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Pulmonary Endarterectomy for Chronic Thromboembolic Pulmonary Hypertension (CTEPH):

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Chronic thromboembolic pulmonary hypertension (CTEPH)

• ~ 3.2% of acute PE survivors

Right lung

• Incomplete resolution of pulmonary thromboemboli and fibrotic transformation

Right side of the heart has too much pressure

• Narrowing/occlusion proximal pulmonary arteries

• Pulmonary vascular resistance (PVR) \uparrow

- 1. Proximal obstruction
- 2. Secondary microvasculopathy

Pulmonary Hypertension (PH)

• RV-failure

5-year survival:

- mPAP > 40 mmHg: 30%
- mPAP > 50 mmHg: 10%



Simonneau G, Torbicki A, Dorfmüller P, et al. The pathophysiology of chronic thromboembolic pulmonary hypertension. Eur Respir Rev 2017; 26: 160112 [https://doi.org/10.1183/ 16000617.0112-2016].

Clinical presentation CTEPH: not specific!

- Exercise intolerance and/or exertional dyspnea
 - \blacktriangleright Cardiac Output \downarrow
 - Dead space ventilation \uparrow
- Accentuated pulmonary component 2nd heart sound

• RV-dysfunction

- Lower extremity swelling
- Chest pain or pressure
- Exertional light-headedness
- Hepatomegaly and ascites
- TI murmur

• Hemoptysis



https://www.uhn.ca/PatientsFamilies/Health_Information/Health_Topics/Documents/What_i s_Chronic_Thromboembolic_Pulmonary_Hypertension_CTEPH.pdf

Risk factors CTEPH

- Acute pulmonary embolism
 - Recurrent
 - Large perfusion defect
 - High mPAP 1st PE
 - Idiopathic

Hemostatic abnormalities

- Increased factor VIII, von Willebrand factor, type 1 plasminogen activator inhibitor
- Abnormal fibrinogen structure
- Antiphospholipid antibodies en Lupus anticoagulant
- Non-type-O blood group
- Increased lipoprotein(a)

Associated medical conditions

- Splenectomy
- Ventriculo-atrial shunt
- Infected intravenous catheters/devices
- Chronic inflammatory diseases
- Hypothyroidy
- Malignancies











1. Diagnosis

2. PEA

- 3. Operability assessment
- 4. Patient selection
- 5. Results



Massive UNDERDIAGNOSIS of CTEPH



Chronic Thrombotic Obstruction of Major Pulmonary Arteries*

Report of a Case Successfully Treated by Thrombendarterectomy, and a Review of the Literature

Lt. CMDR. VERNON N. HOUK, MC, USN, CHARLES A. HUFNAGEL, M.D., Bethesda, Maryland Washington, D. C.

CMDR. JAMES E. MCCLENATHAN, MC, USN and KENNETH M. MOSER, M.D. Bethesda, Maryland Washington, D. C.

Houk et al. Am J Med 1963;35:269-82.

> Pneumonol Alergol Pol. 1993;61(3-4):171-6.

[Pulmonary thromboembolism--random analysis of autopsy material]

[Article in Polish] A Panasiuk ¹, J Dziecioł, H F Nowak, A Kemona, M Barwijuk-Machała

- 240 cases
- Only six correctly diagnosed before death

- 13,216 patients
- CTEPD in 5.5 % of autopsies (31.3% in elderly)



CTEPH – Underdiagnosis



Estimated incidence

of new CTEPH

17 per million inhabitant/year

Based on:

- PE incidence = 1 per 1000 inh/year¹
- CTEPH incidence post-PE = 3%²
- 57% already have CTEPH, 43% not³
- 75% have a history of PE, 25% not⁴
- 1000 * 3% * 43% * 100/75 = 17 per million

Observed incidence of CTEPH

5-6 per million inhabitants/year

Based on:

Registry data⁵⁻⁶

- 1. Goldhaber SZ et al. Lancet. 1999;353:1386-9,
- 2. Ende-Verhaar YM et al. Eur Respir J 2017;49:1601792.
- 3. Guerin L et al. Thromb Haemost 2014;112:598–605.
- 4. Pepke-Zaba J et al, Circulation 2011;124:1973-81,
- 5. Kramm T et al. Clin Res Cardiol 2018;107:548-53,
- 6. Delcroix M et al. Ann Am Thorac Soc. 2016;13 Suppl 3:S201-6



Diagnostic Delay of CTEPH





CrossMark

Determinants of diagnostic delay in chronic thromboembolic pulmonary hypertension: results from the European **CTEPH Registry**

Klok FA et al. Eur Respir J.2018;52:1801687.

