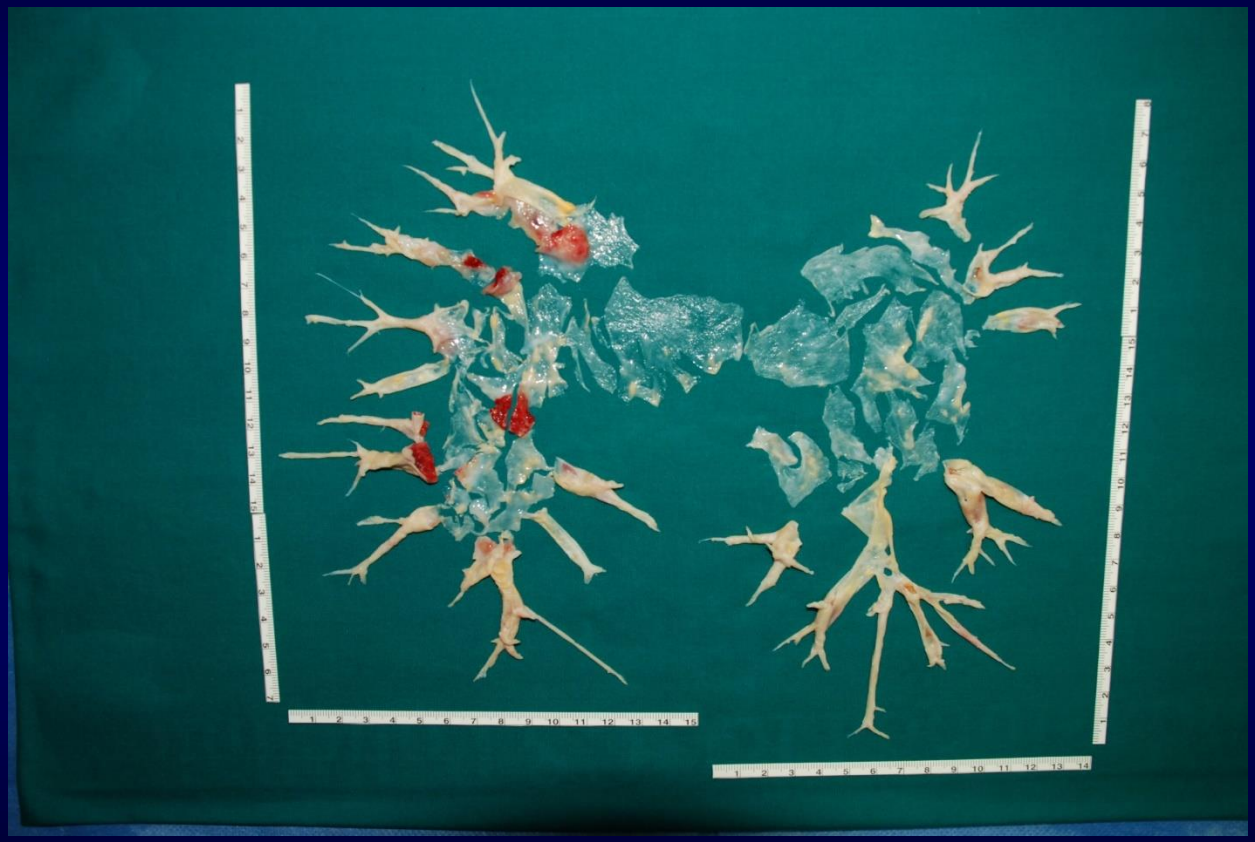
ASSOCIATION OF FUNCTIONAL DATA AT 3 MONTHS AND THE NUMBER OF REOPENED BRANCHES

	Number of Reopened branches subgroups (tertiles)					Number of Reopened branches (continuous		
	(a) Branches reopened 7-26	(b) Branches reopened 27-41	(c) Branches reopened 42-100	Univariable Model P value*	Multivariable Model P value**	Mean ± SD	Univariable Model P value*	Multivariable Model P value**
WHO class **I/II** **III/IV**	5 (9%)	4 (4%)	0 (0%)	0.000	0.17	24 ± 7		
6 mWD (m) **≥400** **<400**	19 (38%)	42 (45%)	71 (64%)	0.003 a vs b 1.00 a vs c 0.009 b vs c 0.023	0.036 a vs b 1.00 a vs c 0.06 b vs c 0.20	 43 ± 16 37 ± 15	0.004	0.013
Bruce (m) **≥400** **<400**	18 (43%)	39 (48%)	76 (72%)	<0.000 a vs b 1.00 a vs c 0.003 b vs c 0.003	0.021 a vs b 1.00 a vs c 0.047 b vs c 0.083	 44 ± 16 36 ± 15	<0.001	0.003

