ICA International CTEPH Association

INTERNATIONAL **CTEPH** CONFERENCE **2021**

10 – 11 December 2021 • Hotel Dolce by Wyndham, Bad Nauheim, Germany

CONFERENCE PROGRAMME

www.cteph-association.org

INTERNATIONAL **CTEPH** CONFERENCE **2021**

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ICC 2021 SCIENTIFIC COMMITTEE

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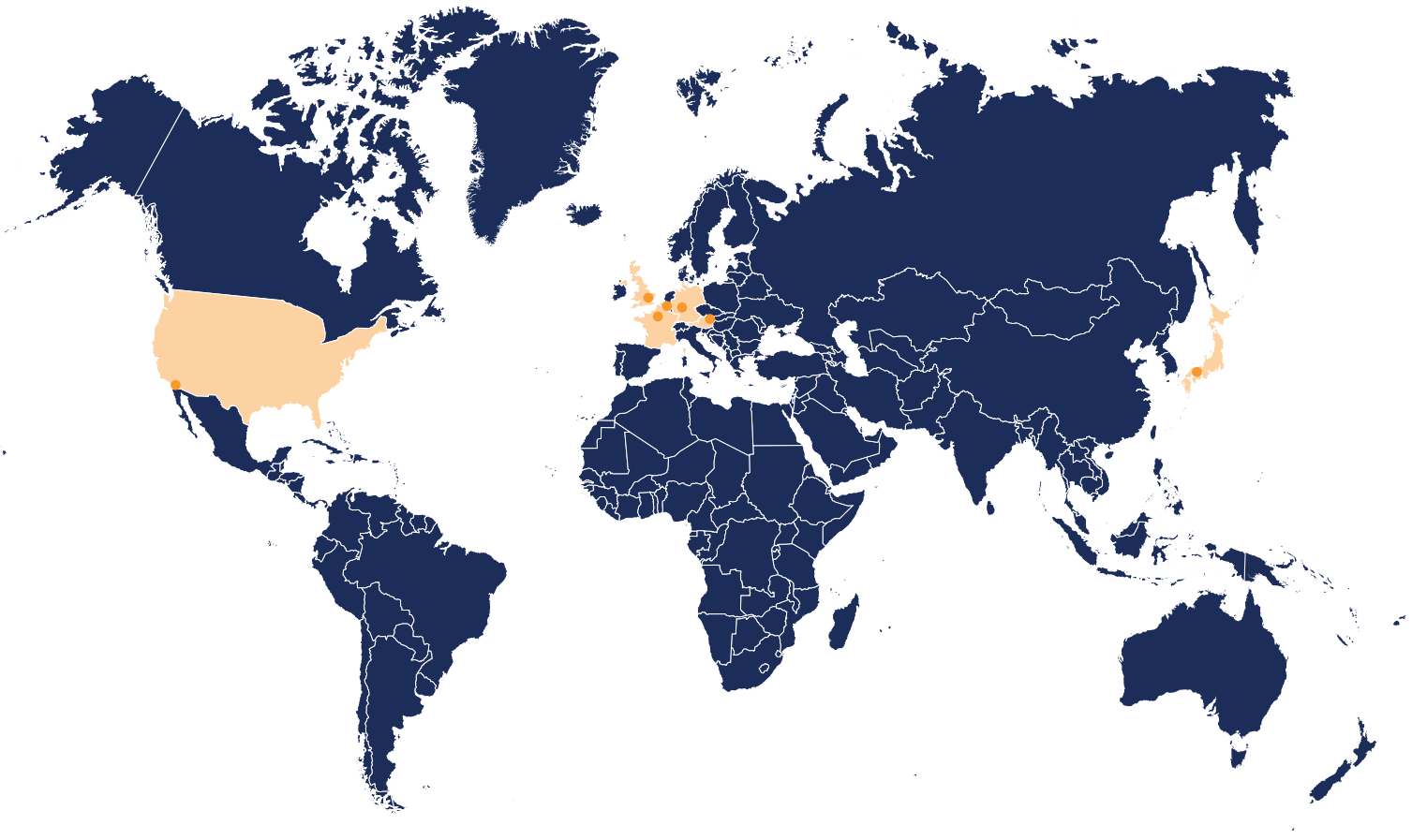


WELCOME LETTER

DEAR COLLEAGUES AND FRIENDS,

On behalf of the International CTEPH Association (ICA), we would like to extend a warm welcome to all participants of the International CTEPH Conference (ICC) 2021. The ICA is very pleased that the conference can take place despite the challenges of the ongoing coronavirus pandemic. For the first time in its history, the ICC is held in a hybrid format, allowing both on-site and virtual participation.

Over the last few years, interventional treatment has become the standard in CTEPH worldwide, and extensive research is ongoing into the optimal use of existing treatment modalities depending on patient profiles. The meeting programme encompasses all aspects of the disease, from pathophysiology and epidemiology to diagnosis and surgery, interventional treatment, medical and multimodal therapy.

We trust that the conference will provide an excellent opportunity for the presentation of original research and the exchange of state-of-the-art knowledge regarding CTEPH, to raise awareness of CTEPH and to help scientists and clinicians translate the latest findings into improvements in patient care. We are convinced that, thanks to the latest advances in virtual technology, clinicians, surgeons, intensivists, radiologists and researchers will be able to interact effectively and exchange ideas, as they have at all previous conferences.

On this occasion, we would like to express our sincere thanks to the pharmaceutical companies who have provided funding for this event despite current uncertainties. The sponsors had no influence on the selection of the faculty or the content of the scientific programme.

We hope that you will enjoy this conference, regardless of whether you participate on-site in Bad Nauheim's beautiful Art Nouveau setting, or virtually.

Yours sincerely,

Prof Gérald Simonneau

Prof Eckhard Mayer

SCIENTIFIC PROGRAMME

In compliance with EACCME® guidelines, all speakers/chairpersons participating in this programme have disclosed potential conflicts of interest that might cause a bias in the presentations.

Friday, 10 December 2021

08:15 – 09:00	Registration	
09:00 – 09:10	Welcome and introduction	E. Mayer
09:10 – 09:35	Developing concept and definition of CTEPH	G. Simonneau
Plenary 1: Pathophysiology, epidemiology (Chairs: M. Delcroix and G. Simonneau)		
09:35 – 10:00	Early diagnosis of CTEPH after acute PE in the pre- and post-COVID era	E. Klok
10:00 – 10:25	What have we learned from GWAS?	M. Toshner
10:25 – 10:50	The role of the bronchial circulation and microvasculopathy	E. Fadel
Coffee break and poster viewing		
Plenary 2: Diagnosis and imaging (Chairs: J. Pepke-Zaba and E. Fadel)		
11:20 – 11:45	Mechanisms of cardiac dysfunction in CTEPH	A. Vonk Noordegraaf
11:45 – 12:10	Beyond V/Q scan: cutting edge imaging modalities	N. Screaton
12:10 – 12:35	How to select treatment modalities – PEA vs BPA	E. Mayer
Lunch break and poster viewing		
Plenary 3: Pulmonary endarterectomy (Chairs: E. Mayer and N. Kim)		
14:15 – 14:40	Segmental/subsegmental endarterectomy	M. Madani
14:40 – 15:05	Management of peri-operative complications	D. Jenkins
Coffee break and poster viewing		
Plenary 4: Balloon pulmonary angioplasty (Chairs: H. Matsubara and I. Lang)		
15:35–16:00	State of the art techniques and complication management	H. Matsubara
16:00–16:25	BPA learning curve: the French experience	P. Brenot
16:25–16:50	International BPA registry	N. Kim
16:50–17:05	Poster award and end-of-day conclusion	J. Pepke-Zaba

SCIENTIFIC PROGRAMME

In compliance with EACCME® guidelines, all speakers/chairpersons participating in this programme have disclosed potential conflicts of interest that might cause a bias in the presentations.

Saturday, 11 December 2021

07:45 – 10:15	Registration	

Plenary 5: Medical and multimodal therapy (Chairs: D. Jenkins and M. Delcroix)

10:15 – 10:35	Role of medical therapy in CTEPH	A. Ghofrani
10:35 – 10:55	Medical vs BPA in non-operable patients	X. Jaïs
10:55 – 11:15	Multimodal interventions	C. Wiedenroth
11:15 – 11:30	**Panel discussion: multimodal therapy strategies** D. Jenkins, M. Delcroix, A. Ghofrani, X. Jaïs and C. Wiedenroth	

Lunch break and poster viewing

Plenary 6: Hot topics (Chairs: M. Madani and I. Lang)

13:10 – 13:25	New insights into CTEPH pathogenesis: the role of neutrophil extracellular traps	I. Lang
13:25 – 13:40	Anticoagulant options in CTEPH	M. Hoeper
13:40 – 13:55	CTEPD without PH: exercise haemodynamics and treatment evidence	S. Guth
13:55 – 14:10	Pulmonary artery denervation after PEA	A. Chernyavskiy
14:10 – 14:20	Closing remarks	N. Kim

ACCREDITATION

The EACCME® has granted 7 credit points to the International CTEPH Conference 2021. Each medical specialist should claim only those hours of credit that he/she actually spent in the educational activity.

INDUSTRY SYMPOSIA

Friday, 10 December 2021

13:15 – 14:45 **Bayer Lunch Symposium**
Putting theory into practice: A case-based masterclass on CTEPH

A case-based journey from acute PE to CTEPH	E. Klok
Contemporary treatment strategies for CTEPH: Insights from the Kerckhoff Klinik	C. Wiedenroth
Recent learnings for optimizing CTEPH patient care – roundtable discussion and Q&A	E. Klok, C. Wiedenroth and E. Mayer

Saturday, 10 December 2021

08:15 – 09:45 **AOP Orphan Breakfast Symposium**
Value of prostacyclins in the CTEPH therapy concept
Chairs: I. Lang and M. Humbert

Treatment goals with medical treatment	M. Humbert
Trepulmix for CTEPH patients: What do we know – what can we expect?	P. Jansa
A special case (presented & discussed)	I. Lang and K. Karlocai
How do we combine mechanical and medical treatment?	I. Lang, M. Humbert, P. Jansa and K. Karlocai

12:15 – 13:00 **Janssen Lunch Symposium**
Bringing the world together to strengthen and to accelerate advances in CTEPH
Chairs: J. Pepke-Zaba and G. Simonneau

A CTEPH patient's journey and the role of referring providers in the ICA Board regions	I. Lang, D. Jenkins, M. Madani and H. Matsubara
ICA efforts	M. Delcroix and E. Fadel
Post-COVID challenges and opportunities for the ICA mission	N. Kim and E. Mayer

SPONSORS

The Executive Board members of the International CTEPH Association express their sincere gratitude to all sponsors for their contribution. The ICC sponsors did not have any influence on the selection of the faculty or the content of the scientific programme.

ENDORSEMENT

The scientific programme of the ICC 2021 is endorsed by

EXHIBITORS

The following companies will exhibit at the ICC 2021:

- AOP Orphan Pharmaceuticals AG
- Bayer AG and Merck Sharp & Dohme
- Janssen Pharmaceuticals Ltd
- Kaneka Medical Europe N.V.

The ICA does not take responsibility for the content displayed at the exhibitor booths.

ABSTRACTS SELECTED FOR POSTER PRESENTATION

National CTEPH management strategies

ICC2021-C1: STATUS OF CTEPH MANAGEMENT IN DENMARK

A Andersen[1], MJ Andersen[1], S Mellemkjær[1], G Andersen[2], L Ilkjær[3], KE Klaaborg[3], JE Nielsen-Kudsk[1]

[1]Department of Cardiology, Aarhus University Hospital, Denmark
[2]Department of Radiology, Aarhus University Hospital, Denmark
[3]Department of Thoracic Surgery, Aarhus University Hospital, Denmark

Objective: To provide an overview of current CTEPH management in Denmark.

Methods: The current status of CTEPH management in Denmark is based on data from the National Danish CTEPH center.

Results: The population of Denmark is 5.7 mill. people. Surgical and interventional CTEPH treatment is centralized at the Danish National CTEPH center at Aarhus University Hospital. The center receives referrals from Denmark, Iceland, Faeroe Islands, Greenland and parts of Sweden. Patients referred are evaluated by a multidisciplinary team of cardiothoracic surgeons, chest radiologists and cardiologists and encompasses out- and in-patient, medical, interventional, and surgical service. The surgical pulmonary endarterectomy program was initiated in 1994 and have operated > 300 patients with approximately ~ 20 patients operated annually. Since 2011 > 100 patients have been operated with a perioperative mortality < 2.5 % and for patients operated from 2004 and forth, 5 y survival is > 80 %. In 2015 the service initiated a balloon pulmonary angioplasty program for inoperable CTEPH patients and a total of 59 patients have completed BPA treatment with a reduction in pulmonary vascular resistance, improved 6 minutes walking distance, improved WHO functional class and a survival similar to patients operated by pulmonary endarterectomy.

Conclusions: Surgical and interventional treatment of CTEPH in Denmark is centralized at the Danish National CTEPH center at Aarhus University Hospital operating ~ 20 patients with PEA annually and treating ~ 15 – 20 patients annually with BPA.

National CTEPH management strategies

ICC2021-C2: PULMONARY ENDARTERECTOMY IN SEVERE CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION – THE TORONTO EXPERIENCE

M de Perrot, K McRae, L Donahoe, E Abdelnour-Berchtold, J Thenganatt, J Granton, the Canadian CTEPH Working Group

Toronto CTEPH Program, Toronto General Hospital, UHN, University of Toronto, Canada

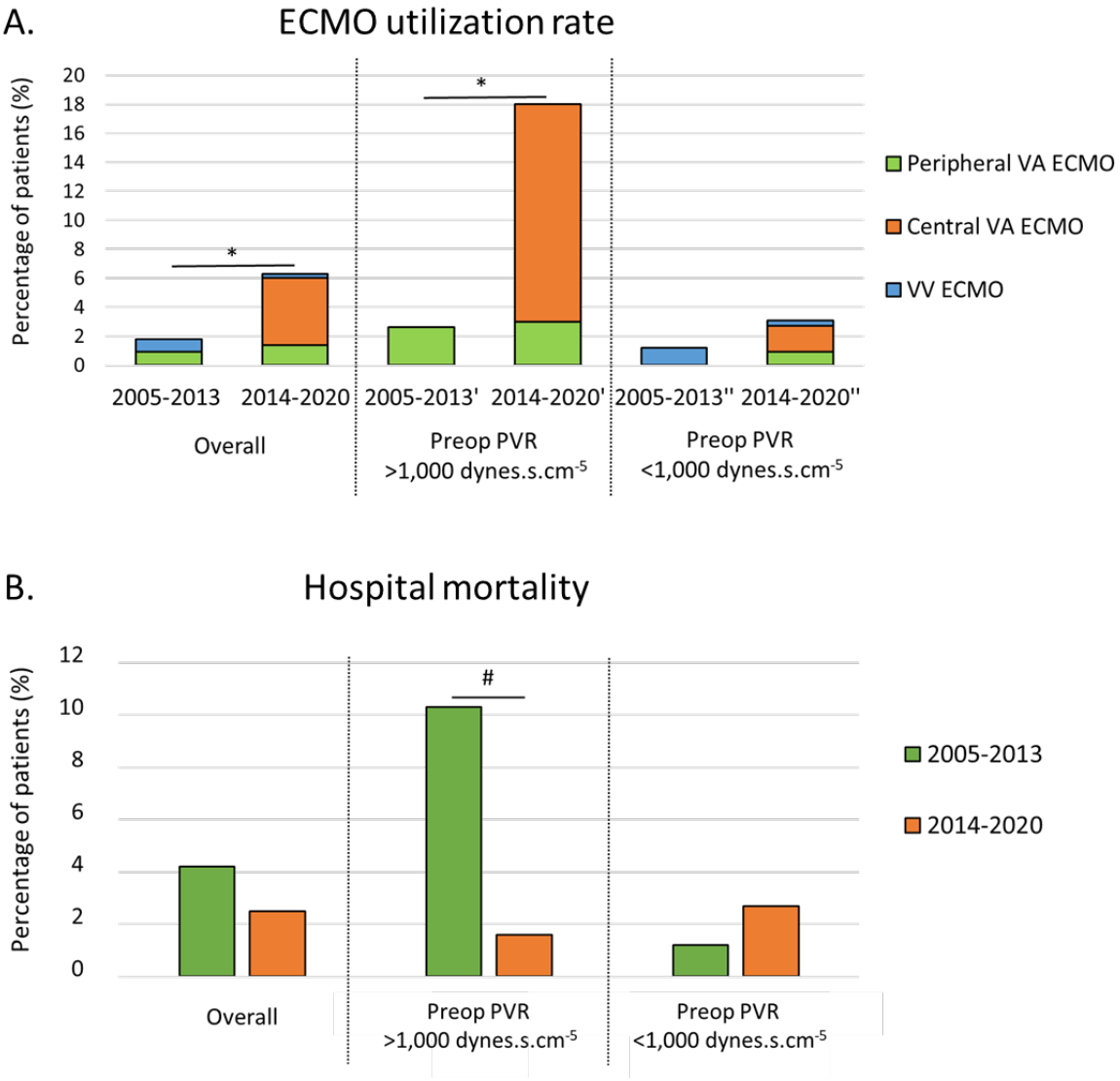
Background: We reviewed our experience in pulmonary endarterectomy (PEA) for severe chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: Retrospective analysis of 401 consecutive patients undergoing PEA at the Toronto General Hospital between 08/2005 and 03/2020. Severe CTEPH was defined by PVR > 1,000 dynes.s.cm^{-5} at the time of diagnosis.