AGORA RESEARCH LETTER

Early diagnosis and referral to CTEPH center = critical for optimal treatment

Diagnostic delay ↑ \rightarrow hemodynamic profile \downarrow , survival↓

Chronic Thromboembolic Pulmonary Hypertension (CTEPH) **Results From an International Prospective Registry**

> Pepke-Zaba J et al. Circulation. 2011;124:1973-81.



Median delay of 14 months between clinical presentation and diagnosis



Massive underdiagnosis and diagnostic delay of CTEPH



- 1. Nonspecific clinical presentation and subtle physical examination findings
- 2. Diagnostic misclassifications as acute PE or other conditions
- 3. Discount possibility of CTEPD in absence of history of VTE
- 4. Lack of awareness
- 5. Cumbersome diagnostic process







Screening after acute PE





European Society doi:10.1093/eurheart/ehz405

ESC GUIDELINES

2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS)

TTE 3-6 months after PE if persistent dyspnea and/or predisposing conditions for CTEPH



Original Articles

Prospective cardiopulmonary screening program to detect chronic thromboembolic pulmonary hypertension in patients after acute pulmonary embolism

Klok FA et al. Haemtatologica.2010;95:970-5.

TTE for all PE survivors:

- Low diagnostic yield
- Overdiagnosis
- Cost-ineffective

Prevalence and potential determinants of exertional dyspnea after acute pulmonary embolism

Klok FA et al. Respir Med. 2010;104:1744-9,

CTEPH ~ 3.2% of acute PE survivors \$\$ 50% persistent dyspnea after PE



Base Booi	ed on th n G et al.	e InShape II study Thorax 2021	results	DIAGNOSIS OF AC	JTE PE	***					
• /	Acurate	e and early exclu	sion of	\downarrow							
(CTEPH	after acute PE		Anticoagulat	e	~	Findings of	pre-			
• ,	Avoids	TTE in 81% of pa	tients	Ļ		CTEPH prediction sco	CT pulmor	nary			
		Findings of pre-existin	g CTEPH on computed tomograph	ny pulmonary angiograph	1	Unprovoked PE	angiograph	ny to	+ 6 points		
• \	Vast ma	Direct vascular signs				Known hypothyr	diagnose act	ute PE	+3 points		
	1 mont	Eccentric wall-adhe	rent filling defect(s), which may ca	alcify; different from the c	entral filling defects	Symptom onset	< 2 weeks before PE d	iagnosis	+ 3 points		
2	+ monu	within a distended	lumen, which are the hallmark of	acute PE		Right ventricular	Right ventricular dysfunction on GT or TTE				
		Abrupt tapering an	d truncation			Known diabetes	mellitus		- 3points		
		Complete occlusion	and pouch defects			Thrombolytic the	erapy or embolectomy	v for the acute PE event	- 3points		
		Intimal irregularity									
		Linear intraluminal	filling defects (intravascular webs	and bands)							
		Stenosis and nost-s	tenotic dilatation			-					
		Vessular tertuseitu				-	ţ				
							Defer to CTEDI	Looptor			
		Indirect vascular signs					Refer to CTEPT	n center			
		Significant RV hype	rtrophy, RA dilatation				6				
		Pericardial effusion				- lalponton l	mahandh -	Min James - hom			
		Dilatation of pulmo pulmonary artery	nary artery (> 29 mm in men and	> 27 mm in women) and/o	or calcifications of	I <mark>/↓</mark> 3 / 2	VR V	1 S ¥ ¥4	1 1		
		Systemic collateral vessels)	arterial supply (bronchial arterial o	collaterals towards pulmo	nary post-obstructive		VI I				
СТ	EPH syn	nptoms without				3 1	Onset o	of CIEPH symp	otoms		
	history	of acute PE	of the lung parenchyma resulting	in geopgraphical variation	n in perfusion		> 3 mo	nths after diag of acute PE	nosis		
		Konstantinides SV et al. Eu	r Heart J. 2020;41:543-603, and Klok FA	m V a							