SURGICAL SPECIMENTS – J1



SURGICAL SPECIMENTS – J2



SURGICAL SPECIMENTS – J3

RESULTS

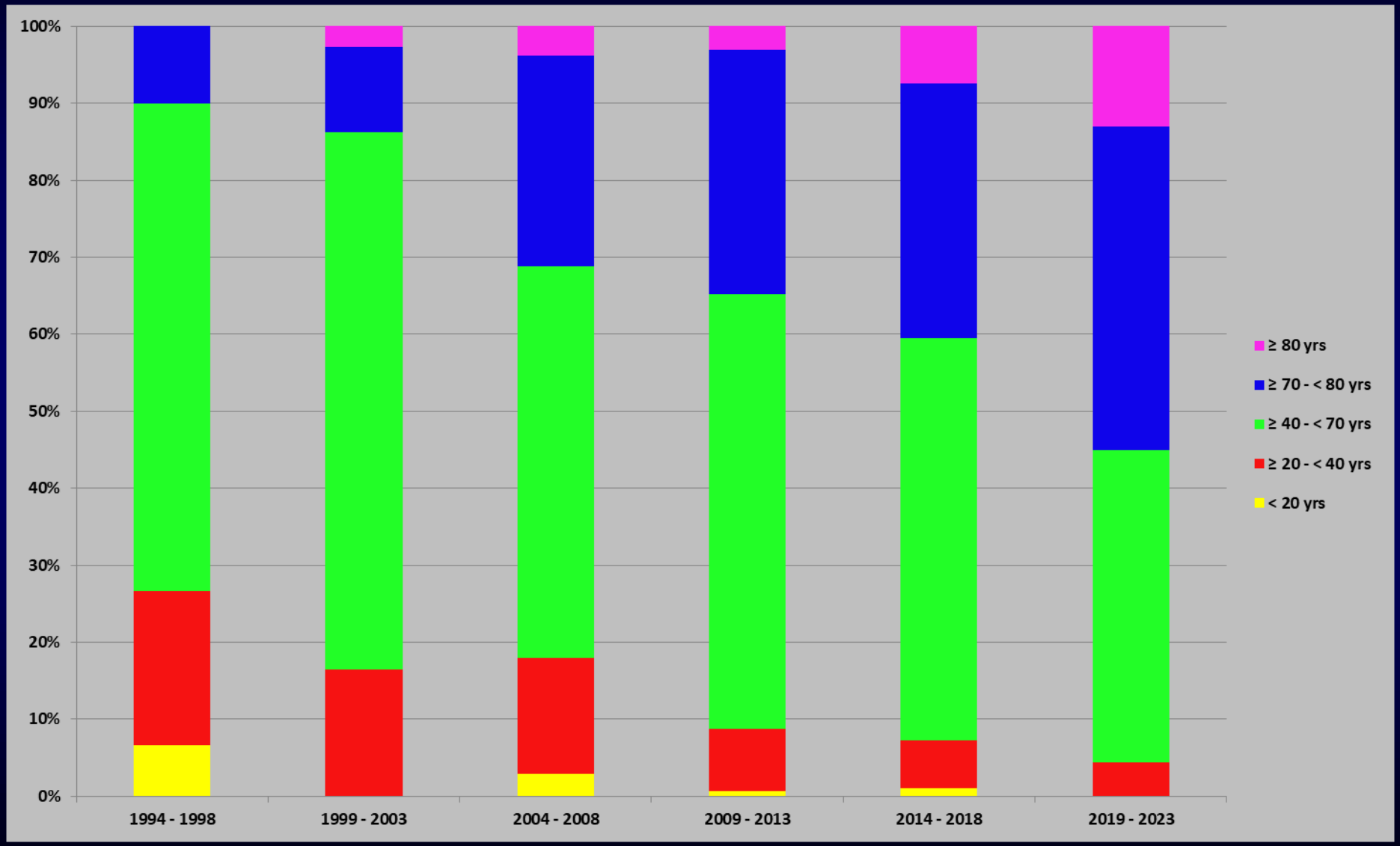
Our study shows a *clear correlation* between the *number* of *reopened pulmonary artery branches* and *hemodynamic values* and *functional data (pO2, NYHA functional class, 6mwt and modified Bruce test) already at 3 months*

CONCLUSIONS

In our hands a *longer TCA time* allows the surgeon to explore *all the pulmonary vascular bed*, find *unexpected chronic thromboembolic material* and *clean more branches* even in more complex clinical conditions as well as in *distal vassels*

AGE

OF 975 PEAs



PAVIA CTEPH PROGRAM

January, 1st – December, 31st 2018 → 462

NewEvaluations (215 pts) CTEPH-PEA FUP (245 pts) PAS-PEA FUP (2 pts)

CONFIRMED (121 pts - 56%)

- PROXIMAL LESIONS (115 pts)
  - 66 PEAs (3 pts evaluated in 2017)
  - 13 waiting for PEA
  - 10 refused evaluation for PEA
  - 3 refused PEA
  - 19 with severe co-morbidities (1 pt evaluated in 2017)
  - 3 died before evaluation or before PEA
  - 1 complete occlusion with vessel retraction
  - 2 asyntomatic CTED
  - 2 bridge to candidacy

OPERABILITY RATE ***thecnically 95%***
+ comorbidity 79%
+ refused 69%

- BPA program (6 pts)
  - 1 waiting for BPA
  - 5 too early for BPA → Riociguat

OTHER DIAGNOSIS (94 pts - 44%)

- RECENT APE (23 pts)
  - 22 medical therapy - 1 embolectomy
- PREVIOUS APE WITHOUT SIGNS (7 pts)
  - 7 medical therapy
- APE OVER CTE LESIONS (3 pts)
  - 3 3-month m.t.→new evaluation
- MINIMAL CTE LESIONS WITHOUT/LOW PH (16 pts)
  - 16 medical therapy
- PULMONARY ARTERY SARCOMA (5 pts)
  - 4 inoperable - 1 refused evaluation or PEA
- PULMONARY ARTERY ANEURYSM (3 pts)
  - 2 medical therapy - 1 interventional therapy
- MISCELLANEOUS (37 pts)

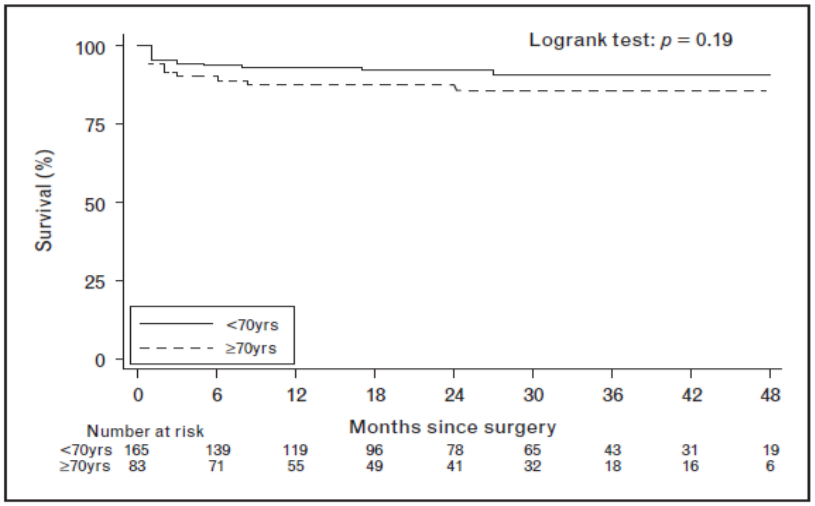
ELDERLY PATIENTS

Pulmonary endarterectomy in the elderly: safety, efficacy and risk factors

Nicola Vistarini[a], Marco Morsolini[a], Catherine Klersy[b], Gabriella Mattiucci[a], Valentina Grazioli[a], Maurizio Pin[a], Stefano Ghio[c] and Andrea Maria D'Armini[a]