Results: A greater proportion of patients with PVR > 1,000 dynes.s.cm^{-5} were treated with targeted PH medical therapy (38 % vs 18 %, p < 0.0001), admitted to hospital for advanced right heart failure (RHF) (26 % vs 4.5 %, p < 0.0001), and initiated on inotropic support (7 % vs 0.3 %, p < 0.0001) before PEA. Since 2014, the utilization of central veno-arterial extracorporeal membrane oxygenation (VA ECMO) as a bridge to recovery after PEA in patients with advanced RHF having difficulty separating from cardiopulmonary bypass has been associated with a reduction in hospital mortality in patients with PVR > 1,000 dynes.s.cm^{-5} from 10.3 % in 2005 – 2013 to 1.6 % in 2014 – 2020 (Figure), while the hospital mortality in patients with PVR < 1,000 dynes.s.cm^{-5} remained stable (1.2 % in 2005 – 2013 vs 2.7 % in 2014 – 2020, p = 0.4). The overall survival reached 84 % at 10-year in patients with severe CTEPH compared to 78 % in the remaining patients, but a greater proportion of patients were initiated on targeted PH medical therapy after PEA in severe CTEPH (31 % vs 15 %, respectively; p = 0.0003).

Conclusions: The early and long-term results of PEA in patients with severe CTEPH are excellent despite greater postoperative risks due to more advanced RHF. Central VA ECMO as a bridge to recovery after PEA can be useful in patients with advanced RHF.

Figure



A. The use of central VA ECMO increased after 2014 in patients with PVR > 1,000 dynes.s.cm^{-5}, while it did not significantly changed in PVR < 1,000 dynes.s.cm^{-5} during the same time period.
B. The hospital mortality decreased from 10.3 % to 1.6 % after 2014 in patients with PVR > 1,000 dynes.s.cm^{-5}, while the hospital mortality did not significantly changed in patients with PVR < 1,000 dynes.s.cm^{-5}. *p = 0.02, #p = 0.05

National CTEPH management strategies

ICC2021-C3: CTEPH IN AUSTRALIA AND NEW ZEALAND: UNDERIDENTIFYING PEA CANDIDATES IS THE KEY ISSUE

TJ Williams[1,3], D McGiffin[2,3], A Doi[2], S Marasco[2,3], H Whitford[1]

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[3]Monash University, Melbourne, Australia

Approved therapies for Chronic Thromboembolic Pulmonary Hypertension (CTEPH) are now generally available in Australia and New Zealand. These include Pulmonary Endarterectomy surgery (PEA), Balloon Pulmonary Angioplasty, Riociguat and Lung Transplantation (LTx). Low PEA servicing rates (0.4 per million per year) are apparent for the last 3 decades.
Since the early 1990's a few CTEPH patients received LTx in Australia or referred to UCSD for PEA funded by a national "act of grace" scheme. Progressively a number of centres (The Prince Charles Hospital in Brisbane, Royal Prince Alfred in Sydney, St Vincent's Hospital in Sydney, Royal Perth Hospital and Green Lane Hospital Auckland) offered PEA surgery. No centre performed > 6 PEA per year nor nationally 10 cases per year (25 million population). Despite this survival was surgical group 72 % at 10 years and non-operated CTEPH patients 42 % at 10 years (PHSANZ registry). The Alfred Hospital in Melbourne commenced a PEA program in 2014 with case numbers (total 94 to date with 1.1 % mortality) rising to 20 per year.
BPA is now available in three centres across Australia with St Vincent's Hospital in Sydney having the most experience, reporting the first 35 cases as of mid-2018.
A recent concerted effort to offer a national (including New Zealand) approach to CTEPH commenced at The Alfred with a regular virtual CTEPH meeting with participants from around Australia and New Zealand, with PEA performed at the Alfred. The present rate of PEA surgery (20 per year) remains well short of the expected 50 – 60 cases per year.

References

Bart et al JHLTx 2020; 39(4):s170 (abstract)
Malyasena et al Pulmonary Circulation 2012;2(3):359-364.
Kearney et al JHLTx 2020;40(4):s460 (abstract)

National CTEPH management strategies

ICC2021-C4: EXPERIENCE DOES MATTER FOR PULMONARY ENDARTERECTOMY SURGERY: TURKEY EXPERIENCE

B Yildizeli

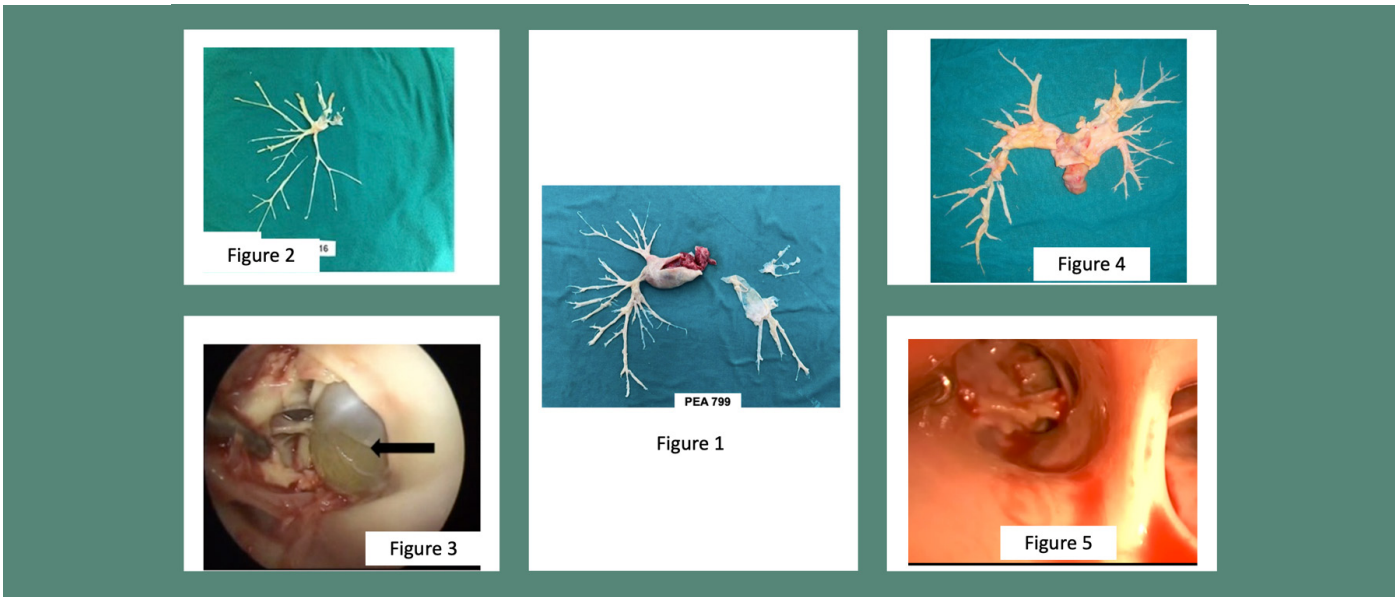
Marmara University School of Medicine, Department of Thoracic Surgery, Istanbul, Turkey

Objective: Pulmonary endarterectomy (PEA) is the treatment of choice for patients with chronic thromboembolic pulmonary hypertension (CTEPH). The aim of this study was to review our country experience since our center is the only expert center in Turkey according to the international guidelines.

Methods: Data were collected prospectively on all patients who underwent PEA between March 2009 and September 2021. Operability is performed by our multidisciplinary CTEPH team.

Results: 808 patients (420 male, 388 female, mean age 47.7 years [8 – 85]) underwent surgery. The overall mortality rate was 6.6 %. With the improvement in surgical techniques, perioperative mortality has decreased from almost 15 % in the early years to 5 % in our center. Unfortunately, during the COVID-19 pandemic, 2 patients died in the early postoperative period due to COVID-19 infection and 3 patients also died during the postoperative follow-up period. Institutional experience includes 808 patients (Figure 1), with diagnosis of 'isolated pulmonary vasculitis' in nine patients (Figure 2), pulmonary arterial hydatidosis in nine (Figure 3), pulmonary artery sarcoma in 11 (Figure 4), and non-thrombotic pulmonary embolism due to foam sclerotherapy in three (Figure 5). Recurrent/persistent pulmonary hypertension after surgery was observed in 13 % of our patients. Balloon pulmonary angioplasty (BPA) was performed for 13 patients with improved hemodynamic results. Thirty patients (3.7 %) were lost to follow up.

Conclusions: Improving a pulmonary endarterectomy program with acceptable mortality and morbidity rates and satisfactory early-term outcomes increases awareness of the CTEPH and surgery. We now operate 90 cases/year. With increasing surgical experience and improvements in instruments and procedures, an increasing number of patients are now considered operable. All patients diagnosed with CTEPH should be referred for consideration of PEA in an expert CTEPH center.



National CTEPH management strategies

ICC2021-C5: CLINICAL CHARACTERISTICS AND MANAGEMENT OF PATIENTS WITH CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION IN KOREA: A REGISTRY DATA

J-M Song[1], S-A Chang[2], JS Lee[1], D-H Kim[1], S-A Lee[1], Y Kim[1], H-J Chang[3]

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[2]Division of Cardiology, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, South Korea
[3]Cardiology Division, Yonsei Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, South Korea

Objectives: We aimed to evaluate clinical features of patients with chronic thromboembolic pulmonary hypertension (CTEPH) in Korea.

Methods: A prospective and retrospective registry was constituted from December 2018 including CTEPH patients in three large tertiary referral hospitals in Seoul, Korea. An interim analysis of data was performed.

Results: A total of 78 patients (37 females, age: 56 ± 14 years, range: 26 – 79 years) have been enrolled. Thrombophilia including antiphospholipid syndrome, protein S deficiency, and Factor V variant was detected in 4 patients (5.1 %), and malignancy was found in 7 patients (9.0 %). For anticoagulation, warfarin was used in 78.2 %, while direct oral anticoagulants were used in 20.5 %. Mean pulmonary artery pressure was 45 ± 12 mmHg, and pulmonary vascular resistance was 10.0 ± 5.7 WU. For the treatment, pulmonary endarterectomy (PEA) was performed in 47 patients (60 %), while balloon pulmonary angioplasty (BPA) was conducted in 31 patients (40 %). Among the patients who underwent PEA, 11 patients were treated with BPA after PEA. BPA was performed in 1 to 10 times to a single patient. A six-minute walk test (6 MWT) was followed up after 31.7 ± 24.8 months in 56 patients, and echocardiography was repeated after 30.3 ± 23.7 months in 71 patients. The walk distance in 6 MWT was increased after follow-up (387 ± 115 to 471 ± 107 meters, $p < 0.001$), and the maximal velocity of tricuspid regurgitation (TRVmax) was reduced (4.3 ± 0.7 to 3.0 ± 0.7 m/s, $p < 0.001$). The improvement was significant in both PEA and BPA groups, and decrement of TRVmax was greater in PEA group than BPA group (-1.6 ± 0.8 vs. -0.7 ± 0.6 m/s, $p < 0.001$).

Conclusion: Our data indicate that Korean CTEPH patients are appropriately treated using surgical and interventional treatments along with anticoagulation resulting in symptomatic improvement.

National CTEPH management strategies

ICC2021-C6: CHRONIC THROMBOEMBOLIC PULMONARY HYPERTESION IN SAUDI ARABIA: PRELIMINARY RESULTS FROM THE SAUDIPH REGISTRY

AM Aldalaan[1], S Saleemi[1], I Weheba[1], H Pekka[2], M Aleid[3], F Alzubi[1], H Zaytoun[1], N Alharbi[1], A Abdelsayed[1]

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[3]Department of Biostatistics, Epidemiology & Scientific Computing, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia

Objective: Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare, progressive vascular disease with poor prognosis if left untreated. This study aims to assess the patient characteristics, treatment approach and clinical and survival outcomes for CTEPH patients enrolled in the Systematic Prospective Follow Up for Better Understanding of Clinical Characteristics of Patients with Pulmonary Hypertension Disease (SAUDIPH) registry.

Methods: This study presents a sub analysis of CTEPH patients enrolled in the SAUDIPH registry. This registry enrolled patients with pulmonary hypertension, established through right heart catheterization, under clinical management at a specialized tertiary care center. Patients received standard care during the period of the registry.

Results: At the time of this analysis, 64 CTEPH patients were enrolled in the registry. Mean age at diagnosis was 39.7 years and there was a female predominance (67.6 %). At baseline, most patients were in World Health Organization functional classes III or IV (70.1 %). At the last follow-up visit, most patients (63.2 %) had undergone endarterectomy, showing significant improvement in disease severity from baseline. Patients who underwent endarterectomy showed numerically higher ($p = 0.126$) probability of survival at 1 year (97.5 %) versus those who did not undergo endarterectomy (94.4 %).

Conclusion: Patients were diagnosed at relatively young age, but still showed high disease severity, suggesting delay in diagnosis. Patients who underwent surgical treatment showed substantial improvements in clinical and haemodynamic parameters, while the remaining patients tended to show disease progression. The 96.6 % 1-year cumulative probability of survival was high compared to previous studies.

Change in clinical and haemodynamic parameters from baseline to last follow-up visit.