- CT pulmonary angiography (2)
- Right heart catheterization (3)
- Intimal irregularities (A)
- Abrupt, often angular narrowing (A)
- B. Pouch defects (B)
- 4. Webs or bands (C)
- 5. Complete obstruction of main, lobar, or segmental vessels at point of origin (D)

Mahmud E et al. J Am Coll Cardiol. 2018;71 20468 ight Tom Verbelen, UZ Leuven





DISADVANTAGES

1. V/Q 2D images: segmental defects missed

- 2. V/Q + ≈ other etiologies of pulmonary malperfusion
 → Additional diagnostic imaging
- 3. Always Pulmonary angiography AND CTPA

4. Radiation and contrast exposure and costs are high

Single-photon emission computed tomography (SPECT)



Roach PJ et al. Semin Nucl Med, 2010;40:455-466,

ECG-gated CT



Dual Energy CT (DECT)



Hoey ET et al. AJR Am J Roentgenol.2011;196:524-32.

Contrast-enhanced MR angiography (ce-MRA)



C

Phase-Resolved Functional Lung (PREFUL)-MRI



Pöhler GH et al. J Magn Reson Imaging. 2020;52:610-9.

Ultimate goal: one single imaging tool to screen, diagnose and assess operability



- Qualitative and quantitative assessment of pulmonary perfusion
- High spatial resolution assessment of pulmonary and coronary arteries
- Morphologic and quantitative assessement of heart
- Lower radiation exposure
- Lower cost

Pulmonary Circulation

Review Article

Optimizing the diagnosis and assessment of chronic thromboembolic pulmonary hypertension with advancing imaging modalities

Seth Kligerman and Albert Hsiao Cardiothoracic Imaging, University of California San Diego, La Jolla, CA, USA

Single ECG-gated dual energy CTPA and coronary CT angiography exam







1. Diagnosis

2. PEA

- 3. Operability assessment
- 4. Patient selection
- 5. Results

Pulmonary (Thrombo)EndArterectomy (PEA) (PTE)

- ≠ Trendelenburg
- Removal of fibrotic transformed intima via a dissection plane

Why?

- 1. Hemodynamic: RV function ↑
- 2. Respiratory: death space \downarrow
- 3. Prophylactic: progressive RV-dysfunction ar retrograde extension of obstruction
- 4. Prophylactic: secondary arteriopathy



Pulmonary (Thrombo)EndArterectomy (PEA) (PTE)

- ≠ Trendelenburg
- Removal of fibrotic transformed intima via a dissection plane

How? 4 basic principles

- 1. Bilateral: median sternotomy
- 2. Identification correct dissection plane
- 3. Complete endarterectomy
- 4. CPB + cooling (20°C) + circulatory arrest (max 20 min)





CTEPD with or without PH





- 1. Diagnosis
- 2. PEA
- 3. Operability assessment
- 4. Patient selection
- 5. Results



= patient selection



Operability assessment for PEA



- 1. Technical operability
 - Anatomic location of CTEPD
 - Skill and experience of surgeon

Surgically accessible and \approx PVR

Operability assessment for PEA UCSD classification



Madani M et al. Ann Am Thorac Soc. 2016;13 Suppl 3:S240-7.



Operability assessment for PEA



Experienced PTE surgeon:

- > 20 in year starting to assess study cases
- > 20 in the year before starting to assess study cases
- > 40 in 3 years before starting to assess study cases

Jenkins D et al. J Thorac Cardiovasc Surg. 2016;152:669-74.e3.

Expertise of a CTEPH center:

- Surgical mortality < 5% (level I)
- Surgical volume ≥ 50 PTE's/year (level II)
- Ability to operate on distal disease and to provide PTE, BPA and medical therapy (level III)

Jenkins D et al. Eur Respir Rev. 2017;26 (143),

One experienced CTEPH center

- 40-50 million population
- ≥ 50 PTE's/year
- In-hospital mortality rates < 5%

Jenkins D et al. Eur Respir Rev. 2017;26 (143),



Operability assessment for PEA





2017-2021: in-hospital mortality 3.6%



CTEPH care in a single center !



Circulation Volume 124, Issue 18, 1 November 2011; Pages 1973-1981 https://doi.org/10.1161/CIRCULATIONAHA.110.015008

American Heart Association.