J Cardiovasc Med 2016, 17:144–151

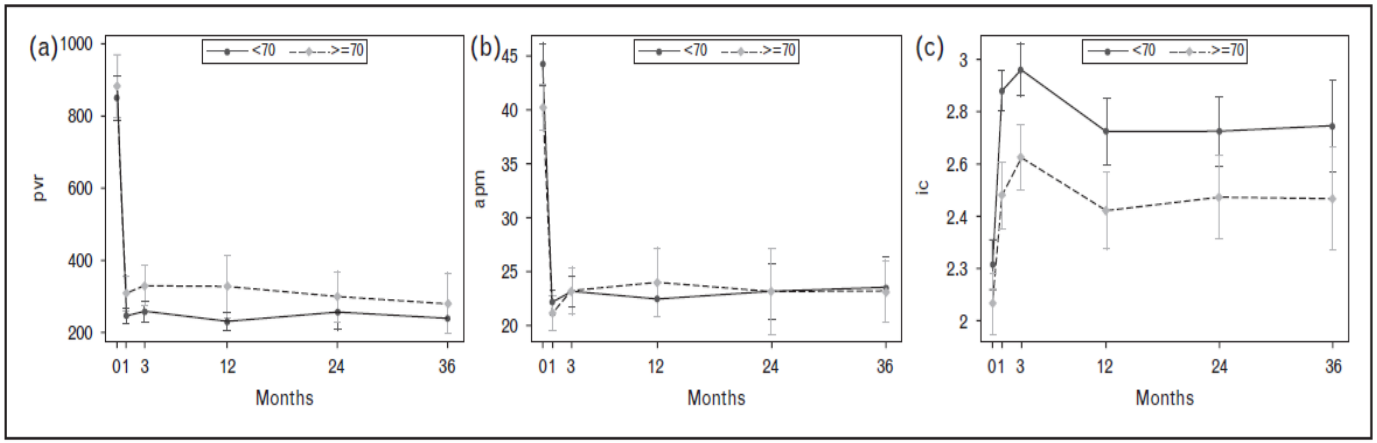
AGE



Kaplan–Meier curves for survival after pulmonary endarterectomy, dichotomized by age.

J Cardiovasc Med 2016, 17:144–151

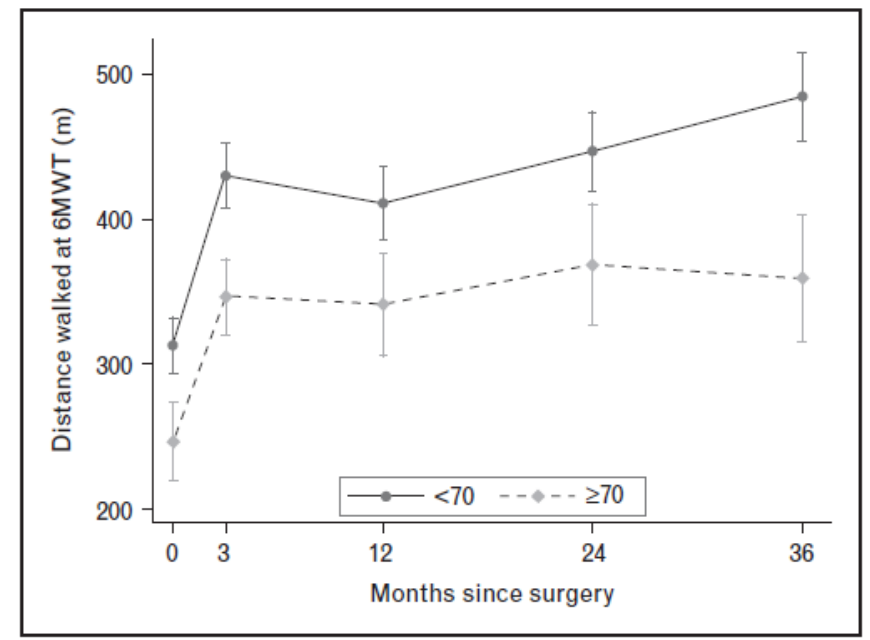
AGE



Hemodynamic evaluations over time in the two study populations. (a) Pulmonary vascular resistances (pvr); (b) pulmonary arterial pressure (apm); (c) cardiac output (ic).