			Surgical Treatment			
	Overall CTEPH (n = 68)		No endarterectomy (n = 25)		Endarterectomy (n = 43)	
Characteristics	**Baseline**	**Last Visit**	**Baseline**	**Last Visit**	**Baseline**	**Last Visit**
WHO FC, n (%)						
I/II	20 (29.9)	45 (67.2)	9 (36.0)	7 (29.2)	12 (27.9)	38 (88.4)*
III/IV	47 (70.1)	22 (32.8)	16 (64.0)	17 (70.8)	31 (72.1)	5 (11.6)
6 MWD, meters	273.3 (159.4)	345.1(148.6)*	255.4 (167.8)	179.4 (112.1)	282.7 (157.8)	428.0 (78.2)
Borg Dyspnoea, Borg units	3.5 (2.1)	2.6 (2.4)	4.1 (1.4)	4.7 (1.9)	3.1 (2.4)	1.6 (2.0)
Borg Fatigue, Borg units	3.4 (2.1)	2.6 (2.4)	3.9 (1.4)	4.7 (1.9)	3.1 (2.4)	1.6 (2.0)
Syncope, n (%)	5 (7.5)	2 (3.0)	3 (12.0)	1 (4.2)	2 (4.7)	1 (2.3)
NT-proBNP, pg/mL	702.5 (119.2, 1645.2)	221.0 (102.0, 1112.5)	702.5 (209.8, 1806.8)	500.0 (177.0, 1674.5)	696.0 (94.8, 1275.5)	147.5 (70.8, 321.2)
Heart Failure, n (%)	1 (1.5)	1 (1.5)	0 (0.0)	1 (4.2)	1 (2.3)	0 (0.0)
Haemodynamic						
CI, L/min/m^2	2.0 (1.7, 2.3)	2.0 (1.8, 2.7)	2.0 (1.8, 2.2)	2.5 (1.9, 3.0)	2.0 (1.7, 2.3)	2.0 (1.8, 2.6)
CO, L/min	3.9 (1.2)	4.4 (1.7)	3.9 (0.9)	4.9 (3.9)	3.9 (1.3)	4.3 (1.6)
mPAP, mmHg	49.6 (14.3)	41.8 (15.9)	49.9 (14.2)	53.5 (17.7)	49.5 (14.5)	40.4 (15.7)
O_2 Sat – Base, %	96.2 (2.3)	96.7 (2.2)	96.4 (1.8)	96.0 (3.0)	96.2 (2.5)	97.0 (1.6)
O_2 Sat – Min, %	89.6 (5.6)	92.0 (4.8)	90.9 (5.4)	89.8 (5.9)	89.0 (5.7)	93.0 (3.9)*
PADP, mmHg	28.0 (23.0, 38.0)	23.5 (16.8, 36.8)	29.0 (23.2, 33.5)	34.5 (27.8, 41.2)	28.0 (22.5, 38.5)	23.5 (16.2, 35.2)
PASP, mmHg	78.9 (26.1)	61.6 (26.9)	79.9 (23.4)	76.5 (16.3)	78.3 (27.6)	59.9 (27.6)
PCWP, mmHg	15.0 (11.0, 18.0)	15.0 (11.8, 17.5)	15.0 (11.2, 21.0)	23.5 (20.2, 26.8)	14.5 (10.0, 18.0)	14.5 (11.2, 16.8)
PVR, WU	9.7 (4.9, 13.1)	4.1 (2.6, 14.7)	8.1 (5.4, 11.6)	12.2 (6.8, 17.5)	9.8 (4.9, 13.5)	4.1 (2.7, 13.7)
RAP, mmHg	13.0 (6.1)	11.5 (4.9)	13.1 (6.0)	18.0 (1.4)#	12.9 (6.2)	10.8 (4.6)#
SV, mL/beat	50.9 (18.0)	57.3 (28.3)	53.8 (15.7)	73.3 (58.5)	49.5 (19.0)	55.4 (25.5)
SVR, WU	19.8 (7.4)	20.7 (9.5)	17.8 (4.6)	18.3 (13.4)#	20.7 (8.3)	21.0 (9.5)#
TPR, WU	14.0 (8.0, 17.4)	8.1 (5.8, 18.8)	13.5 (8.0, 16.4)	18.1 (11.7, 24.5)	14.1 (8.1, 17.9)	8.1 (5.9, 17.7)

Results are presented as mean (SD) for normal continuous variables or median (Q1, Q3) for non-normal continuous variables, considering only patients who had last visit assessments. Change through last visit: *p-value < 0.05; **p-value < 0.01; ***p-value < 0.001. # It was not possible to perform comparison due to data inconsistency.
c = Chronic thromboembolic pulmonary hypertension; mPAP = mean pulmonary arterial pressure; NT-proBNP = N-terminal pro-B-type natriuretic peptide; PADP = pulmonary artery diastolic pressure; PASP = pulmonary artery systolic pressure; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; RAP = right atrial pressure; SV = stroke volume; SVR = systemic vascular resistance; TPR = total pulmonary resistance; WHO FC = World Health Organization Functional Class.

Aldalaan et al. ERJ Open Res 2020; 6:00218-2019

National CTEPH management strategies

ICC2021-C7: CTEPH EXPERIENCE FROM INDIA

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We report our experience of nearly 600 Chronic Thromboembolic Pulmonary Hypertension (CTEPH) cases from India since 2004. The incidence of development of Pulmonary Embolism (PE) following Deep Vein Thrombosis (DVT) and development of CTEPH following DVT (39.5 % and 20 % respectively) is higher compared to what is reported in world literature. Late presentation, several years after onset of the disease and more advanced disease at the time of presentation, with high mean Pulmonary Artery Pressure and (mPAP) Pulmonary vascular resistance (PVR) is still common due to the disease not being diagnosed early. Lack of knowledge that curative treatment is available also contributes to late referrals, resulting in operability of under 50 % of diagnosed patients. Many patients are treated with targeted PH medications with the intend to avoid surgery. Median age at the time of PTE is lower at 38 years and male to female ratio is 2.6:1. The requirement of ECMO was also higher at 13.9 %. Concomitant procedures included treatment of pulmonary hydatidosis as a cause of obstruction of pulmonary arteries resulting in CTEPH, treatment of renal cell carcinoma and requirement for homograft replacement of pulmonary valve following surgery for congenital heart disease in childhood. The poster presentation will also show the post-operative outcomes as measured by Pulmonary artery systolic pressures and six-minute walk distance, effect of the learning curve on the outcomes over different periods and follow up over a median period of 8 months.

National CTEPH management strategies

ICC2021-C8: THE DATA FROM PH REGISTRY AND INITIAL SINGLE-CENTER EXPERIENCE OF PEA AND BPA IN RUSSIAN FEDERATION

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Objective: To assess the results of CTEPH treatment in Russian Federation.

Methods: 320 CTEPH patients entered the PH-registry. The PH-registry formed by volunteer cardiologists to help patients get optimal treatment. The 183 CTEPH patients underwent surgical treatment: Pulmonary endarterectomy (PEA) – 73 patients, balloon pulmonary angioplasty (BPA) – 117 patients and both methods (PEA+BPA) – 15 patients. The rest of the patients were inoperable (74 patients) or reject surgical treatment (63 patients). The fundings for PEA or single BAP session is equal. The decision to operate was based on two modalities mainly – CT angiography and catheterization combined with plain subtraction pulmonary angiography.

Results: The time from onset of HF to surgical treatment was 5 years. The average PVR before PEA was 1002 ± 150 dynes.s.cm^{-5}. The final pulmonary resistance after PEA was 276 ± 98 dynes.cm.s^{-5}, the final mPAP was 26 ±18 5 mmHg. The early mortality was 2.4 % (2 patients). There were 8 cases (9.5 %) of residual PH. Of notice are 10 cases in which transient neurologic complications took place earlier in our series. These and other complications are discussed. 117 patients underwent BPA only. The average number of sessions of BPA per patient was 6. There were no hospital mortality and ECMO usage. Some cases of reperfusion edema and bronchial bleeding were controlled successfully by non-invasive ventilatory support and pharmacological correction. 4 cases of late mortality (3.4 %) were not caused by CTEPH. 15 patients underwent staged approach of PEA and BPA surgery.

Conclusions: Our initial experience of PEA and BPA is encouraging.

National CTEPH management strategies

ICC2021-C9: SINGLE CENTER EXPERIENCE OF PULMONARY THROMBOENDARTERECTOMY FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Objectives: Pulmonary thromboendarterectomy, remains the preferred and potentially curative option for patients with chronic thromboembolic pulmonary hypertension (CTEPH). The objective of this study was to report the result of pulmonary thromboendarterectomy (PEA) surgery performed for chronic thromboembolic pulmonary hypertension (CTEPH) at a single tertiary center.

Method: This study consisted of 29 CTEPH patients who undergoing PEA between September 2015 and September 2017.

Results: The mean PAP and pulmonary vascular resistance before surgery were 42 ± 15 mmHg (range 20 to 64 mmHg) and 769.8 ± 511 dynes · sec-1 · cm-5 (range, 150 to 1850). The main outcome measures were functional (New York Heart Association [NYHA] class, 6-minute walk distance), hemodynamic (right heart catheterization), and outcome data (morbidity and mortality). There were significant improvements in function class (pre 2.6 ± 0.5 vs post 1.08 ± 0.2, p = 0.00), mean PAP (pre 769 ± 515 mmHg vs post 302 ± 141 mmHg, p = 0.004), cardiac output (pre 4.7 ± 1.4 L/min vs post 5.5 ± 1.2 L/min, p = 0.00), pulmonary vascular resistance (769 ± 515 dynes · sec-1 · cm-5 vs 302 + -141 dynes · sec-1 · cm-5, p = 0.00). The 8 (27 %) number of patients experienced complications. The most common complication was reperfusion injury (17 % Hospital mortality post-surgery was 4.2 %.

Conclusion: Pulmonary thromboendarterectomy can be safely performed with relatively low mortality and favorable prognosis. This surgery should be performed in an expert center and under observation of a multidisciplinary team.

National CTEPH management strategies

ICC2021-C10: TEAM MANAGEMENT IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Objective: Current guidelines recommend a multidisciplinary team approach for treatment decision-making in chronic thromboembolic pulmonary hypertension (CTEPH). We have reviewed our experience with the CTEPH Team using combined efforts of two referral centers: for diagnosis – in Kyiv, and for pulmonary endarterectomy (PEA) – in Lviv.

Methods: We performed 152 PEA, the majority over the past 15 years. Since 2014, during the CTEPH Team work, 47 (77 %) patients were assessed as operable, and 14 (23 %) were deemed inoperable. In previous years, Jamieson type I or II lesions were predominant. More recent 23 patients presented with Jamieson type III disease. All but 4 patients underwent operation with deep -18 degrees C – hypothermia and intermittent total circulatory arrest. Concomitant procedures were performed in 5 – 3 coronary artery bypass grafts, and 2 atrium septum defect closures. Three patients underwent reoperative PEA. One patient was a Jehovah's Witness.

Results: The overall mortality after PEA was 5.1 %, with no deaths among the last 25 PEA. Mortality was related only to residual pulmonary hypertension. One patient with redo PEA died regardless radical surgical desobliteration and ECMO use.

Conclusions: CTEPH Team work and preoperative good-quality pulmonary vasculature imaging is essential for increasing the number of patients suitable for PEA. Operability is determined by accessibility of the thrombi, comorbidities, and clinical situation. Operative mortality associated with PEA has lowered due to recent refinements in surgical techniques and postoperative care, although the surgical learning curve is unavoidable.

National CTEPH management strategies

ICC2021-C11: BALLOON PULMONARY ANGIOPLASTY FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: A NATIONAL REGISTRY

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Objectives: Balloon pulmonary angioplasty (BPA) is an emerging treatment modality for patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH). This study aims to investigate the efficacy and safety of BPA for inoperable CTEPH in a national registry from China.

Methods: We conducted a prospective multicenter cohort study using the data from National Rare Disease Registry System of China. Total 140 consecutive patients with inoperable CTEPH who completed BPA between Jan 2016 and Dec 2020 were enrolled. The key efficacy outcomes were changes from baseline to re-evaluation in pulmonary vascular resistance and six-minute walking distance. The safety outcomes were procedure-related complications. The survival outcome was all-cause mortality.

Results: At re-evaluation, the least-squares mean changes from baseline were -5.3 Wood U (95 % CI, -5.9 to -4.6, P < 0.001) in pulmonary vascular resistance, and 87 meters (95 % CI, 74 to 101, P < 0.001) in six-minute walking distance. BPA procedure-related complications occurred in 109 of 650 BPA sessions (16.8 %), but severe complications requiring noninvasive positive pressure ventilation only occurred in 4 (0.6 %) BPA sessions. During a mean follow-up time of 32 ± 14 months, 4 patients died, including 2 peri-procedural deaths, contributing to the survival rates of 97.8 % (95 % CI, 93.4 to 99.3) at 1 year and 96.9 % (95 % CI, 91.9 to 98.8) at 3 and 5 years.

Conclusions: This multicenter registry confirmed that BPA significantly improved the hemodynamic and functional parameters with acceptable safety profiles and might be an important therapeutic option for inoperable CTEPH in China.

Table: Efficacy outcomes of BPA.

	Total patients (n = 140)		Difference (95 % CI)[¶]	P-value
	Baseline	Re-evaluation		
Mean PAP[†], mm Hg	48.6 ± 12.1	30.1 ± 8.3	-18.3 (-19.9, -16.6)	<0.001
PVR[†], Wood U	9.1 ± 4.6	3.8 ± 2.0	-5.3 (-5.9, -4.6)	<0.001
6MWD[†], meter	364 ± 110	450 ± 80	87 (74, 101)	<0.001
Mean RAP[†], mm Hg	8.2 ± 3.9	6.2 ± 2.7	-2.0 (-2.7, -1.3)	<0.001
CI[†], l/min/m^2	2.6 ± 0.7	3.0 ± 0.6	0.4 (0.2, 0.5)	<0.001
SaO_2[†], %	90.1 ± 4.3	93.4 ± 2.7	3.3 (2.6, 4.0)	<0.001
SvO_2[†], %	62.7 ± 8.5	69.9 ± 6.0	7.1 (5.9, 8.4)	<0.001
NT-proBNP*[†]	6.5 ± 1.7	4.9 ± 1.2	-1.7 (-1.9, -1.4)	<0.001
WHO functional class III/IV[‡]	86 (61.4)	16 (11.4)	0.07 (0.04, 0.12)[§]	<0.001

PAP: pulmonary artery pressure; PVR: pulmonary vascular resistance; 6 MWD: six-minute walking distance; RAP: right atrial pressure; CI: cardiac index; SaO_2: peripheral arterial oxygen saturation; SvO_2: mixed venous oxygen saturation; NT-proBNP: N-terminal fragment of pro-brain natriuretic peptide.
*NT-proBNP was log-transformed; [†]mean ± SD; [‡]n (%); [¶]A generalized estimating equation was used to estimate the mean changes with 95 % CIs for continuous variables and odds ratio with 95 % CI for binary variable between baseline and re-evaluation, with time as a study variable, age and sex as covariates, and subject as a random effect; [§]Odds ratio with 95 % CI.