ORIGINAL ARTICLE

Chronic Thromboembolic Pulmonary Hypertension (CTEPH) Results From an International Prospective Registry • Low-volume centers reported more non-operable patients



CTEPH – Multimodality treatment





- 1. PEA
- 2. BPA (Balloon Pulmonary Angioplasty)
- 3. Medicatie



- ✤ Non-operable
- Frailty
- Residual lesions after PEA



CTEPH – Multimodality treatment







CTEPD with or without PH





- 1. Diagnosis
- 2. PEA
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Risk/benefit ratio: likelihood of

- Symptomatic improvement > individual patient expectations
- Hemodynamic improvement > correlation of accessible surgical disease and severity of PH and RV dysfunction



Patient selection for PEA



Severe parenchymal lung disease = only absolute contraindication

Case Report	Pulmonary Circulation					
Pulmonary endarterectomy in a comorbidities	a 12-vear-old bov with multiple RESEARCH ARTICLES: HEART FAILURE					
Tom Verbelen ¹ , Bjorn Cools ² , Zina Fejzic ³ , R Marion Delcroix ⁶ and Bart Meyns ¹	Pulmonary endarterectomy in the octogenarian population: safety and					
	OUTCOMES Grazioli, Valentina ^a ; Ghio, Stefano ^b ; Pin, Maurizio ^a ; Sciortino, A Anna ^a ; Silvaggio, Giuseppe ^a ; Monterosso, Cristian ^a ; Turco, Ann Catherine ^c ; Merli, Vera N. ^a ; Vanini, Benedetta ^{a,d} ; D'Armini, And Author Information Journal of Cardiovascular Medicine: July 2021 - Volume 22 - Iss	Baseline Body Mass Index Does Not Significantly Affect Outcomes After Pulmonary Thromboendarterectomy Timothy M. Fernandes, MD, MPH, William R. Auger, MD, Peter F. Fedullo, MD, Nick H. Kim, MD, David S. Poch, MD, Michael M. Madani, MD, Victor G. Pretorius, MD, Stuart W. Jamieson, MD, and Kim M. Kerr, MD				
		Divisions of Pulmonary and Critical Care Medicine and Cardiothoracic Surgery, University of California, San Diego, San Diego, California				



Patient selection for PEA



Severe parenchymal lung disease = only absolute contraindication

Relative contraindications:

- Absent history of DVT or PE
- Signs of RV-failure
- Significant pulmonary or left heart disease
- WHO functional class IV
- Inconsistency on imaging modalities
- Absence of appreciable lower lobe disease
- PVR > 1,200 dynes.s/cm⁵ (> 15 WU) out of proportion to imaging
- Higher diastolic PAP

Kim NH et al. Eur respir J. 2019;53 (1).

vs potential benefits by multidisciplinary CTEPH team



Patient refusal for PEA = 20%



Gall H et al. Pulm Circ. 2016;6:472-82.

- ➤ ≈ need for ongoing education and better understanding of CTEPH treatment
- \succ ≈ delay or lack of referral
- \rightarrow Refer to CTEPH center as early as possible!
 - After each TTE with high PH probability
 - After V/Q scan with mismatched perfusion defects, the latest.



Patient refusal for PEA = 20%



Gall H et al. Pulm Circ. 2016;6:472-82.

- ➤ ≈ need for ongoing education and better understanding of CTEPH treatment
- \succ ≈ delay or lack of referral

→ Consultation regarding decision to surgery by member of CTEPH team

- Preferably by performing surgeon
- Information about
 - Improvement of exercise capacity and QoL
 - Low mortality rates (4.7% international CTEPH registry, 2.2% UCSD)
 - 5-year survival = 53% for PEA refusers vs 83% for patients that underwent PEA

Quadery SR et al. Eur Respir J. 2018;52(3)



CTEPH operability assessment and patient selection



Subjective

- CHEST-1 study: 22% initially inoperable \rightarrow operable Jenkins D et al. J Thorac Cardiovasc Surg. 2016;152:669-74.e3.
 - ightarrow 60% CTEPH patients operable (international CTEPH registry): \uparrow

> 10-15% of CTEPH cases ultimately undergo PEA

Gall H et al. Pulm Circ. 2016;6:472-82.