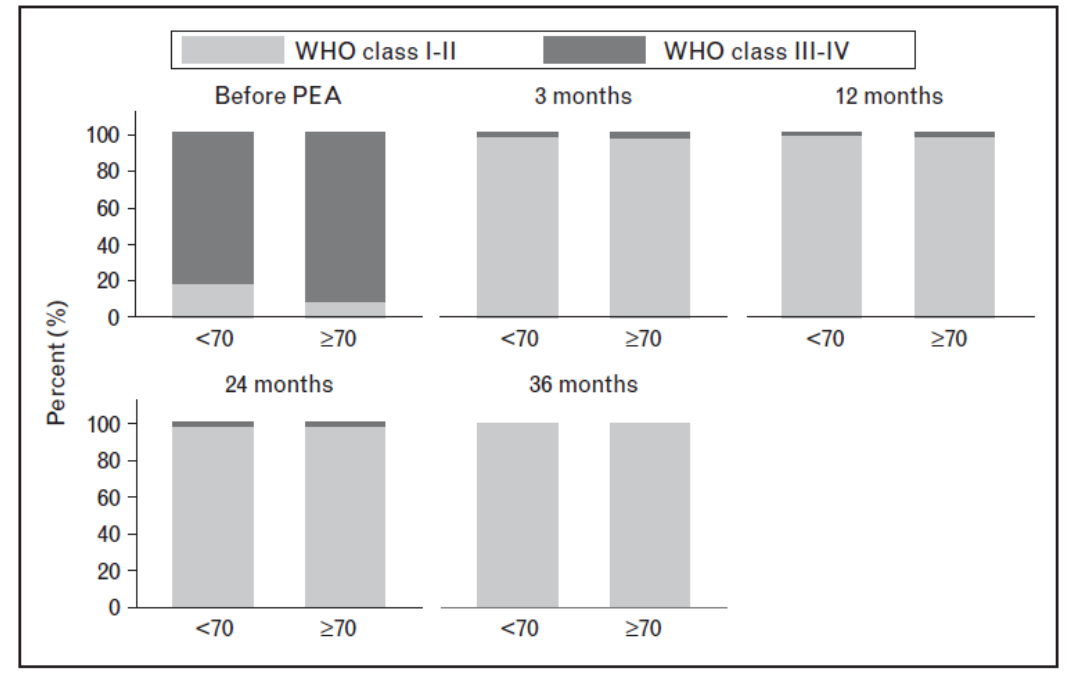
J Cardiovasc Med 2016, 17:144–151

AGE



J Cardiovasc Med 2016, 17:144–151

ELDERLY PATIENTS



J Cardiovasc Med 2016, 17:144–151

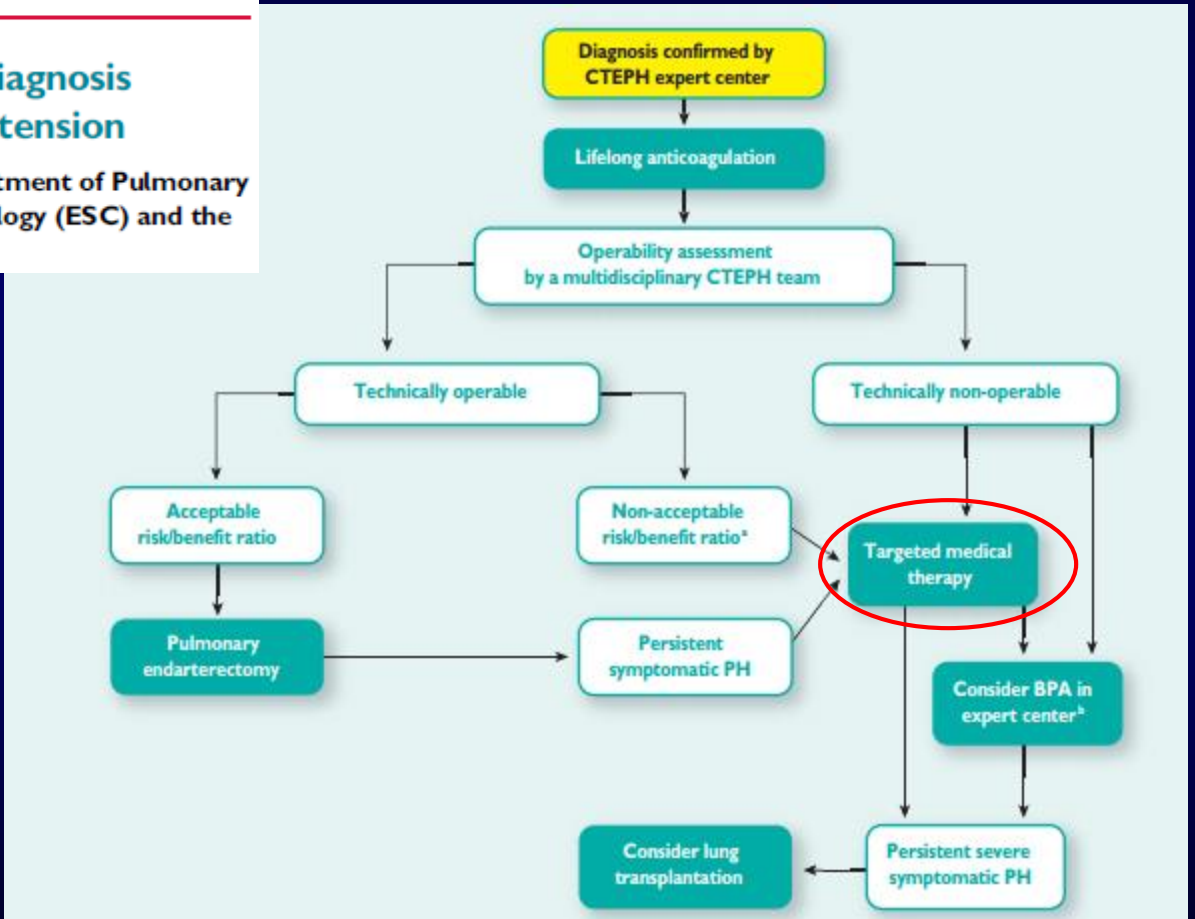
TARGETED MEDICAL THERAPY IN THE GUIDELINES FOR CTEPH

European Heart Journal
doi:10.1093/eurheartj/ehv317

ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)



BPA = balloon pulmonary angioplasty; CTEPH = chronic thromboembolic pulmonary hypertension; PH = pulmonary hypertension.
[a]Technically operable patients with non-acceptable risk/benefit ratio can be considered also for BPA.
[b]In some centers medical therapy and BPA are initiated concurrently.