Basic mechanisms of disease

ICC2021-19: MICRORNA EXPRESSION IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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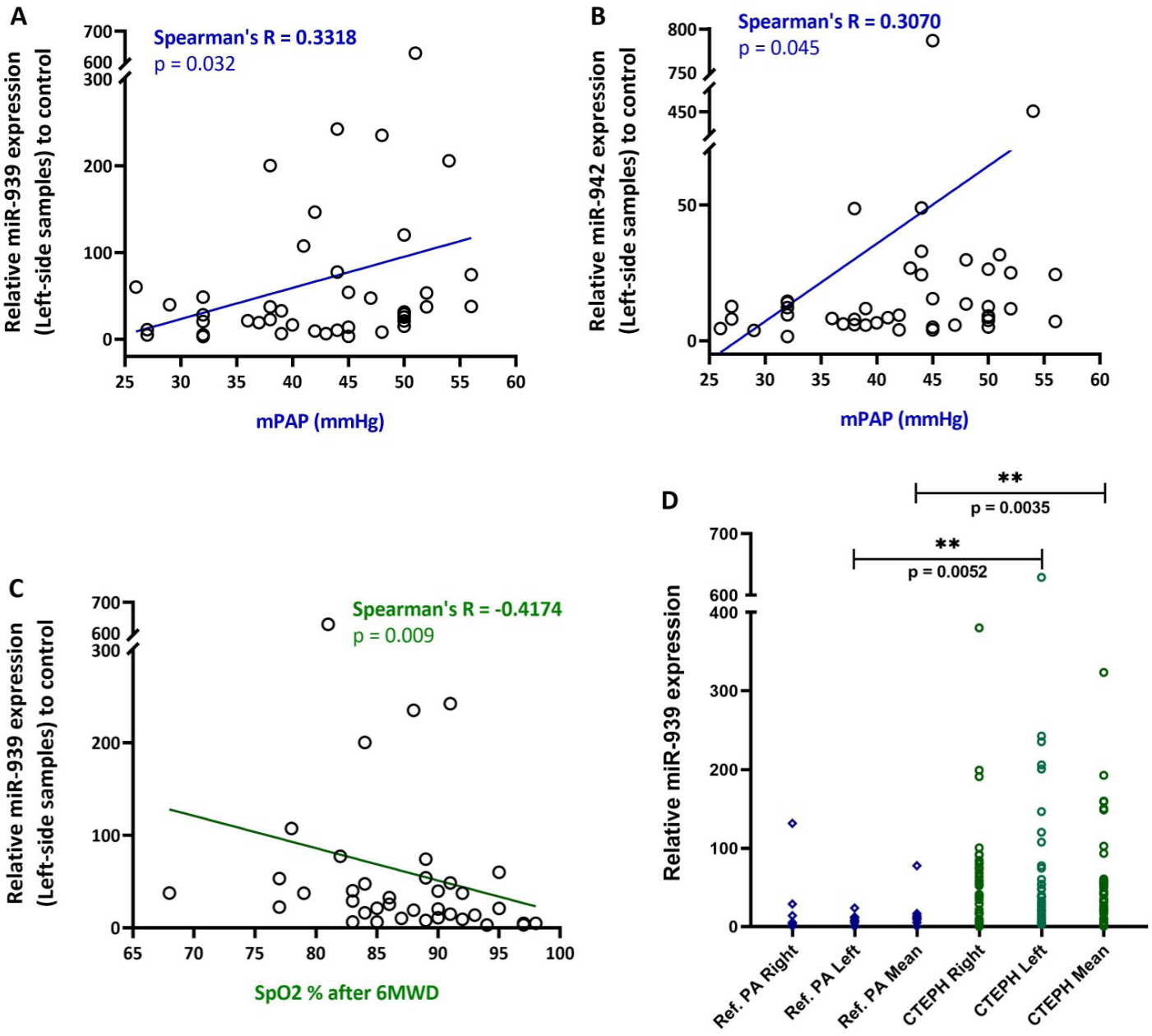
Objective: Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare, disease characterized by pathological changes that obstruct both sides of the pulmonary arteries (PA). The underlying molecular and pathophysiological mechanisms of CTEPH are so far only poorly understood. Aiming to understand a possible contribution of microRNAs to CTEPH development, we analysed the expression of microRNAs in pulmonary endarterectomy (PEA) specimens.

Methods: Expression of miR-939 and miR-942 was analysed in PEA specimens of 46 CTEPH patients and in 10 PAs resected from explant lungs of transplant recipients (predominantly COPD, including n = 4 with PH). Associations between microRNA expression and clinical presentation (not all factors available for every patient) were assessed by Spearman correlation, and differences in expression between CTEPH and reference PAs were compared by Mann Witney test.

Results: A positive correlation with mPAP was observed for both miR-939 (n = 42, R = 0.33, p = 0.032, Fig. 1A), and miR-942 (n = 43, R = 0.31, p = 0.045, Fig. 1B) in left-side PEA-tissue. MiR-939 also correlated negatively with oxygen saturation (SpO_2) at peak 6-minute walk distance (n = 38, R = -0.41, p = 0.009, Fig. 1C). Furthermore, both microRNAs showed elevated expression in CTEPH compared to reference PAs, reaching significance for mean miR-939 (n = 46 CTEPH vs n = 10 Reference, p = 0.0035) and left-sided miR-939 expression (n = 44 CTEPH vs n = 8 Reference, p = 0.0052, Fig. 1D).

Conclusions: The significant elevation of microRNAs in CTEPH compared to reference PA implies that microRNA dysregulation might be involved in CTEPH pathophysiology, possibly through altering of endothelial and inflammatory processes. Furthermore, our results suggest that microRNAs may be associated with clinical presentation of CTEPH.

Figure 1: Correlations between microRNA expression and clinical factors in PEA and reference PA specimens.



MiR-939 (n = 42) **(A)** and miR-942 (n = 43) **(B)** levels from left-side PEA specimens showed a significant positive correlation with pre-operative mPAP values. A significant negative correlation was found between miR-939 levels (n = 38) and SpO_2 after the 6-minute walking distance test **(C).** Mean and left-side levels from PEA and reference PA specimens showed significant differences in miR-939 expression **(D).**

Basic mechanisms of disease

ICC2021-28: NOCTURNAL HYPOXEMIA AND HIGH CIRCULATING TNF-A LEVELS IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Objective: CTEPH is a form of pulmonary hypertension caused by persistent thromboemboli of the pulmonary arteries, and one of its etiological factors may be inflammation. Sleep disordered breathing (SDB) is reportedly an important complication of pulmonary hypertension. However, the association between SDB and inflammation in CTEPH has been undefined. This prospective observational study analyzed the association between the severity of SDB, pulmonary hemodynamic parameters and the systemic inflammation level in patients with CTEPH.

Methods: CTEPH patients admitted for a right heart catheter (RHC) examination were consecutively enrolled from November 2017 to June 2019 at the pulmonary hypertension center in Chiba University Hospital. Patients with idiopathic pulmonary arterial hypertension (IPAH) were also enrolled as a control group. All patients underwent a sleep study using a WatchPAT 200 during admission.

Results: The CTEPH patients showed worse nocturnal hypoxemia, oxygen desaturation index (ODI), and apnea-hypopnea index than the IPAH patients. Among these factors, only the nocturnal mean SpO_2 was negatively correlated with the pulmonary hemodynamic parameters. The circulating tumor necrosis factor-alpha (TNF-α) level was also high in the CTEPH group, and a multivariate analysis showed that the nocturnal mean SpO_2 was the most important predictive factor for a high TNF-α level.

Conclusions: We showed that CTEPH patients had high serum TNF-α levels and that the nocturnal mean SpO_2 was a predictive factor for serum TNF-α levels. Further investigations focused on nocturnal hypoxemia and the TNF-α level may provide novel insight into the etiology and new therapeutic strategies for CTEPH. (Intern Med 2020;59:1819-1826).

Basic mechanisms of disease

ICC2021-29: IMPAIRMENT OF ANGIOGENESIS-DRIVEN CLOT RESOLUTION IS A KEY EVENT IN THE PROGRESSION TO CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: VALIDATION IN A NEW RABBIT MODEL

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Objective: Chronic thromboembolic pulmonary hypertension (CTEPH) is a life-threatening condition and rare complication of acute pulmonary embolism. The reason why clots do not resolve and further result in fibro-thrombotic obstruction of the pulmonary arterial bed remains poorly understood. Since defective angiogenesis is able to prevent clot resolution and has been observed in surgical material from CTEPH patients, we aimed to validate its crucial pathogenic role by local inhibition of angiogenesis in a CTEPH animal model.

Methods: Weekly embolization of autologous blood clots containing an antifibrinolytic agent, tranexamic acid, or an inhibitor of angiogenesis, SU5416, was performed in adult male New Zealand White rabbits. Right ventricular (RV) pressure was monitored by telemetry, RV function was investigated by transthoracic echocardiography and a complete pulmonary hemodynamic evaluation was performed by right heart catheterization before animal sacrifice. Circulating markers of inflammation, endothelial dysfunction, heart failure and fibrinolysis were measured in plasma. Pulmonary vessel remodeling was analyzed.

Results: Inhibition of angiogenesis within repeatedly embolized autologous blood clots resulted in elevated mean pulmonary arterial pressure (38 mmHg), increased indexed pulmonary vascular resistance and enhanced RV hypertrophy (80 %, 1.9-fold and 36 %, respectively compared with rabbits embolized with clots containing an antifibrinolytic agent). This was caused by both obstruction of large pulmonary arteries with fibro-thrombotic material and muscularization of pulmonary microvessels, and was accompanied by an increase in circulating endothelin-1.

Conclusion: We showed that inhibition of angiogenesis within repeatedly embolized clots in rabbits induced more sustained and progressive pulmonary hypertension than inhibition of fibrinolysis.

Epidemiology

ICC2021-7: THE DIFFERENCES BETWEEN CENTRAL AND PERIPHERAL CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Objective: Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by obstruction of segmental pulmonary artery combined with distal small vessel remodeling. Lesions location is crucial for the treatment modality (surgical, interventional, medical or combination). The aim of the study is to investigate the presence of other than morphological differences.

Patients and methods: The study group consisted of 101 patients (60 male/41 female) with confirmed CTEPH. Due to lesion location they were divided into CENTRAL (65 patients; 64 %) vs. PERIPHERAL type (36 patients; 36 %). Compared were demographic, functional, echocardiographic and hemodynamic data, the risk profile as well as.

Results: Significant difference between CENTRAL and PERIPHERAL was found in gender (M = 73 % vs. F = 47 %; P = 0.0198). No difference was revealed in age, functional class or echocardiographic parameters. Hemodynamic parameters showed significant difference in mean pulmonary arterial pressure (45 vs. 59 mmHg; P = 0.0002), transpulmonary gradient (33 vs. 48 mmHg; P = 0.0005), cardiac index (2.03 vs. 2.6 L. min.m2; P = 0.02) but not in pulmonary vascular resistance. In risk profile the only significant difference was found in history of pulmonary embolism (93 % vs. 61 %; P = 0.0002) and of malignancy (1.9 % vs. 14 %; P = 0.0426).

Conclusions: Our study CENTRAL vs. PERIPHERAL CTEPH showed in addition to anatomical also hemodynamic differences. This may indicate that the PERIPHERAL form in contrast to the CENTRAL develops over a much longer time and so enables compensatory mechanisms to preserve better cardiac output, even despite the presence of more severe pulmonary hypertension. Moreover, some risk factors may also play a role also in the localization of CTEPH lesions.

Epidemiology

ICC2021-15: EPIDEMIOLOGY OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH): RESULTS FROM THE CZECH REGISTRY

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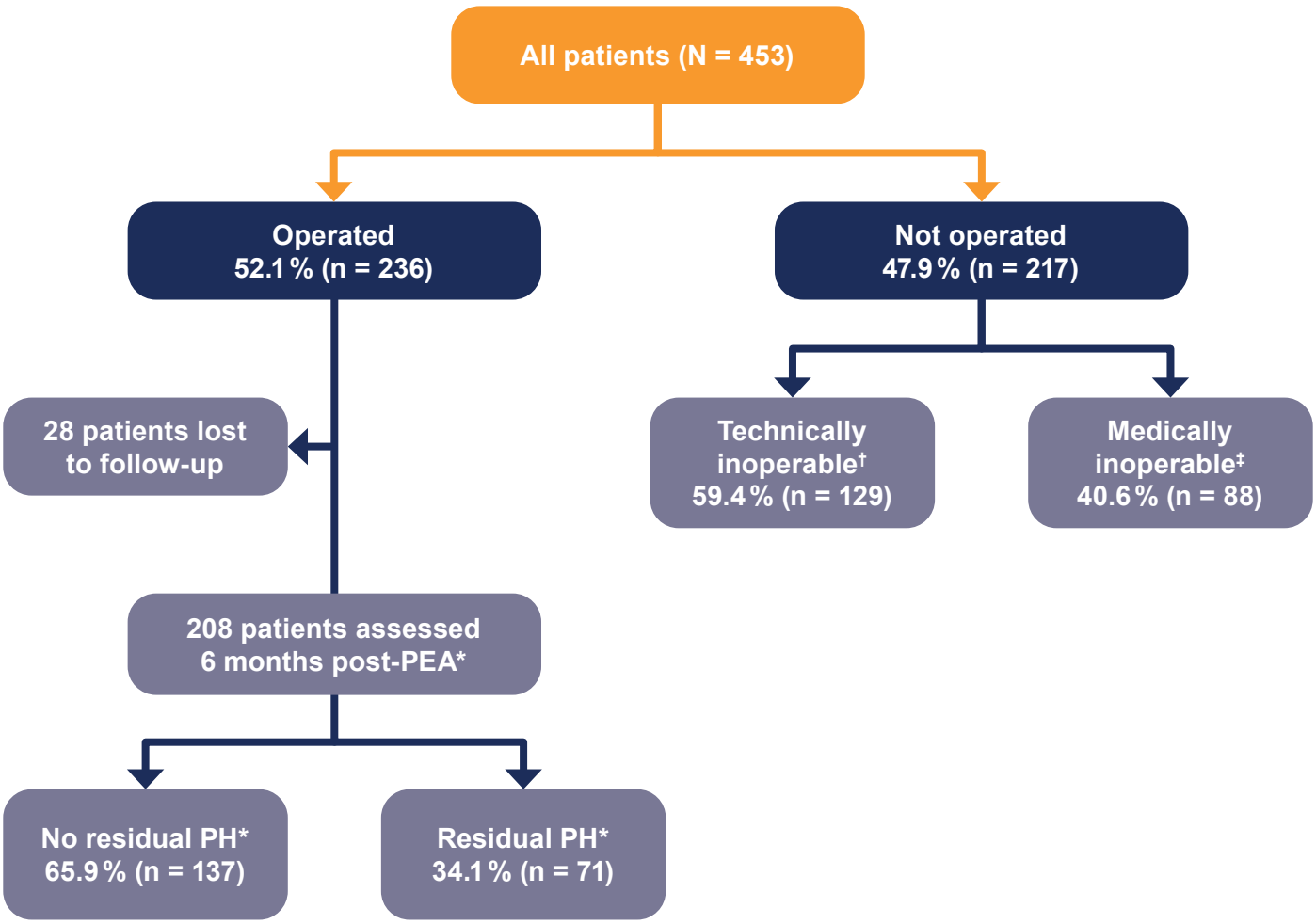
Objective: Referral of CTEPH patients to expert centres is of paramount importance. We report the epidemiology of all adult CTEPH patients diagnosed between 2003 – 2016 in the Czech Republic, where diagnosis and management are centralised in a single expert centre.

Methods: Patients were categorised according to operability (Figure). During the study, the main treatment option was pulmonary endarterectomy (PEA), the gold standard treatment for CTEPH. Medical therapy was limited to riociguat since 2015, and to participation in clinical trials with other drugs, as off-label use is not allowed in Czech Republic. Balloon pulmonary angioplasty (BPA) was introduced in 2016. Incidence/prevalence rates were calculated using the adult general population as denominator.

Results: Patient characteristics (N = 453) at diagnosis were: median (Q1 – Q3) age of 65.2 years (56.3 – 72.4), 54.5 % male, 91.8 % New York Heart Association functional class III – IV, and median 6-minute walk distance of 335.5 m (267.0 – 417.5). Median time from diagnosis to last follow-up was 6.1 years (2.8 – 9.4). CTEPH incidence (2006 – 2016) was 4.47/1,000,000 person-years and prevalence was 37.43 (2016). 236 (52.1 %) patients underwent PEA; 208 patients were evaluated 6 months after PEA via echocardiography and 34.1 % (n = 71) had residual PH (estimated pulmonary artery systolic pressure ≥ 40 mmHg). Of the not-operated patients (n = 217), 59.4 % (n = 129) were technically inoperable (distal disease) and 40.6 % (n = 88) were medically inoperable (comorbidities/refusal).

Conclusions: This analysis identified a high proportion of inoperable patients and operated patients with residual PH, in a setting with limited use of BPA/medical treatment options, providing insight into CTEPH management.



*Residual PH was determined by echocardiographic estimation of pulmonary artery systolic pressure (≥40 mmHg).
†Due to distal disease. ‡Due to comorbidites or refusal.