- Delay in and/or lack of referral to CTEPH centers
- Subjective operability assessment
- Refusal of surgery by suboptimal informed patients



CTEPH operability assessment and patient selection



Highest PEA a year: 2.7/million inhabitants (Papworth 2017)

Estimated incidence CTEPH = 17/million inhabitants a year at least 60% operable

 \rightarrow 10 PEA/million inhabitants a year

Belgium: 113/year \leftrightarrow <u>20/year</u>



CTEPD with or without PH





- 1. Diagnosis
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PEA – Patients



Mean ± SD Median (range) Median [Q1, Q2]	UZL 2018	Papworth, UK Cannon, 2016	Pavia D'Arma	Pavia, Italy D'Armani, 2016		0, USA 2012	CTEPH Registry Pepke-Zaba 2011
Period	1999-2018	1997-2012	2008-	2008-2013		2006-2010	2007-2009
			Prox Dist				
n	209	880	221	110	1,000	500	427
Age, y	60 (10-92)	57±15	61±15 60±14		52±15	51±15	63 [51-72]
Gender, % male	47	53	46 33		NA	NA	53
NYHA (I-II-III-IV), %	3-32-47-6	0-9-68-23	0-12-53-35 0-15-54-31		2-11-79-8	1-7-83-10	1-19-68-12
6MWD, m	341±138	260±126	277±118	289±112	-	-	329 [245, 427]
PAP, mmHg	46±11	47±11	44±10	46±10	46±11	46±11	47 [38, 55]
CI, L/min/m2	2.13±0.53	-	2.1±0.6	2.1±0.6 2.2±0.6		4.3±14*	2.2 [1.8, 2.7]
PVR, dsc-5	810±380	830±382	876±392	926±337	861±446	719±383	717 [495,963]



28-11-2018

* Cardiac output

PEA- Age-distribution



28-11-2018

PEA – In-hospital outcome

Median (mean±SD) Median (range)	UZL 2018	Papworth, UK Cannon 2016	Pavia D'Armi	n , Italy ni, 2014	UCSD, USA Madani, 2012		
Period	1999-2018	1997-2012	2008	-2013	1999-2006	2006-2010	
			Proximal Distal				
n	209	880	221	221 110		500	
DHCA total, min	40 ± 17	-	84±32 102±28		35±12	36±12	
MV, days	3 (1-75)	1 (2.5±4)	2 (1-3) 2 (1-4)		-	-	
ICU, days	6 (1-75)	3 (7±9)	4 (3-7) 4 (3-8)		-	-	
Hospitalization, days	19 (1-117)	16 (20±14)	13 (10-16)	13 (11-17)	-	-	
ECMO, n	19 (†9)	-			-	-	
Mortality, %	7.6	10.5	6.9	6.9	5.2	2.2	

ECMO: 58% survival

PEA = 253 - In-hospital death = 17 (6.7%)

#	Year	Day	Cause	Age	PVRpre	PVRpostOT
1	1999	D1	RHF	51	1125	847
2	2000	D0	RHF	69	1752	1852
3	2003	D15	bleeding	28	824	840
4	2003	D14	RHF	56	705	357
5	2003	D75	mediastinitis	92	671	412
6	2004	D19	RHF	68	1890	754
7	2005	D4	RHF? Inflamm reaction	33	472	476
8	2006	D9	RHF	71	1213	711
9	2008	D29	ARDS	55	1906	855
10	2008	D7	bleeding	46	1231	NA
11	2010	D14	MOF	68	692	NA
12	2011	D13	Sepsis	75	1233	NA
13	2014	D30	unknown	71	929	NA
14	2015	D14	RHF	72	1502	565
15	2017	D57	sepsis	63	519	309
16	2018	D69	unknown	38	852	NA
17	2021	D11	RHF	79	713	NA
				61 ± 17	1072 ± 464	725 ± 425