BENEFiT STUDY

CLINICAL RESEARCH Clinical Trials

Bosentan for Treatment of Inoperable Chronic Thromboembolic Pulmonary Hypertension

BENEFiT (Bosentan Effects in iNopErable Forms of chronIc Thromboembolic pulmonary hypertension), a Randomized, Placebo-Controlled Trial

Xavier Jaïs, MD,* Andrea M. D'Armini, MD,† Pavel Jansa, MD,‡ Adam Torbicki, MD,§ Marion Delcroix, MD,‖ Hossein A. Ghofrani, MD,¶ Marius M. Hoeper, MD,# Irene M. Lang, MD,** Eckhard Mayer, MD,†† Joanna Pepke-Zaba, MD,‡‡ Loïc Perchenet, PHD,§§ Adele Morganti, MSC,§§ Gérald Simonneau, MD,* Lewis J. Rubin, MD,‖‖ for the BENEFiT Study Group

Clamart, France; Pavia, Italy; Prague, Czech Republic; Warsaw, Poland; Leuven, Belgium; Giessen, Hannover, and Mainz, Germany; Vienna, Austria; Cambridge, United Kingdom; Allschwil, Switzerland; and La Jolla, California

J Am Coll Cardiol 2008 Dec16;52(25):2127-34

CHEST STUDY

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Riociguat for the Treatment of Chronic Thromboembolic Pulmonary Hypertension

Hossein-Ardeschir Ghofrani, M.D., Andrea M. D'Armini, M.D., Friedrich Grimminger, M.D., Marius M. Hoeper, M.D., Pavel Jansa, M.D., Nick H. Kim, M.D., Eckhard Mayer, M.D., Gerald Simonneau, M.D., Martin R. Wilkins, M.D., Arno Fritsch, Ph.D., Dieter Neuser, M.D., Gerrit Weimann, M.D., and Chen Wang, M.D., for the CHEST-1 Study Group*

N Engl J Med 2013 Jul25;369(4):319-29

CHEST STUDY

ORIGINAL ARTICLE
PULMONARY VASCULAR DISEASES

Riociguat for the treatment of chronic thromboembolic pulmonary hypertension: a long-term extension study (CHEST-2)

Gérald Simonneau[1], Andrea M. D'Armini[2], Hossein-Ardeschir Ghofrani[3,4], Friedrich Grimminger[3], Marius M. Hoeper[5], Pavel Jansa[6], Nick H. Kim[7], Chen Wang[8], Martin R. Wilkins[9], Arno Fritsch[10], Neil Davie[10], Pablo Colorado[11] and Eckhard Mayer[12]

Eur Respir J 2015 May;45(5):1293-302

MERIT-1 STUDY

Macitentan for the treatment of inoperable chronic thromboembolic pulmonary hypertension (MERIT-1): results from the multicentre, phase 2, randomised, double-blind, placebo-controlled study

*Hossein-Ardeschir Ghofrani, Gérald Simonneau, Andrea M D'Armini, Peter Fedullo, Luke S Howard, Xavier Jaïs, David P Jenkins, Zhi-Cheng Jing, Michael M Madani, Nicolas Martin, Eckhard Mayer, Kelly Papadakis, Dominik Richard, Nick H Kim, on behalf of the MERIT study investigators**

Lancet Respir Med 2017 Oct;5(10):785–94

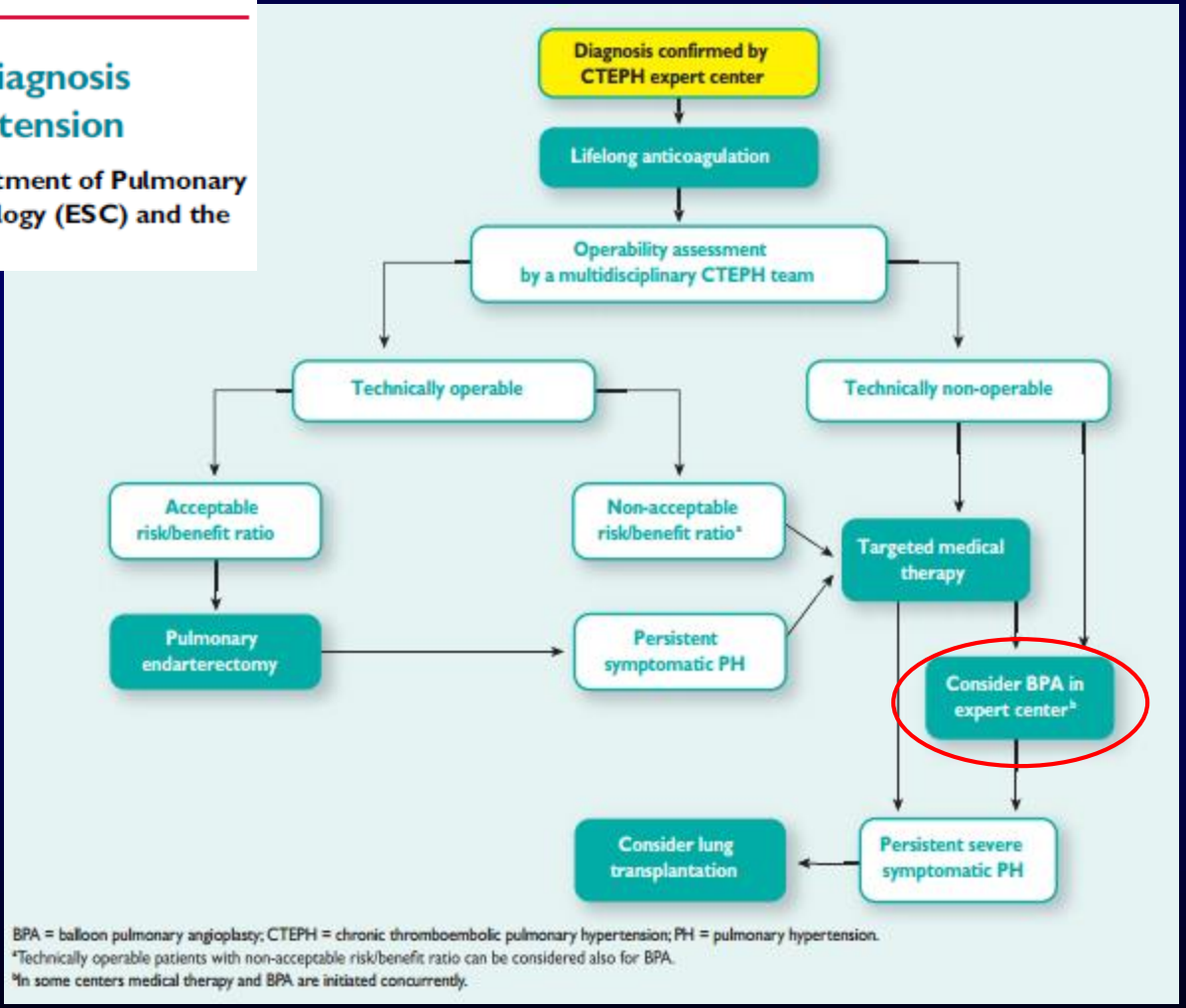
BPA IN THE GUIDELINES FOR CTEPH

European Heart Journal
doi:10.1093/eurheartj/ehv317

ESC/ERS GUIDELINES

2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension

The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS)



BPA = balloon pulmonary angioplasty; CTEPH = chronic thromboembolic pulmonary hypertension; PH = pulmonary hypertension.
[a]Technically operable patients with non-acceptable risk/benefit ratio can be considered also for BPA.
[b]In some centers medical therapy and BPA are initiated concurrently.