Conflicts of Interest
P Jansa has received fees and grants from Actelion Pharmaceuticals Ltd, AOP Orphan and MSD.
D Ambrož has no conflicts of interest to declare.
M Kuhn has no conflicts of interest to declare.
V Dytrych has no conflicts of interest to declare.
A Linhart has no conflicts of interest to declare.
J Lindner has no conflicts of interest to declare.
A Muller is an employee of Actelion.

Epidemiology

ICC2021-23: DYSPNEA AFTER PULMONARY EMBOLISM: A NATION-WIDE POPULATION BASED STUDY

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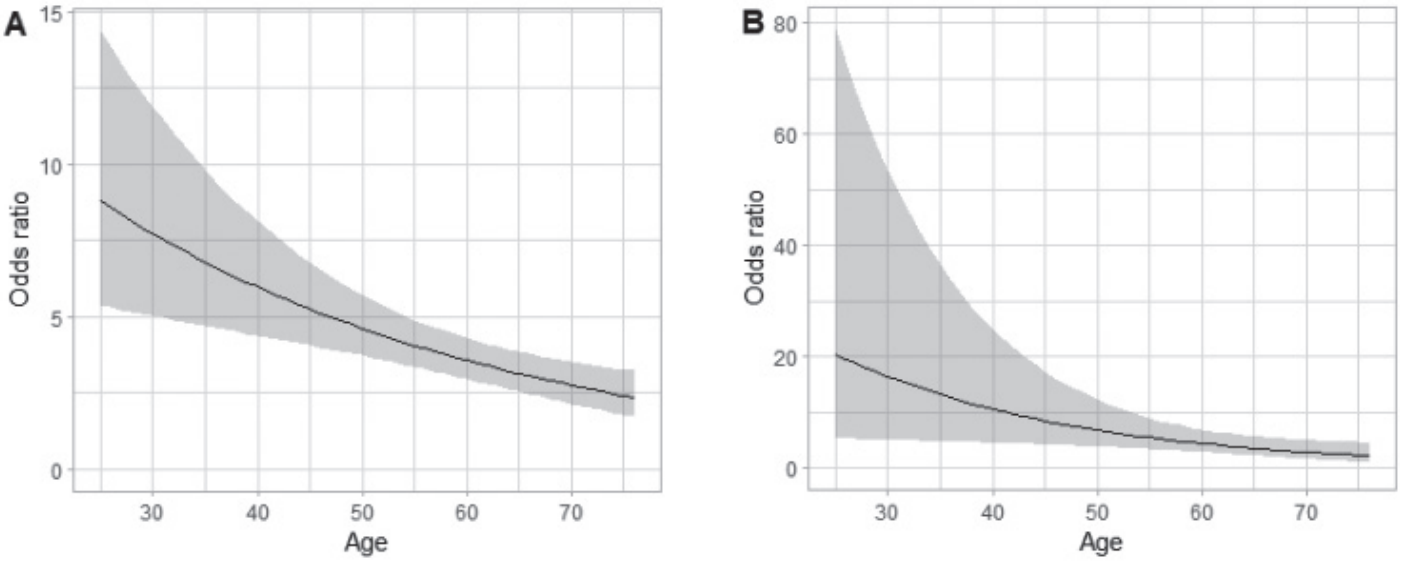
Objectives: Dyspnea is common after a pulmonary embolism (PE). Often, but not always, the dyspnea can be explained by pre-existing comorbidities, and only rarely by chronic thromboembolic pulmonary hypertension (CTEPH). CTEPH is probably the extreme manifestation of a far more common condition, called the post-PE syndrome. The purpose of this retrospective study was to investigate the prevalence and predictors of dyspnea among Swedish patients that survived a PE, compared to the general population.

Methods: All Swedish patients diagnosed with an acute PE in 2005 (n = 5793) were identified via the Swedish National Patient Registry (NPR). Patients that lived until 2007 (n = 3510) were invited to participate. Of these, 2105 patients responded to a questionnaire about dyspnea and comorbidities. Data from the general population (n = 1905) were acquired from the multinational MONItoring of trends and determinants in CArdiovascular disease (MONICA) health survey, conducted in 2004.

Results: Patients with previous PE had higher prevalences of both exertional dyspnea (53.0 % vs. 17.3 %, OR: 5.40, 95 % CI: 4.61 – 6.32) and wake-up dyspnea (12.0 % vs. 1.7 %, OR: 7.7, 95 % CI: 5.28 – 11.23) compared to control subjects. These differences remained after adjustments and were most pronounced among younger patients. The increased risk for exertional dyspnea and wake-up dyspnea remained after propensity score matching (OR [95 % CI]: 4.11 [3.14 – 5.38] and 3.44 [1.95 – 6.06], respectively), Figure 1A – B.

Conclusions: This population-based, nation-wide study demonstrated that self-reported dyspnea was common among patients with previous PE. This finding suggested that a post-PE syndrome might be present, which merits further investigation.

Figure 1



Odds ratio for (A) exertional dyspnea and (B) wake-up dyspnea comparing post-PE group to the MONICA control group, conditioned on age and adjusted for propensity scores. The grey band represents the 95 % confidence interval.

Epidemiology

ICC2021-32: CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION. EXPERIENCE OF A REFERENCE CENTER IN ARGENTINA

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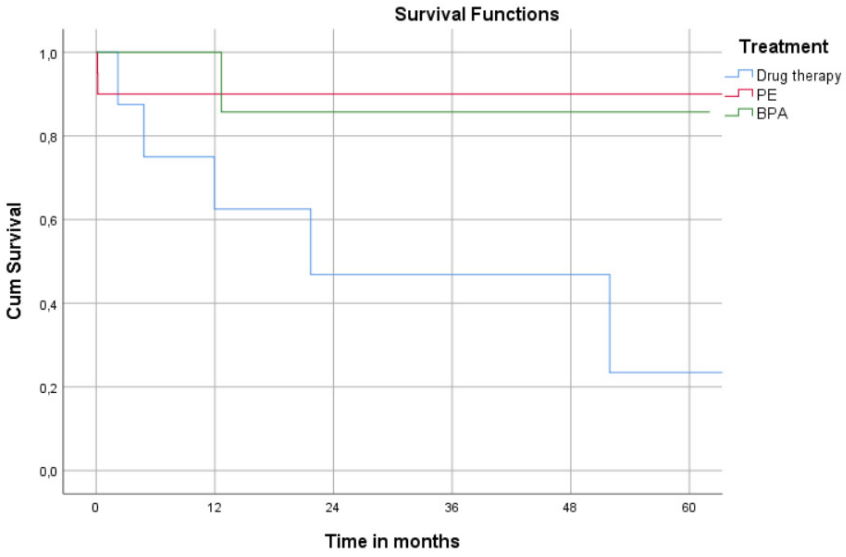
Objectives: To describe clinical characteristics, treatment and follow-up of patients (p) with chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: Of 93 patients diagnosed with PH, 36 had CTEPH (January-2010 to January-2021). One patient was lost at follow-up, total analyzed: 35 patients.

Results: Mean age was 54 ± 17 years old (69 % females). Median follow-up was 25.4 months (IQR25-75: 12.8 – 52.7). At diagnosis, 26 patients (74 %) were in functional class (FC) III/IV and 16 (45 %) had clinical right ventricle failure. Regarding right-cath, median mPAP: 48 mmHg (IQR25-75: 34 – 58), PVR: 722 dynes.sec.cm^{-5} (IQR25-75: 434 – 1250), CI: 2.5 L/min/m^2 (IQR25-75: 1.6 – 3.3) and RAP: 9.5 mmHg (IQR25-75: 6.7 – 14); 22 patients were eligible for pulmonary endarterectomy (PE), 1 patient rejected it and 1 died while waiting: 20 patients (57 %) underwent PE. Twelve (34 %) underwent balloon pulmonary angioplasty (BPA): 7 patients with high risk surgery and 5 patients after PE due to residual PH; 8 (23 %) patients did not receive any invasive treatment: 1 patient died waiting for surgery and the other 7 patients received drug therapy (DT) due to high clinical risk. Of these, 6 received monotherapy and 1 received triple therapy with sildenafil + bosentan + iloprost. At follow-up, a better survival in PE and PBA compared with DT was observed (p=0.02) (Figure).

Conclusions: This registry showed that this population had an advance disease at diagnosis due to most of the patients were in high FC and almost 50 % had clinical right heart failure. Nevertheless, at right heart catheterization, CI and RAP values were not compatible with poor prognostic parameters. At follow-up, PE and BPA were associated with better survival, as published before.

Figure: Kaplan-Meyer survival according to treatment assigned.



Blue line: drug therapy, red line: PE: pulmonary endarterectomy, BPA: balloon pulmonary angioplasty. P = 0.02.

Diagnosis

ICC2021-42: SUCCESSFUL OUTCOMES IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION USING NON-INVASIVE IMAGING APPROACH

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Background: Chronic thromboembolic pulmonary hypertension (CTEPH) is potentially curable by pulmonary endarterectomy (PEA). Therefore, identification of patients suitable for surgery is of utmost importance in the treatment of the disease. Current guidelines recommend conventional pulmonary angiography (CPA) as the final step in the diagnostic pathway. The aim of this study was to identify whether a non-invasive imaging approach in conjunction with right heart catheterisation could be used to aid treatment decisions in CTEPH with comparable outcomes to the published literature using CPA techniques.

Methods: Imaging data was analysed for CTEPH patients identified from the ASPIRE Registry between 2001 and 2014.

Results: A total of 507 patients were identified. The mean age was 63±15 years, mean pulmonary artery pressure 46 ± 11 mmHg and pulmonary vascular resistance 7.6 ± 4.2 WU. Of the patients, 94 % underwent multimodality imaging, 96 % CT-pulmonary-angiography, 84 % perfusion-MR-angiography, 78 % ventilation-perfusion or perfusion-only-lung-imaging, and 2 % CPA. 82 % (n = 418) of patients identified with CTEPH had technically operable disease. Of this 61 % (n = 256) of the patients underwent PEA surgery with a peri-operative mortality of 3 % and five-year survival of 85 %.

Conclusion: By using a non-invasive multimodality imaging approach in CTEPH similar proportion of patients with technically operable disease can be identified as compared to approaches based on CPA. In addition, selection of patients for surgery using a non-invasive imaging approach was associated with a low peri-operative mortality and excellent long-term outcome. These results highlight the value of a non-invasive multi-modality imaging approach to assess patients with CTEPH for consideration of PEA.

Table 1: Imaging modalities used to establish a diagnosis of CTEPH.

Imaging modality	CTEPH whole cohort (n = 507)	CTEPH operated (n = 256)	CTEPH not operated (n = 251)
CTPA, Perfusion MRA, Scintigram	334 (68 %)	185 (72 %)	159 (63 %)
CTPA, Perfusion MRA	74 (15 %)	34 (13 %)	40 (16 %)
CTPA, Scintigram	53 (10 %)	20 (8 %)	33 (13 %)
CTPA only	18 (4 %)	4 (2 %)	14 (6 %)
Perfusion MRA, Scintigram	8 (2 %)	5 (2 %)	3 (1 %)
CTPA, Perfusion MRA, DSA	8 (2 %)	7 (3 %)	2 (1 %)
CTPA, Scintigram, DSA	1 (0.2 %)	1 (0.5 %)	0 (0 %)
DSA only	0 (0 %)	0 (0 %)	0 (0 %)
Scintigram only	0 (0 %)	0 (0 %)	0 (0 %)

Definition of abbreviations: n = number of patients; CTPA = computer tomographic pulmonary angiogram; Perfusion MRA = 3D magnetic resonance perfusion map and magnetic resonance angiogram; DSA = digital subtraction angiography (conventional pulmonary angiogram); Values are expressed as mean (standard deviation) or percentage.

Treatment

ICC2021-3: UNILATERAL CHRONIC THROMBOEMBOLIC PULMONARY DISEASE: DO THEY BENEFIT FROM SURGERY?

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Objectives: Chronic thromboembolic pulmonary hypertension (CTEPH) is considered to be an extreme variant of pulmonary thromboembolism. Unilateral CTEPH is extremely uncommon. It is not clear if these patients benefit from pulmonary thromboendarterectomy (PTE). Here we report 3 cases of CTEPH who underwent successful PTE.

Methods: In this case series we report three symptomatic patients with CTEPH and CTED patients with unilateral involvements. All the patients underwent pulmonary thromboendarterectomy successfully. There were no other reasons for patient's symptoms. PFT were normal as well.

Results: All the patients were young women between the age of 30 and 37. The patients underwent PTE because dyspnea which was otherwise unexplained. First patient was a 37-year-old woman with exertional dyspnea in FC 2. Her VQ scan showed unilateral defect in LLL. Six months after surgery, she was in FC.1. Her 6 MWD increased from 328 m to 441 m. Also, her mPap decreased from 25 mmHg to 19 mmHg. There was no defect in VQ scan 6 months after the surgery. Second patient was a 30-year-old woman with history of PE and DVT. She had dyspnea in FC 2. VQ scan revealed unilateral segmental defect in LLL. One year after surgery she was in FC 1. Her 6MWD improved from 395 m to 474 m without desaturation. Also, her VQ scan test improved completely. The third case was a 30-year-old woman with APS positive. She had history of PE, DVT and CVA. She was symptomatic in FC 2. Her mean Pap at rest was 19 mmHg and after exercise that increased to 32 mmHg. One year after PTE, she was in FC.1. Her 6MWD increased from 260 m to 302 m and mean Pap after exercise decreased from 30 mmHg to 24 mmHg.

Conclusion: Although unilateral symptomatic CTEPH is uncommon, but this diagnosis should be considered in evaluation of patients with unexplained shortness of breath, since some of them may get benefit from PTE.

Treatment

ICC2021-4: SURVIVAL IN PATIENTS WITH CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION IN THE MODERN MANAGEMENT ERA

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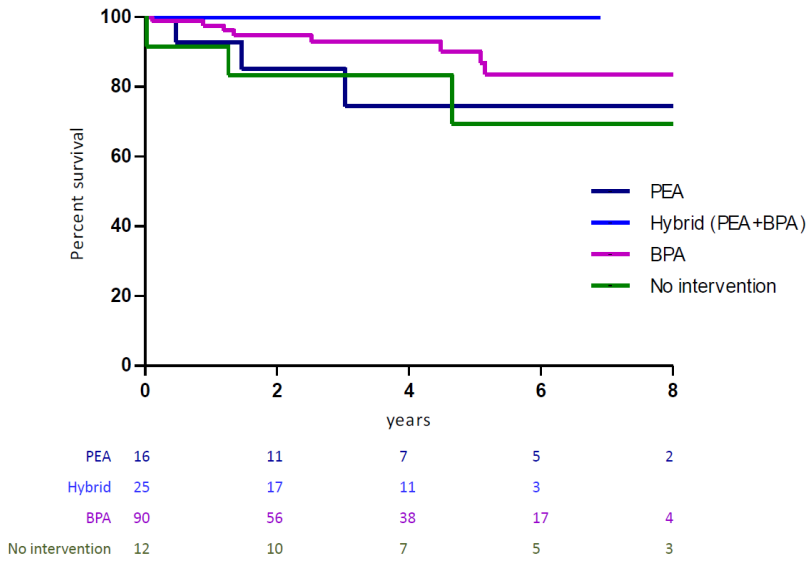
Objective: The management of non-operable chronic thromboembolic pulmonary hypertension (CTEPH) has recently evolved with the availability of balloon pulmonary angioplasty (BPA) and pulmonary vasodilators. We launched BPA program since 2011. The aim was to analyze survival and treatment efficacy in the modern management era.

Methods: We retrospectively reviewed data from 143 consecutive CTEPH patients diagnosed in our university from January 2011 (i.e. after the availability of BPA) to December 2019. Forty-one patients underwent pulmonary endarterectomy (PEA), in these 25 patients underwent additional BPA (Hybrid group) and other patients were treated with only PEA (PEA group). Ninety patients underwent BPA (BPA group), remaining 12 patients had not undergone any interventional treatments.