13-12-2021

1365 ± 438 848 ± 521

PEA = 253	- In	-hospi	ital	deat	:h =	17	(6.7%	6)
	n		%					

11.5

52

1999-2004

13-12-2021

PEA – Results

mean±SD	UZ LEUVEN		Papworth, UK Cannon, 2016		Pavia, Italy D'Armani, 2016				
					Proximal		Distal		
	PRE	POST	PRE	POST	PRE POST		PRE	POST	
n	209	143	880	748	221	198	110	99	
6MWD, m	341 ± 138	434 ± 134	260±126	353±118	277±118 -		289±112	-	
PAP, mmHg	$\textbf{46} \pm \textbf{11}$	28±10	47±11	27±10	44±10	44±10 24±9			
CI, L/min/m ²	2.13 ± 0.53	$\textbf{2.55} \pm \textbf{0.52}$	-	-	3.9±1.3* 5.2±1.1*		3.7±1.2*	5.0±1.2*	
PVR, dsc ⁻⁵	810 ± 380	342 ± 214	830±382	317±239	876±392	270±175	926±337	300±139	

Post: measured after 3-6 months; *cardiac output

PEA – Long-term results

Pre-op (n=188), 6m (n = 168)

PEA – Long-term survival

UZ Leuven, 2018

Papworth, UK; Cannon 2016

PEA – Long-term survival

center	n	1-year	3-year	5-years	10-years
San Diego Madani, 2012	1410	-	-	82%	75%
Papworth Cannon, 2016	880	86%	84%	79%	72%
Pavia D'Armani, 2016	331	-	-	-	-
CTEPH Registry Delcroix, 2016	404	93%	89%	-	-
UZ Leuven	209	90%	86%	84%	69%

Circulation, 2016 Mar 1;133(9):859-71. doi: 10.1161/CIRCULATIONAHA.115.016522. Epub 2016 Jan 29.

Long-Term Outcome of Patients With Chronic Thromboembolic Pulmonary Hypertension: Results From an International Prospective Registry.

Delcroix M¹, Lang I², Pepke-Zaba J², Jansa P², D'Armini AM², Snijder R², Bresser P², Torbicki A², Mellemkjaer S², Lewczuk J², Simkova I², Barberà JA², de Perrot M², Hoeper MM², Gaine S², Speich R², Gomez-Sanchez MA², Kovacs G², Jaïs X², Ambroz D², Treacy C², Morsolini M², Jenkins D², Lindner J², Dartevelle P², Mayer E², Simonneau G².

- Mortality 个
 - Operative complications
 - Postop residual PH
 - Additional cardiac procedures
 - History of cancer
 - High NYHA class, high RAP, dialysis dependent
- PEA: strongest independent predictor for survival!

PEA – Key Message

 \leftrightarrow

5-year survival untreated CTEPH:

mPAP > 40 mmHg: 30%
mPAP > 50 mmHg: 10%

5-year survival PEA UZ Leuven (mPAP 46±11 mmHg)

84%

Significant 个 6MWD & NYHA

Consider CTEPH as possible cause of dyspnea → quick diagnosis and PEA

 \rightarrow avoidance of multiple deaths a year

PEA = only <u>curative</u> treatment: best chance on \uparrow survival and \uparrow functional status

08/06/2022: first reported PEA via ministernotomy

FOCUSED ISSUE

PTE in Chronic Thromboembolic Pulmonary Hypertension and Disease

Guest Editors: Sofia Martin-Suarez and Antonio Loforte, Bologna, Italy

SYSTEMATIC REVIEW

Pulmonary thromboendarterectomy for chronic thromboembolic pulmonary hypertension: a systematic review John D. L. Brookes, *et al.*

KEYNOTE LECTURE SERIES

Chronic thromboembolic pulmonary hypertension: diagnosis, operability assessment and patient selection for pulmonary endarterectomy Tom Verbelen, *et al.*

FEATURED ARTICLES

Pulmonary thromboendarterectomy —the Royal Papworth experience David P. Jenkins, *et al.*

EDITORIAL

End-stage chronic thromboembolic pulmonary hypertension: is there still room for lung transplantation?—the past, the present and the future Eleonora Faccioli, *et al.*

ART OF OPERATIVE TECHNIQUES

Pulmonary endarterectomy: technique and pitfalls Stefan Guth, et al.

MASTERS OF CARDIOTHORACIC SURGERY

Surgical management of "ab-extrinseco" main stem left coronary compression during pulmonary thromboendarterectomy Sofia Martin-Suarez, *et al.*

Chronic thromboembolic pulmonary hypertension: diagnosis, operability assessment and patient selection for pulmonary endarterectomy

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© Maren Hötten, Master Thesis in Scientific Illustration "Chronic Thromboembolic Pulmonary Hypertension: Diagnosis and Treatment", University of Maastricht, 2016.

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