BPA FOR CTEPH

Pulmonary Vascular Disease

Novel Angiographic Classification of Each Vascular Lesion in Chronic Thromboembolic Pulmonary Hypertension Based on Selective Angiogram and Results of Balloon Pulmonary Angioplasty

Takashi Kawakami, MD, PhD; Aiko Ogawa, MD, PhD; Katsumasa Miyaji, MD, PhD; Hiroki Mizoguchi, MD, PhD; Hiroto Shimokawahara, MD, PhD; Takanori Naito, MD; Takashi Oka, MD; Kei Yunoki, MD, PhD; Mitsuru Munemasa, MD, PhD; Hiromi Matsubara, MD, PhD

(*Circ Cardiovasc Interv*. 2016;9:e003318. DOI: 10.1161/CIRCINTERVENTIONS.115.003318.)

BPA FOR CTEPH

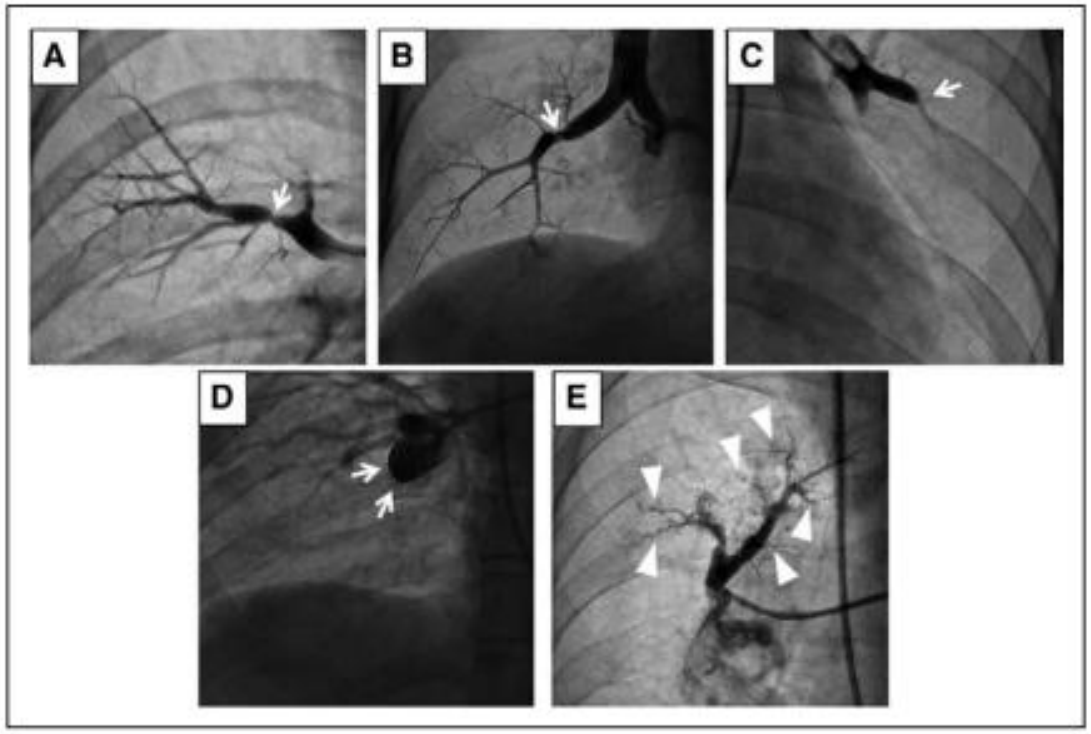


Figure 1. Angiographic classification of lesion morphology based on the lesion opacity and the blood flow distal to the lesion. **A**, Ring-like stenosis lesion. **B**, Web lesion. **C**, Subtotal lesion. **D**, Total occlusion lesion. **E**, Tortuous lesion. Type A–D lesions are located proximal to the subsegmental pulmonary artery, namely, the segmental and subsegmental arteries. Type E lesions are located distal to the subsegmental artery.

(*Circ Cardiovasc Interv*. 2016;9:e003318. DOI: 10.1161/CIRCINTERVENTIONS.115.003318.)