Results: The 1- and 5-year survival rates of operated patients (n = 41) were 97.4 % and 90.0 %, compared to 96.9 % and 86.9 % in not-operated patients (n = 102), respectively (p = 0.579). There was no death in Hybrid group. Survival of each treatment groups was shown in Figure. Percent decrease of pulmonary vascular resistance in PEA group, Hybrid group, BPA group were -75.4 ± 9.9 %, -74.3 ± 11.8 %, -56.3 ± 22.2 %, respectively (p < 0.01, one-way ANOVA). Absolute decrease of mean pulmonary artery pressure in each group were -20.3 ± 9.5 mmHg, -24.5 ± 8.8 mmHg, -16.4 ± 9.2 mmHg, respectively (p < 0.01, one-way ANOVA).

Conclusions: There was no longer significant difference of long-term survival between operated and not-operated CTEPH. Moreover, Hybrid approach might have the potential to lead notable improvement in the prognosis of CTEPH. BPA and PEA would be mutually complementary therapies in the modern management era.

Figure



Treatment

ICC2021-5: DIFFERENTIAL EFFECT OF ANTICOAGULANT TREATMENT ON VASCULAR MORPHOLOGY IN PATIENTS WITH ACUTE PULMONARY EMBOLISM

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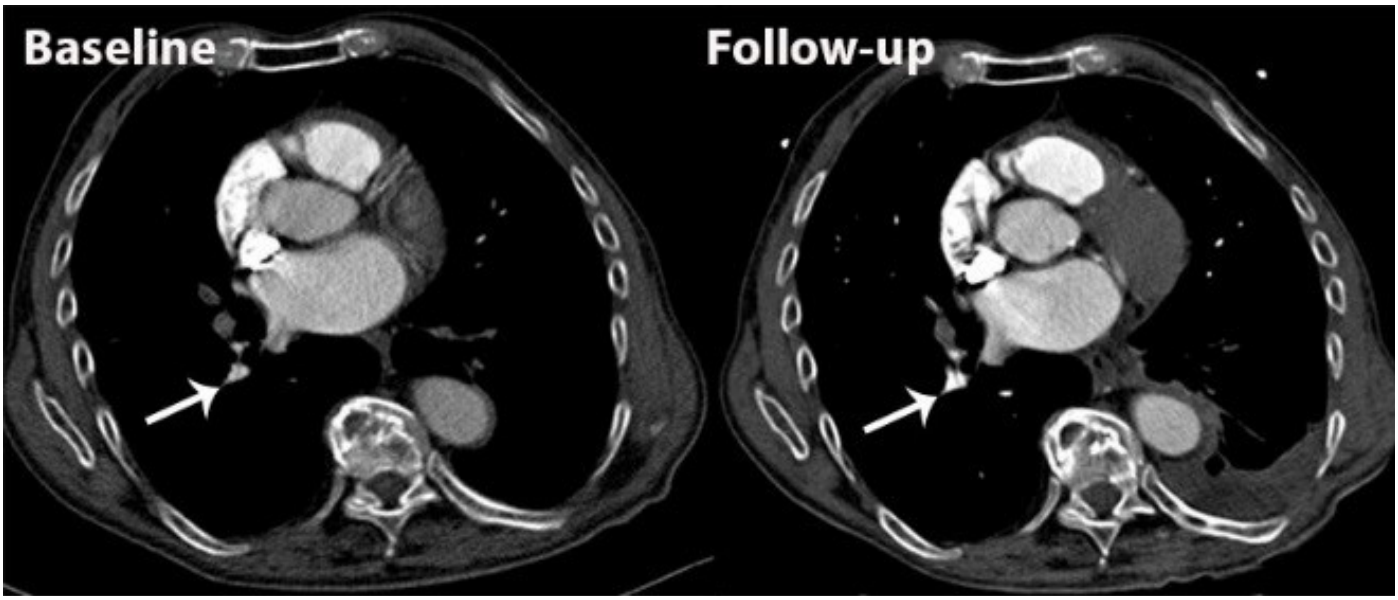
Objective: The relevance of chronic lesions (as seen in chronic thromboembolic pulmonary hypertension (CTEPH) on CT pulmonary angiogram (CTPA) used to diagnose acute pulmonary embolism (APE) is unknown. We aimed to investigate the effect of anticoagulant treatment on CTPA-derived vascular morphological abnormalities in APE patients.

Methods: We selected 30 CTEPH patients with a history of a first APE episode and 116 patients with CTPA performed 6 months after first APE episode in the context of a clinical trial (den Exter 2015). Baseline and follow-up CTPA was available for all patients before and after anticoagulant treatment. Experienced chest radiologists morphologically assessed 20 segmental pulmonary arteries per patient and pulmonary arteries of the entire cohort were merged for analysis.

Results: At baseline CTPA, 1647 (56 %) of the 2920 pulmonary segmental vessels were affected. Almost all central thrombi resolved after oral anticoagulant treatment (1103/1191 = 93 %). Webs (n = 85) and tapered pulmonary arteries (n = 57) did not change in morphology at follow-up (Figure 1). Most vessels totally occluded by a thrombus resolved completely (156/280 = 56 %), changed to a tapered pulmonary artery (26 %) or a web (7 %). Mural thrombi remained unchanged (16/34 = 47 %), resolved completely (29 %) or became a web (24 %).

Conclusions: After anticoagulant treatment for APE almost all central thrombi completely resolved, whereas mural thrombi or total occlusions by thrombi resolved or transformed to a web or tapered pulmonary artery. Interestingly, none of the webs and tapered pulmonary arteries resolved after anticoagulant treatment. Therefore, webs and tapered pulmonary arteries at time of APE diagnosis indicate a chronic PE state.

Figure 1: Web at baseline and follow-up.



Treatment

ICC2021-8: SEVERE INOPERABLE CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION CURABLE BY BALLOON PULMONARY ANGIOPLASTY – A CASE REPORT

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Objectives: Chronic thromboembolic pulmonary hypertension (CTEPH) is a progressive disease caused by organizing thrombo-emboli and vascular remodelling. In addition to surgery and pharmacotherapy is balloon pulmonary angioplasty (BPA) a novel method, improving the pulmonary hemodynamics comparable to surgery but less invasive, effecting much greater mortality and life quality than pharmacotherapy alone. Only few reports have demonstrated the efficacy of BPA as a completely curable intervention like in a our patient with severe inoperable CTEPH.

Results: 30 yrs man, with thrombophilia (fibrinogen and PAI-1 gene mutation) and repeated pulmonary thromboembolism, 4yrs anti-coagulated by VKA, presented with progressive dyspnoe/WHO III. Echo showed severe pressure overloaded right ventricle, right heart catheterization severe PAH (mean PAP 40 mmHg, PCWP 8 mmHg, PVR 8.6 WU), pulmonary angiography bilateral segmental irregularities, subsegmental multiple defects of the branches to the lower lobes. The lesions were estimated as inoperable, medication with riociguat was initiated with temporary (28 months) improvement of exercise capacity (WHO II, 6 MWD + 120 m) and NT-proBNP (-500 ng/l). Despite s.c. treprostinil the patient critically worsened: WHO IV, NT-proBNP 6000 ng/l, mPAP 52 mmHg, PVR 12.3 WU. High risk BPA was performed with immediate improvement in all parameters. After 11 sessions in 25 months a complete normalization of PAP, clinical status and exercise capacity was achieved: mPAP 26 mmHg, PVR 3 WU, WHO I, NT-proBNP 56 ng/l, 6 MWD 620 m.

Conclusion: BPA procedure provides hemodynamic and functional improvement because it is able to resolve obstruction even in distal arteries and achieve substantial decrease of PAP, in our patient even the normalization.

Treatment

ICC2021-13: LIFE EXPECTANCY AFTER PULMONARY ENDARTERECTOMY FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: A SWEDISH SINGLE-CENTER STUDY

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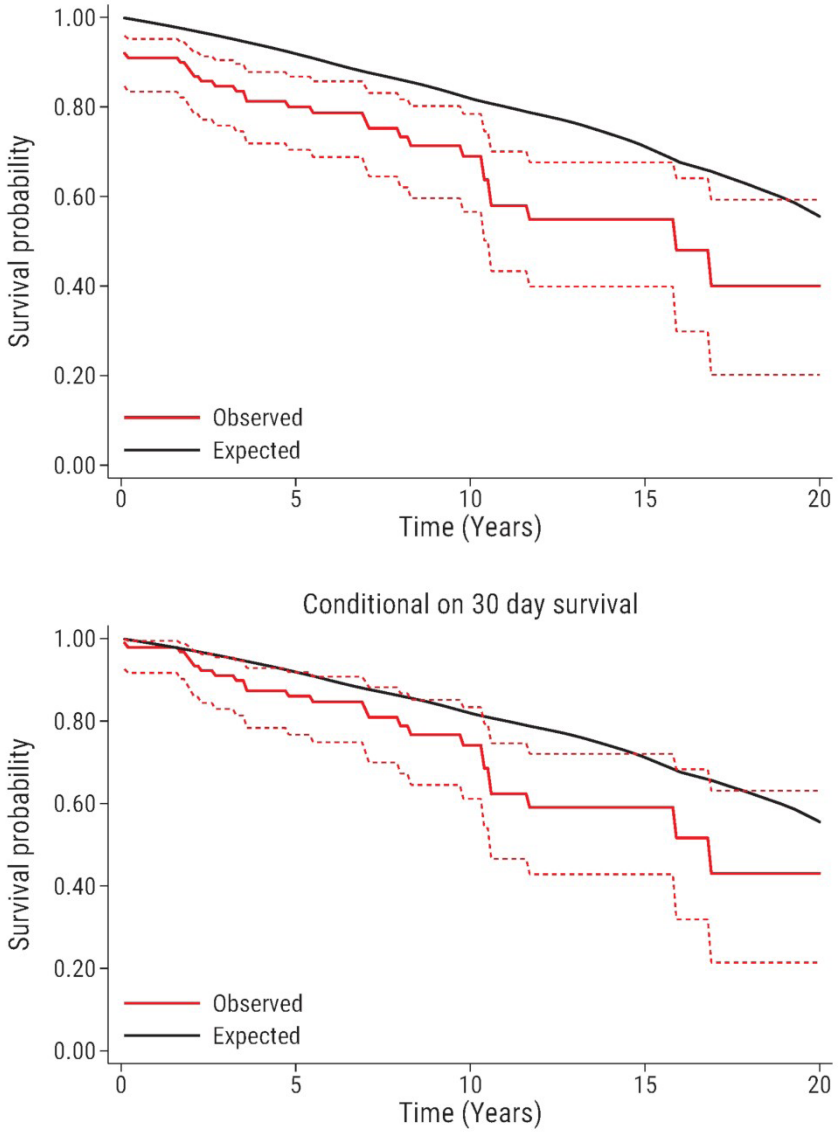
Objective: Pulmonary endarterectomy (PEA) is the guideline recommended treatment for chronic thromboembolic pulmonary hypertension (CTEPH), in addition to life-long anticoagulation therapy. The aim was to analyze long-term relative survival after PEA for CTEPH.

Method: We included all patients who underwent PEA for CTEPH at Karolinska University Hospital between 1997 – 2018 (n = 100). We obtained baseline characteristics and vital status from patient charts and national health-data registers. The expected survival from the general Swedish population matched by age, sex and year of surgery was obtained from the Human Mortality Database. The relative survival was used as an estimate of cause-specific mortality.

Results: The mean age of the patients was 62 years and 39 % were women. Most patients were severely symptomatic (95 % in New York Heart Association functional class III – IV) and mean preoperative systolic/diastolic (mean) pulmonary artery pressure was 78/27 (45) mmHg. The mean and maximum follow-up time was 7.2 and 22.1 years, respectively. Early (30-day) mortality was 7 %. The 15-year observed, expected, and relative survival was 55 % (95 % CI: 40 % – 68 %), 71 %, and 77 % (95 % CI: 56 % – 95 %), respectively. The 15-year relative survival conditional on 30-day survival was 83 % (95 % CI: 60 % – 100 %).

Conclusions: Although the life expectancy following PEA was shorter compared to the general population, the difference was small in those who survived the operation and the early post-operative period. Patients with CTEPH who are surgical candidates should undergo PEA to improve prognosis.

Figure 1: Survival after pulmonary endarterectomy (PEA).



The observed survival (95 % confidence interval) in patients after PEA (red solid line and red dashed lines) compared to the expected survival of an age-, sex-, and calendar-year matched Swedish population (black line). The upper panel show the survival in the total study population (n = 100) and the bottom panel show the survival conditional on patient survival beyond 30 days post-PEA (n = 93).

Treatment

ICC2021-16: INITIAL EXPERIENCE WITH BPA IN THE COMPLEX CTEPH CENTRE

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Objective: Surgical pulmonary endarterectomy (PEA) is the treatment modality that is indicated for 60 – 70 % of patients with confirmed CTEPH. Patients considered as inoperable and patients with persistent/recurrent CTEPH have the option of either undergoing balloon pulmonary angioplasty (BPA) and/or specific pharmacotherapy. Here we present the initial experience with BPA in patients diagnosed and treated in the complex CTEPH centre.

Methods: In total, 25 consecutive patients (11 males and 14 females, mean age 63 ± 10 years) underwent 74 BPA sessions. NYHA functional class, 6-minute walking distance (6 MWD), right heart catheterization, N-terminal probrain natriuretic peptide (NTproBNP) and quality of life (EQ5D-5L questionnaire) were performed at baseline and 4 months (median) after the last BPA session.

Results: The following significant improvements from baseline were observed: NYHA functional class improvement in 75 % of patients, increase of 6 MWD by 54 m, decrease in mean pulmonary artery pressure (PAP) and in pulmonary vascular resistance (PVR) by 18 % and 32 %, respectively, decrease of NTproBNP by 26 % and improvement of quality of life (EQ5D-5L score and overall health status). Non-fatal complication rate was 11.8 %. No death was observed.

Conclusions: BPA is effective procedure improving significantly functional class, exercise capacity, hemodynamics and quality of life in patients treated in expert centre with existing PEA program.

Treatment

ICC2021-18: BALLOON PULMONARY ANGIOPLASTY IN PATIENTS WITH RENAL IMPAIRMENT

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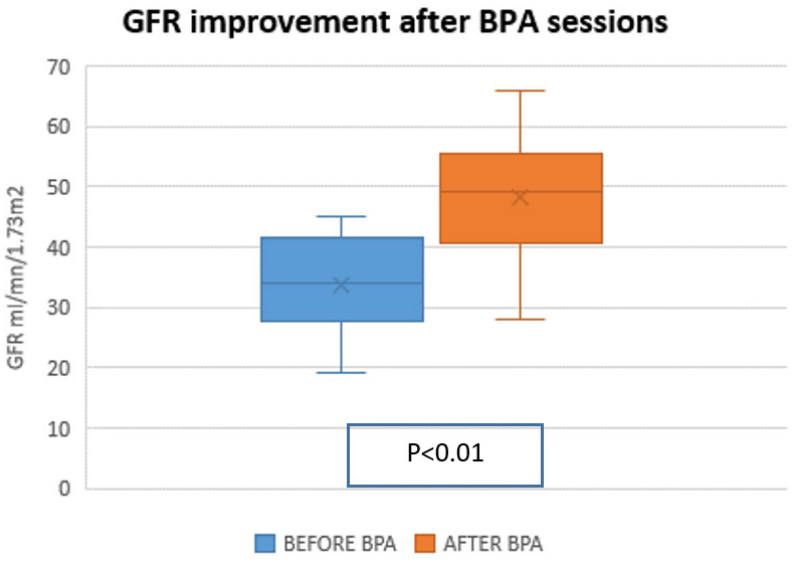
Objective: BPA technic requires repeated sessions with contrast injection. This may be an obstacle in patients with renal dysfunction. Series in the literature have reported that renal function tends to ameliorate after BPA but no data are available for moderate or severe renal impairment. We report the evolution of renal function in patients with renal dysfunction and CTEPH treated with BPA.