BPA FOR CTEPH

Table 3. Numbers and Distribution of Pulmonary Thromboembolic Lesions

Lesion Type	A	B	C	D	E
Description of Lesion Type	Ring-Like Stenosis	Web	Subtotal	Total Occlusion	Tortuous
Number, n	248	1235	342	67	44
Bifurcation lesion, n (%)	248 (100)	1092 (88.4)	301 (88.0)	61 (91.0)	0 (0)
Distribution (upper/middle or lingular/lower)					
Right lung, n	103/7/46	215/172/367	64/42/118	6/16/24	5/3/9
Left lung, n	29/0/63	61/22/398	13/6/99	0/2/19	6/1/20
QVA					
PRD, mm	3.7 (1.3–9.5)	3.7 (0.3–9.3)	3.8 (0.7–12.9)	4.8* (0.8–17.1)	2.8† (1.5–6.4)
DRD, mm	3.5 (0.3–8.2)	2.3‡ (0.1–11.1)	…	…	2.0‡ (0.8–4.4)
RD, mm	3.9 (0.7–8.3)	3.1‡ (0.1–8.3)	…	…	2.4‡ (1.1–5.0)
MLD, mm	1.6 (0.2–5.6)	1.6 (0.1–6.5)	…	…	1.6 (0.2–4.6)
%DS, %	58 (16–91)	45‡ (2–95)	…	…	39‡ (1–99)
Lesion length, mm	4.6 (1.4–14.8)	12.8‡ (2.0–49.6)	…	…	12.8‡ (0.2–27.8)
Used balloon					
Size, mm	4.0 (1.5–8)	3.5‡ (1.5–8)	3.5‡ (1.25–7)	4.0 (1.5–8)	2.0† (1.5–4.5)
Inflated pressure, atm	12 (2–22)	8‡ (2–18)	10 (2–20)	12 (3–18)	10 (2–16)
Success, n (%)	248 (100)	1219 (98.7)	296§ (86.5)	35‖ (52.2)	28 (63.6)
~~Complication, n (%)~~	~~4 (1.6)~~	~~27 (2.2)~~	~~53* (15.5)~~	~~4 (6.0)~~	~~19 (43.2)~~
Type of complication					
Balloon injury, n	3	7	5	0	0
Wire injury/perforation, n	0	12	41	4	19
Dissection of vessels, n	1	8	7	0	0

~~Values are presented as the median and the range. DRD indicates distal reference diameter; %DS, percent diameter stenosis; MLD, minimal lumen diameter; PRD,~~ proximal reference diameter; QVA, quantitative vascular analysis; and RD, reference diameter.

*$P<0.05$ vs ring-like stenosis, web and subtotal lesions.

†$P<0.01$ vs ring-like stenosis, web, subtotal and total occlusion lesions.

‡$P<0.01$ vs ring-like stenosis.

§$P<0.01$ vs ring-like stenosis and web lesion.

‖$P<0.01$ vs ring-like stenosis, web and subtotal lesions.

BPA FOR CTEPH

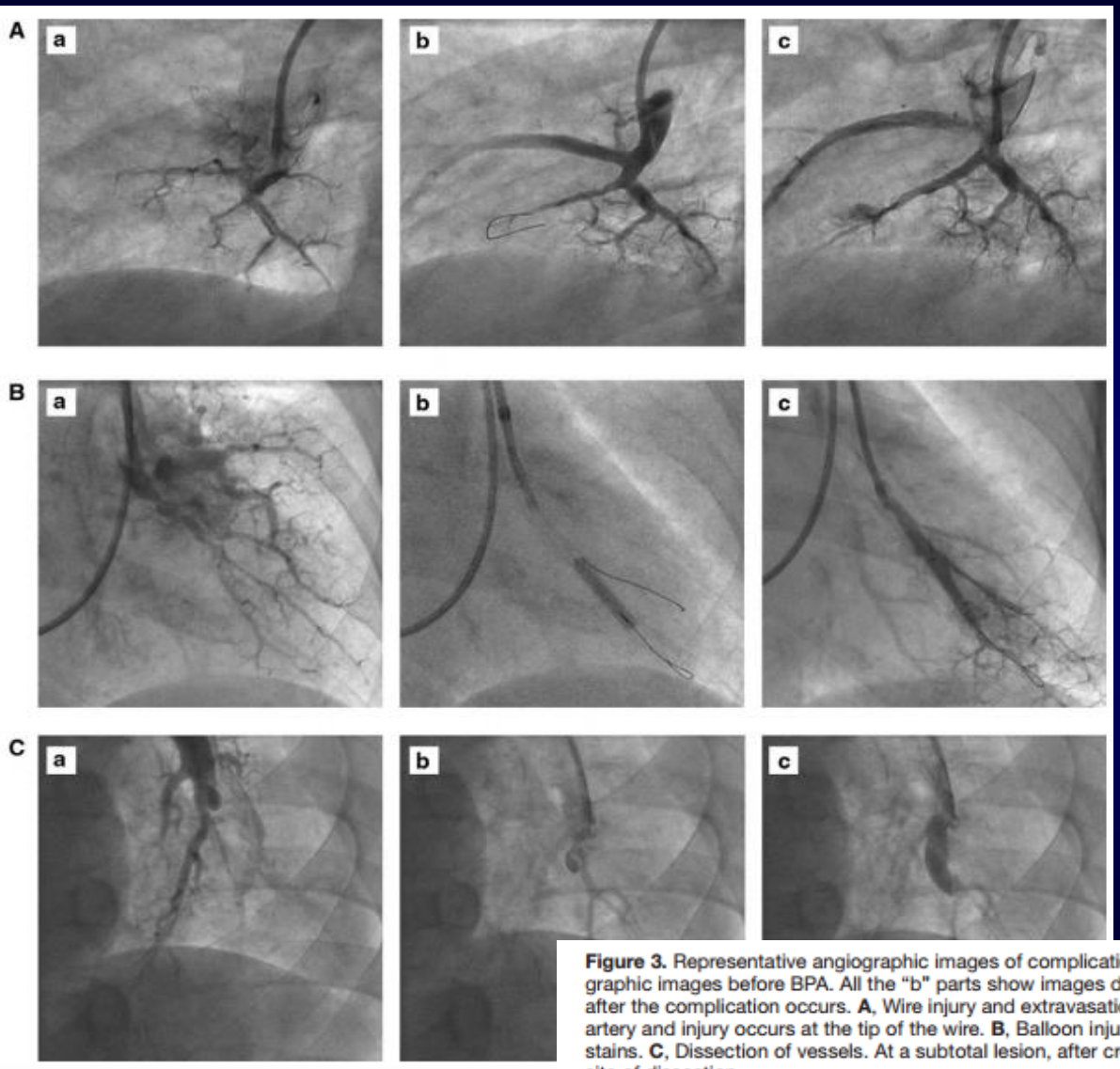


Figure 3. Representative angiographic images of complications of balloon pulmonary angioplasty (BPA). All the "a" parts show angiographic images before BPA. All the "b" parts show images during BPA when the complication occurs. All the "c" parts show images after the complication occurs. **A**, Wire injury and extravasation of contrast medium. At a subtotal lesion, the wire extends to the distal artery and injury occurs at the tip of the wire. **B**, Balloon injury. A web lesion, after inflation of the balloon, contrast medium pools, and stains. **C**, Dissection of vessels. At a subtotal lesion, after crossing the wire, dissection occurs, and the contrast medium stays at the site of dissection.