Methods: In our series of 52 patients, we checked renal function before and after each BPA session and at the end of the treatment. All reversible potential causes of renal insufficiency, other than the one due to CTEPH, were search and corrected when possible.

Results: Before BPA, 8 patients had a GFR below 45 ml/mn/1.73 m^2 (Mean 33.6 ± 8.6), 13 had a GFR below 60 (Mean 39.5 ± 10.9). Mean amount of contrast received during each BPA procedures was 176 ± 21 ml. The improvement on systolic pulmonary pressure (PAP), Mean PAP and pulmonary vascular resistance was not different in the sub group of patients whatever their renal function. GFR measured after the end of treatment improved from 33.6 to 48 ± 10.9 ($p < 0.01$) and from 39.5 to 53 ± 12.9 ($p < 0.01$) in patients initially below 45 and 60 ml/mn/1.73 m^2 respectively. None of our patient worsened his renal function. All improved their GFR value of at least 25 %.



Conclusion: In patients with severe CTEPH, renal dysfunction should not be considered as an absolute contra indication for BPA. Improvement of hemodynamic conditions have a positive impact on kidney function and may outweigh the potential iodine nephrotoxicity.

Treatment

ICC2021-20: LAUNCHING OF BPA AND BIOBANK PROGRAM FOR PH PATIENTS IN LATVIA

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Objective: Recent meta-analysis has shown that treatment with balloon pulmonary angioplasty (BPA) for inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) results in a greater improvement of functional and hemodynamic parameters than vasodilator therapy [1].
The importance of biobanks for research in rare diseases has been recognized on European Commission level for more than a decade [2].
The aim of this study is to summarize baseline characteristics of CTEPH patients who are selected to potentially undergo BPA and to be included in biobank program at a university hospital.

Methods: Latvian PH registry study summarizing demographic, clinical and hemodynamic parameters of symptomatic, non-operable or recurrent CTEPH patients, with baseline assessment from May-December 2020 who were deemed eligible by multidisciplinary CTEPH team to potentially undergo BPA (starting summer/autumn 2021) within the framework of scientific project approved by Latvian Council of Science.
Additionally, these patients will be offered to voluntarily donate biological samples (blood, stool) to Latvian national biobank before and after BPA treatment [3].
Most recent right heart catheterization, functional capacity test and laboratory data were used.

Results: 15 patients were prospectively deemed as potential candidates for BPA. Baseline characteristics are depicted in the table.

Conclusions: According to European Society of Cardiology/European Respiratory Society guidelines [4], study patients have several risk factors associated with high mortality.
Creation of the first BPA center in the Baltic States would offer additional treatment options for this patient cohort. Furthermore, a PH patient biobank would open new possibilities for future studies and increase collaboration with other centers.

Table: Baseline characteristics of potential BPA candidates among Latvian CTEPH patients.

Parameter	
Number of patients	15
Females	8 (53 %)
Age, years	65 ± 12
NYHA class I-II/III/IV, %	4/10/1
Six-minute walking distance, m	267 ± 59
Mean pulmonary artery pressure, mmHg	49 ± 8
Pulmonary vascular resistance, Wood units	9.1 ± 2.2
Cardiac index, L/min/m^2	2.09 ± 0.24
B-type natriuretic peptide, pg/mL	386 ± 190

Values are shown as frequencies and proportions (%) or mean ± standard deviation.

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Treatment

ICC2021-21: PROCEDURAL-LEVEL HAEMODYNAMICS IN PATIENTS UNDERGOING BALLOON PULMONARY ANGIOPLASTY COMPLICATED BY LUNG REPERFUSION INJURY

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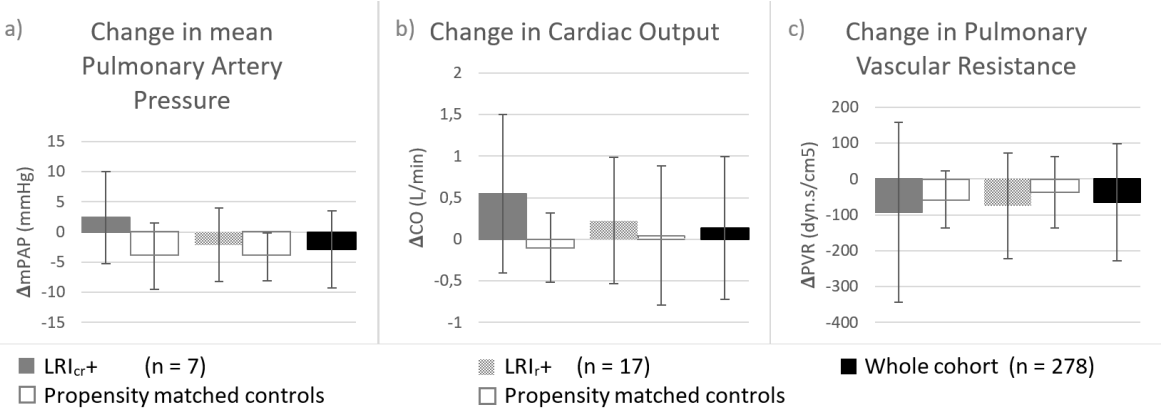
Objective: To assess patients with lung reperfusion injury (LRI) after balloon pulmonary angioplasty (BPA) to determine the procedural-level haemodynamic effect. Hypothesis: BPA complicated by LRI results in a greater haemodynamic effect.

Methods: We retrospectively analysed 278 BPA procedures performed on 101 patients with inoperable chronic thromboembolic pulmonary hypertension (CTEPH). Serial right heart catheterisation was performed before each BPA and at 3 months after the final BPA. LRI was defined clinically (O_2 desaturation > 4 %) or radiologically (wedge opacification in the territory treated) on a post-procedure chest radiograph. Patients were subcategorised into 2 groups: those with clinical and radiological features (LRI_{cr}+) and those with radiological features alone (LRI_r+). Propensity-matched controls without LRI were identified, matched for age, sex, stage of BPA, location and number of vessels treated. Change in mean pulmonary artery pressure (ΔmPAP), cardiac output (ΔCO) and pulmonary vascular resistance (ΔPVR) were compared.

Results: LRI_{cr}+ occurred in 7/278 (2.5 %) BPA procedures whereas LRI_r+ occurred in 17/278 (6.1 %). There was no significant difference in ΔPVR between those with LRI and controls (LRI_{cr}+: -93.2 ± 251.2 vs -56.6 ± 79.7 dyn.s.cm^{-5}, p = 0.36; LRI_r+: -74.3 ± 147.1 vs -36.8 ± 98.6 dyn.s.cm^{-5}, p = 0.20), but there was a trend to increased ΔCO in those with LRI (LRI_{cr}+: +0.55 ± 0.95 vs -0.10 ± 0.42 L/min, p = 0.08; LRI_r+: +0.23 ± 0.76 vs +0.05 ± 0.84 L/min, p = 0.27) and increased ΔmPAP (LRI_{cr}+: +2.4 ± 7.6 vs -4.0 ± 5.5 mmHg, p = 0.06; LRI_r+: -2.1 ± 6.1 vs -4.1 ± 4.0 mmHg, p = 0.14).

Conclusions: LRI after BPA results in greater increases in CO and mPAP relative to propensity matched controls. Ongoing analysis will examine factors predisposing to LRI, particularly demographics and prevailing haemodynamics.

Figure 1: Charts show the mean procedural-level absolute changes in a) mean pulmonary artery pressure (mPAP), b) cardiac output (CO) and c) pulmonary vascular resistance (PVR) relative to propensity-matched controls and the whole cohort. Error bars represent ±1 standard deviation.



Treatment

ICC2021-25: BALLON PULMONARY ANGIOPLASTY FOR INOPERABLE CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: INITIAL EXPERIENCE AT A REFERRAL CENTER IN ARGENTINE

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Objective: Balloon pulmonary angioplasty (BPA) is a novel but well known procedure that has showed to be safe and effective for selected patients with chronic thromboembolic pulmonary hypertension (CTEPH). The aim of this study was to analyze hemodynamic, clinical and safety outcomes of the initial experience at a referral center in Argentine.

Methods: From January 2010 to January 2021 we have 36 patients with CTEPH diagnosis. On December 2015, we started BPA program. Patients were discussed at CTEPH Team. We retrospectively analyzed 12 patients that underwent to BPA.

Results: We performed 21 BPA on 12 patients. The mean age was 56 (30 – 84) years old (11 females, 1 male). 7 inoperable patients and 5 with residual pulmonary hypertension. 50 % of the patients received riociguat before the intervention. After BPA mean pulmonary artery pressure (mPAP) decreased 25 % [52 mmHg (IQR 41.5-59.5) – 39 mmHg (IQR 34.2-48); p 0.039], and the pulmonary vascular resistance (PVR) decreased 51 % [1034 Dyne.s.cm^{-5} (IQR736-1338) – 500 Dyne.s.cm^{-5} (IQR349-583); p 0.001]. The cardiac index had non-significant increase [2.09 L/min/m^2 (IQR 1.7-3.1) – 2.8 L/min/m^2 (IQR2.2-3.6); p 0.146]. Only 1 patient had pulmonary artery dissection during BPA that did not require any specific interventions. 33 % had non-clinical relevant reperfusion edema. No other adverse events were observed neither in-hospital mortality. At the time of diagnosis 83 % were on functional class III/IV, at median follow up of 1.12 years since last intervention 83 % were on functional class I/II (p 0.001) and only one death occurred.

Conclusions: This registry showed clinical and hemodynamic improvement after BPA with good safety profile.

Treatment

ICC2021-26: HOW TO NAVIGATE THE LEARNING CURVE? FUNCTIONAL GUIDED PULMONARY ENDARTERECTOMY

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Objective: Pulmonary endarterectomy (PEA) is a technically challenging operation for cardiothoracic surgeons. The majority of centers initiating a PEA program report a significant surgical learning curve. This study examines the outcomes in a single institution, with PEA guided by functional preoperative images.

Methods: A retrospective case review was performed of 20 consecutive PTEs performed from 2013 to 2020 at a single institution. First 10 patients were operated guided only by pulmonary arteriography (Group A, Control group) and were compared with last 10 patients operated by a functional guided approach (Group B, Functional guided PEA). Functional guided PEA consisted in indicating the surgeon, after a fusion of images between the single photon emissions CT (SPECT) V/Q scan and computed tomography pulmonary angiography (CTPA), the lung segments that had perfusion deficit.

Results: The mean age was 44 ± 17 years (Group A) vs 49 ± 9 years (Group B). Both groups were similar in basal characteristics except mean pulmonary artery pressure (Group A 53 ± 19 mmH vs. Group B 35 ± 13 mmHg, P = 0.03). Operative results were different with less circulatory arrest time (45 ± 16 vs. 30 ± 7 minutes, P = 0.01) and although p nonsignificant, less mortality for Group B (20 % vs. 0 %) (Table 1). At median follow up of 2.6 years no deaths occurred, and all patients are in NYHA Class I or II.

Conclusions: Functional image guided PEA may help the surgeon navigate the learning curve allowing to shorten the circulatory arrest time and probably improving postoperative mortality.

Table 1: Preoperative patient characteristics and outcomes.

Characteristics	Control Group (n = 10)	Functional guided PEA (n = 10)	P value
Age, years, mean ± SD	44 ± 17	49 ± 9	ns
Female, n (%)	7 (70)	7 (70)	ns
Preoperative NYHA Functional Class III/IV, n (%)	8 (80)	8 (80)	ns
Previous cardiac surgery	1 (10)	1 (10)	ns
Urgency/emergency surgery	3 (30)	3 (30)	ns
Preoperative 6MWD meters, mean ± SD	408 ± 183	440 ± 26	ns
Preoperative right heart catheterization			
Mean PAP mm Hg, mean ± SD	53 ± 19	35 ± 13	0.03
Right atrial pressure mm Hg, mean ± SD	10 3	7 4	ns
Cardiac index, liters/min/m^2, mean ± SD	2.3 ± 0.7	2.5 ± 0.8	ns
TPR, dynes · sec · cm^{-5}	859 ± 547	603 ± 408	ns
Pre-op targeted PH therapy			
Endothelin receptor antagonists	3 (30)	1 (10)	ns
Phosphodiesterase inhibitor	3 (30)	0	ns
Prostacyclin analogue	2 (20)	0	ns
sGC stimulators	2 (1)	1 (10)	ns
Combination therapy	2 (1)	1 (10)	ns
Total circulatory arrest, mean ± SD	45 ± 16	30 ± 7	0.01
Cross-clamp, mean ± SD	122 ± 17	112 ± 21	ns
Cardiopulmonary bypass, mean ± SD	235 ± 33	202 ± 23	ns
Most proximal surgical specimen			
Jamieson Type I	0	0	ns
Jamieson Type II	1 (10)	2 (20)	ns
Jamieson Type III	8 (80)	8 (80)	ns
Jamieson Type IV	1 (10)	0	ns
Postoperative mean PAP mm Hg, mean ± SD	27 ± 10	24 ± 8	ns
Extubation time days, mean ± SD	3.9 ± 4.5	5.7 ± 9.5	ns
Hospital stay days, mean ± SD	19 ± 20	16 ± 13	ns
Intensive care unit stay days, mean ± SD	8 ± 7	8 ± 9	ns
Hospital operative mortality	2 (20)	0 (0)	ns
6MWD at 6 months, m	420 118	432 46	ns
NYHA Functional Class III/IV at follow up	0	0	ns

Treatment

ICC2021-27: PULMONARY THROMBOENDARTERECTOMY AFTER BALLOON PULMONARY ANGIOPLASTY: SINGLE CENTER USA EXPERIENCE

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Pulmonary thromboendarterectomy (PTE) remains the treatment of choice for chronic thromboembolic pulmonary hypertension (CTEPH). Balloon pulmonary angioplasty (BPA) has emerged as alternative therapy when PTE is not considered an option. We present a series of patients who underwent PTE after prior BPAs at outside institutions for disease initially deemed inoperable by referring providers.

Methods: CTEPH patients with prior BPAs who underwent PTE at the University of California, San Diego between January 2013 and August 2020 were included.

Results: Seven patients were identified. Average number of BPA sessions prior to PTE was four. The most common reason documented for initial BPA was distal disease deemed inoperable. Six patients were on pulmonary hypertension (PH)-targeted therapy prior to PTE. Average circulatory arrest time was 60.4 ± 13.7 minutes. In comparison, PTE cases in 2019 averaged 45.8 ± 17.7 minutes. Post-operatively, there were no deaths. One patient had airway hemorrhage with reperfusion lung injury and two returned to the operating room for bleeding; none required extracorporeal support. Median ICU and post-operative lengths of stay were 3 (range 2 – 25) and 10 (8 – 34) days, respectively. All patients were discharged off PH-targeted therapy. However, one patient was deemed to have significant residual PH (PVR > 425 dynes.s.cm^{-5}) with anticipated need for resuming PH therapy.

Conclusion: PTE can be safely performed in CTEPH patients previously having undergone BPA procedures. However, these cases were associated with longer circulatory arrest times. One patient had post-operative airway hemorrhage and residual PH. Whether the prior BPAs contributed to these complications are unknown.

Table 1: Pre-PTE interventions and Post-PTE outcomes.