BPA IN THE GUIDELINES FOR PH

Table 34 Recommendations for chronic thromboembolic pulmonary hypertension

Recommendations	Class[a]	Level[b]	Ref.[c]
In PE survivors with exercise dyspnoea, CTEPH should be considered	IIa	C	449
Life-long anticoagulation is recommended in all patients with CTEPH	I	C	91
It is recommended that in all patients with CTEPH the assessment of operability and decisions regarding other treatment strategies should be made by a multidisciplinary team of experts	I	C	91
Surgical PEA in deep hypothermia circulatory arrest is recommended for patients with CTEPH	I	C	91
Riociguat is recommended in symptomatic patients who have been classified as having persistent/recurrent CTEPH after surgical treatment or inoperable CTEPH by a CTEPH team including at least one experienced PEA surgeon	I	B	441
Off-label use of drugs approved for PAH may be considered in symptomatic patients who have been classified as having inoperable CTEPH by a CTEPH team including at least one experienced PEA surgeon	IIb	B	437–440

Continued

Table 34 *Continued*

Recommendations	Class[a]	Level[b]	Ref.[c]
Interventional BPA may be considered in patients who are technically non-operable or carry an unfavourable risk:benefit ratio for PEA	IIb	C	57, 444–446, 448
Screening for CTEPH in asymptomatic survivors of PE is currently not recommended	III	C	417

BPA = balloon pulmonary angioplasty; CTEPH = chronic thromboembolic pulmonary hypertension; PAH = pulmonary arterial hypertension; PE = pulmonary embolism; PEA = pulmonary endarterectomy.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

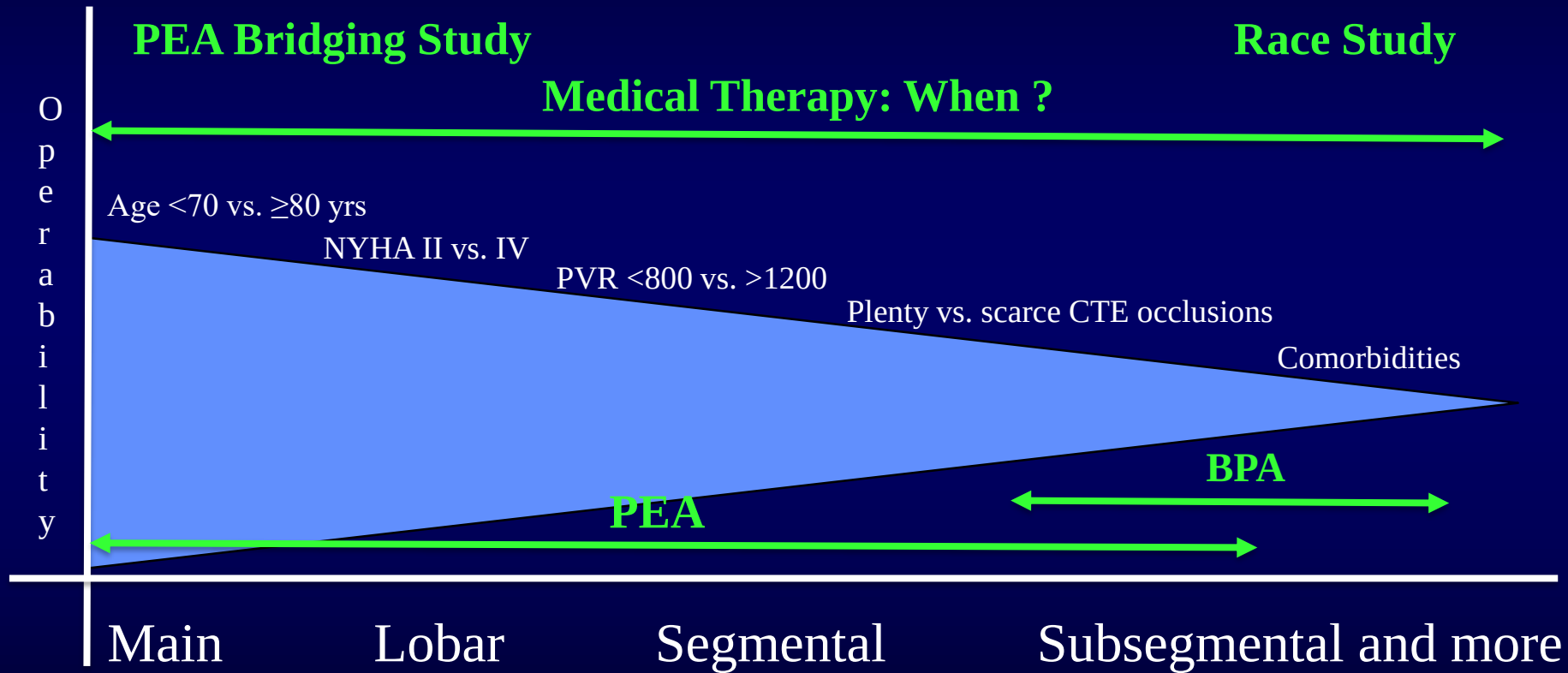
CONCLUSION

- A single characteristic usually is not enough to identify a poor or a good candidate for PEA

- Multidisciplinary CTEPH team (at least one experienced surgeos) is the basis for the correct selection of the patients

- For “less experienced centers” or in general for all centers a second opinion, in absence of PEA score, could be the optimal solution for complex patients

CONCLUSION


PEA Bridging Study
Race Study
Medical Therapy: When ?
Operability
Age <70 vs. ≥80 yrs
NYHA II vs. IV
PVR <800 vs. >1200
Plenty vs. scarce CTE occlusions
Comorbidities
BPA
PEA
Main
Lobar
Segmental
Subsegmental and more