	# BPA sessions	Pre-PTE medications	Post-op complications	Post-op interventions	UCSD Level (R/L)	Days on ventilator	Discharge from ICU	Discharge from Hospital	Discharge with O_2
Patient A	N/A	PDE5	None	N/A	2/2	1	POD 3	POD 8	No
Patient B	4	PDE5, ERA	None	N/A	4/4	1	POD 2	POD 9	No
Patient C	4	ERA, Rio, Inhaled Tre	Hemopericardium	Return to OR	3/4	1	POD 3	POD 21	Yes
Patient D	5	ERA, Rio	Mediastinal hemorrhage	Return to OR	1/2	22	POD 25	POD 34	Yes
Patient E	4	Rio	Airway hemorrhage	iNO	4/4	11	POD 13	POD 19	Yes
Patient F	3	None	None	N/A	1/1	1	POD 3	POD 10	No
Patient G	3	PDE5	None	N/A	2/3	1	POD 3	POD 10	Yes

BPA, balloon pulmonary angioplasty. PTE, pulmonary thromboendarterectomy. Post-op, post-operative. R/L, right/left. ICU, intensive care unit. O_2, oxygen. PDE5, phosphodiesterase type 5 inhibitor. ERA, endothelin receptor antagonist. Rio, riociguat. Tre, Treprostinil. OR, operative room. POD, post-operative day. iNO, inhaled nitric oxide. N/A, not available. UCSD, University of California San Diego. PVR, pulmonary vascular resistance.

Treatment

ICC2021-31: BALLOON PULMONARY ANGIOPLASTY FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: EVALUATION OF EFFICACY OVER TIME AND OF "RESCUE" ANGIOPLASTY SESSIONS

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Objective: In patients undergoing balloon pulmonary angioplasty (BPA) for inoperable chronic thromboembolic pulmonary hypertension (CTEPH), single-centre series from expert centres have recognized a learning curve for magnitude of haemodynamic benefits. We aim at reporting our 7-year experience with BPA, focusing on haemodynamic efficacy over time.

Methods: Inoperable CTEPH patients treated with BPA in our centre between May 2013 and February 2020 who had two complete workups (at baseline [pre-BPA] and 3 – 6 months after the last BPA session [post-BPA]) were analysed. The cohort was separated into two subgroups ("initial period" vs. "recent period"). The effects of "rescue" BPA sessions performed after the "post-BPA" workup in patients considered to have insufficient haemodynamic improvement were also reported.

Results: Among 156 patients treated during the period, 119 had complete evaluations both pre- and post-BPA(Table). In these 119 patients, 646 sessions were performed. The median [interquartile range] duration between pre- and post-BPA was 189 [143 – 284] days. Efficacy was significantly less during the initial than during the recent period (change in mPAP: 8 ± 12 vs. 13 ± 12 mmHg, p = 0.02 and change in PVR: 2.9 ± 3.4 vs. 4.4 ± 3.4 Wood units, p = 0.04). In patients undergoing at least one "rescue" BPA session (n = 47, all from the "initial period"), mPAP further decreased (from 35 ± 9 to 32 ± 7 mmHg, p = 0.046), but PVR did not significantly change (from 5.5 ± 2.8 to 4.3 ± 1.7 Wood units, p = 0.06).

Conclusion: Our analysis is consistent with a learning curve for magnitude of haemodynamic improvements. Rescue BPA sessions seem poorly effective, suggesting the importance to refer patients to experienced centres.

Table: Selected parameters measured in inoperable patients with chronic thromboembolic pulmonary hypertension (CTEPH) before balloon pulmonary angioplasty (pre-BPA) and 3-6 months after the last BPA session (post-BPA).

	Complete cohort (n=119)			Initial period (n=59)			Recent period (n=60)		
	Pre-BPA	Post-BPA	*P*	Pre-BPA	Post-BPA	*P*	Pre-BPA	Post-BPA	*P*
Mono/Bi-/Tri-therapy, %	46/18/0	49/27/0	0.35	24/39/0	42/25/0	0.90	53/13/0	55/20/0	0.23
NYHA FC (I/II/III/IV), %	1/35/55/9	25/62/12/1	<0.001	2/31/56/12	17/64/17/2	<0.001	0/40/53/7	33/60/7/0	<0.001
NT-proBNP (pg/mL)	1 673±1975	522±1 117	<0.001	1 450±1 639	533±907	0.002	1 864±2 235	513±1 286	0.01
Haemodynamics									
mPAP (mmHg)	42±10	31±9	<0.001	43±11	35±9	<0.001	41±10	27±7	<0.001
CI (L/min/m^2)	2.4±0.6	2.7±0.7	<0.001	2.3±0.6	2.4±0.5	0.29	2.5±0.6	2.8±0.7	<0.001
PVR (Wood units)	8.0±3.3	4.2±2.2	<0.001	8.5±3.2	5.6±2.7	<0.001	7.7±3.4	3.3±1.2	<0.001
SvO_2 (%)	63±9	67±6	0.01	63±7	65±9	0.56	63±10	68±6	0.004

BPA: balloon pulmonary angioplasty; NYHA FC: New York Heart Association Functional Class; mPAP: mean pulmonary artery pressure; CI: cardiac index; PVR: pulmonary vascular resistance; SvO_2: mixed venous oxygen saturation.

Treatment

ICC2021-33: ONE CASE OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION COMBINED WITH ATRIAL SEPTAL DEFECT LED TO RADICAL CURE FROM THE SITUATION OF WORLD HEALTH ORGANIZATION FUNCTIONAL CLASS 4

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A 47-year-old female was admitted heart failure with low output syndrome. She was introduced to our hospital for the examination of heart failure at aged 40 year-old and diagnosed as pulmonary hypertension (PH) of atrial septal defect (ASD). After the improvement of heart failure, we re-examined for PH and diagnosed chronic thromboembolic pulmonary hypertension (CTEPH) combined with ASD from right heart catheterization (RHC), pulmonary artery angiography (PAG) and lung perfusion scan. PAG demonstrated that blood-flow in left pulmonary artery was likely to be higher compared to that in patients with primary CTEPH. Six BPAs were performed at Okayama Medical Center during six months. The values of SpO_2 were improved from 90 % on 4 L nasal oxymizer to 98 % on 1 L nasal cannula. Mean pulmonary artery pressure (PAP) was also improved from 44 to 29 mmHg, and oral vasodilators were discontinued. However, ASD closure was considered for radical cure since mild to moderate PH remained consistent. An occlusion test was performed by RHC before operation in terms to determine the hemodynamics after ASD closure. The mean PAP decreased from 35 to 22 mmHg, confirming the closure. RHC and PAG were performed in two weeks after ASD closure, resulting in the improvement of a mean PAP with 20 mmHg. Regarding PAG, blood-flow in left pulmonary artery was significantly improved and lower compared to that seen before the surgery. She was discharged in 18 days after surgery without home oxygen therapy in the state of World Health Organization functional class 1.

Table 1: Hemodynamic effects of BPA and ASD closure in CTEPH combined with ASD.

	Only ASD Sep. 2011	Pre BPA Dec. 2017	Post BPA 6 Jan. 2019	Post closure Feb. 2019	Post BPA 7 Mar. 2020
WHO-functional class	III	IV → III	II	II	I
6 – MWD, m	300	0 → 240	345	440	480
BNP, pg/mL	100.8	227.6	163.5	132.7	52.7
Amount of oxygen	2 L nasal	6 L nasal	1 L nasal	Room air	Room air
Treatment					
ERA; bosentan, mg	–	250	–	–	–
PGI2; beraprost,µg	60	60	–	–	–
PDE5i; sildenafil, mg	60	30	–	–	–
Azosemide, mg	–	30	30	30	15
Spironolactone, mg	–	50	25	25	25
Tolvaptan, mg	–	3.75	–	–	–
Warfarin, mg	–	3.0	3.3	3.5	3.7
RHC data	**Room air**	**4 L nasal**	**Room air**	**Room air**	**Room air**
Heart rate, bpm	88	81	75	82	57
PCWP, mmHg	6	11	7	4	6
Systolic PAP, mmHg	70	79	54	29	24
Diastolic PAP, mmHg	26	24	19	14	14
Mean PAP, mmHg	47	44	31	20	18
RAP, mmHg	5	3	4	4	6
CO, L/min	–	3.85	–	4.33	3.20
CI, L/min/m^2	–	3.32	–	3.48	2.74
PVR, dynes•sec•cm^{-5}	–	872.73	282.49	295.61	224.09
Qp/Qs	1.2	1.4	2.2	–	–
Hemoglobin, mg/dL	13.7	13.4	14.6	11.3	13.8
SvO_2, %	–	78.7	82.6	67.7	72.2
Oxygenation level	**Room air**	**4 L nasal**	**Room air**	**Room air**	**Room air**
SpO_2, %	96.0	88.0	88.0	95.0	96.0
PaO_2, %	81.5	55.9	66.4	75.2	81.1
SaO_2, %	96.6	88.8	93.3	95.4	96.6
Lung perfusion scan data					
RVEF, %	–	36.0	53.0	–	55.0

Abbreviations: BPA – balloon pulmonary angioplasty, ASD – atrial septal defect, CTEPH – chronic thromboembolic pulmonary hypertension, WHO – World Health Organization, 6 MWD – six minutes walk distance, BNP – brain natriuretic peptide, ERA – endothelin receptor antagonist, PGI2 – prostacyclin, PDE5i – phosphodiesterase type5 inhibitor, RHC – right heart catheter, PCWP – pulmonary capillary wedge pressure, PAP – pulmonary artery pressure, RAP – right atrial pressure, CO – cardiac output, CI – cardiac index, PVR – pulmonary vascular resistance, Qp/Qs – pulmonary flow/systemic flow, SvO_2 – mixed venous oxygen saturation, SpO_2 – oxygen saturation of arterial blood measured by pulse oximeter, PaO_2 – partial pressure of arterial oxygen, SaO_2 – oxygen saturation of arterial blood measured by blood gas analysis, RVEF – right ventricular ejection fraction

Treatment

ICC2021-34: APPROPRIATE BALLOON PULMONARY ANGIOPLASTY FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION IMPROVES RIGHT VENTRICULAR EJECTION FRACTION BY LUNG PERFUSION SCAN

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Objectives: Lung perfusion scan (LPS) is required for deciding treatment lesion of appropriate balloon pulmonary angioplasty (BPA) among patients with chronic thromboembolic pulmonary hypertension (CTEPH) and available to measure right heart function. We investigated if BPA improves right heart function by LPS along with pulmonary hemodynamics by right heart catheter (RHC) among CTEPH patients.

Methods: We studied 20 CTEPH patients (mean age 65.0 ± 15.5 years, male 25.0 %) who underwent appropriate BPA. All study sets including RHC, pulmonary artery angiography (PAG), LPS, six-minutes' walk (6 MW) test and blood gas analysis were performed within 5 days before the BPA treatment. All pulmonary hemodynamics by RHC and oxygenation level were measured at room air. Right ventricular ejection fraction (RVEF) was calculated by the first-pass method of LPS. These parameters were compared between before and after BPA.

Results: In total, 98 BPA were performed (mean procedures per patient 4.8 ± 2.6 sessions). Per one BPA session, 6.1 ± 2.4 areas and 10.1 ± 4.0 lesions were treated with the amount of 198.1 ± 53.5 ml contrast media using 1.7 ± 0.5 wires and 2.8 ± 0.8 balloons. There was no complication that required the invasive procedure. World Health Organization functional class, 6 MW distance, pulmonary artery pressure, pulmonary vascular resistance and oxygenation level were significantly improved after BPA (Table 1). Also, RVEF by LPS was significantly improved after BPA (44.4 ± 6.0 to 50.1 ± 2.8, p = 0.001).

Conclusions: In the current study, we found that RVEF by LPS was improved by appropriate BPA along with the other parameters. The relation to prognosis needs to be explored in the future.

Table 1: Hemodynamic effects of BPA in inoperable CTEPH (n = 20).

	Pre BPA	Post BPA	P value
WHO functional class	3.2 ± 0.6	1.5 ± 0.7	**< 0.001**
6 MWD, m	282.6 ± 178.7	413.6 ± 143	**< 0.001**
BNP, pg/ml	189.6 ± 254.3	52.0 ± 57.8	0.057
HOT, n (%)	16 (80.0)	3 (15.0)	**< 0.001**
Treatment			
ERA, n (%)	4 (20.0)	1 (5.0)	
Oral PGI2, n (%)	4 (20.0)	2 (10.0)	
PDE5 inhibitor, n (%)	2 (10.0)	1 (5.0)	
sGC, n (%)	8 (40.0)	6 (30.0)	
Number of PAH targeted drugs: 1, n (%)	7 (35.0)	5 (25.0)	
Number of PAH targeted drugs: 2, n (%)	2 (10.0)	3 (15.0)	
Number of PAH targeted drugs: 3, n (%)	3 (15.0)	0 (0.0)	
CCB, n (%)	4 (20.0)	2 (10.0)	
Diuretics, n (%)	9 (45.0)	11 (55.0)	
Warfarin, n (%)	7 (35.0)	8 (40.0)	
DOAC (only apixaban), n (%)	13 (65.0)	12 (60.0)	
RHC data (room air)			
Heart rate, bpm	76.6 ± 12.8	68.1 ± 14.8	0.012
PCWP, mmHg	8.8 ± 3.3	8.2 ± 2.9	0.602
Systolic PAP, mmHg	67.7 ± 13.3	35.8 ± 6.8	**< 0.001**
Diastolic PAP, mmHg	24.6 ± 6.6	14.5 ± 3.3	**< 0.001**
Mean PAP, mmHg	40.7 ± 7.8	22.5 ± 4.0	**< 0.001**
RAP, mmHg	7.3 ± 4.0	5.7 ± 2.6	0.065
CO, L/min	5.5 ± 3.3	4.9 ± 1.2	0.017
CI, L/min/m^2	3.6 ± 0.8	3.1 ± 0.8	0.018
PVR, dynes • sec • cm^{-5}	500.2 ± 185.6	251.9 ± 112.7	**< 0.001**
Hemoglobin, mg/dL	13.1 ± 1.9	12.6 ± 1.6	0.080
SvO_2, %	59.6 ± 11.2	67.0 ± 4.2	0.008
Oxygenation level (room air)			
SpO_2, %	87.3 ± 5.8	94.2 ± 3.0	**< 0.001**
PaO_2, %	61.0 ± 11.6	78.0 ± 11.0	**< 0.001**
SaO_2, %	89.4 ± 4.4	95.3 ± 1.7	**< 0.001**
Lung perfusion scan data			
RVEF, %	44.4 ± 6.0	50.1 ± 2.8	**0.001**
Average heart rate, bpm	75.9 ± 12.2	75.3 ± 14.2	0.670
ED counts	503.1 ± 279.1	295.8 ± 130.0	**< 0.001**
ES counts	282.6 ± 158.8	147.6 ± 67.1	**< 0.001**

Abbreviations: WHO – World Health Organization, 6 MWD – six minutes walk distance, BNP – brain natriuretic peptide, HOT – home oxygen therapy, PAH – pulmonary artery hypertension, ERA – endothelin receptor antagonist, PGI2 – prostacyclin, PDE5 – phosphodiesterase type5, sGC – soluble guanylate cyclase, CCB – calcium channel blocker, DOAC – direct oral anticoagulant, RHC – right heart catheter, PCWP – pulmonary capillary wedge pressure, PAP – pulmonary artery pressure, RAP – right atrial pressure, CO – cardiac output, CI – cardiac index, PVR – pulmonary vascular resistance, SvO_2 – mixed venous oxygen saturation, SpO_2 – oxygen saturation of arterial blood measured by pulse oximeter, PaO_2 – partial pressure of arterial oxygen, SaO_2 – oxygen saturation of arterial blood measured by blood gas analysis, RVEF – right ventricular ejection fraction, ED – end diastole, ES – end systole

Treatment

ICC2021-35: HAEMODYNAMIC EFFECT OF BPA TREATMENT OF INOPERABLE CTEPH IS GREATER THAN POST-PEA CTEPH

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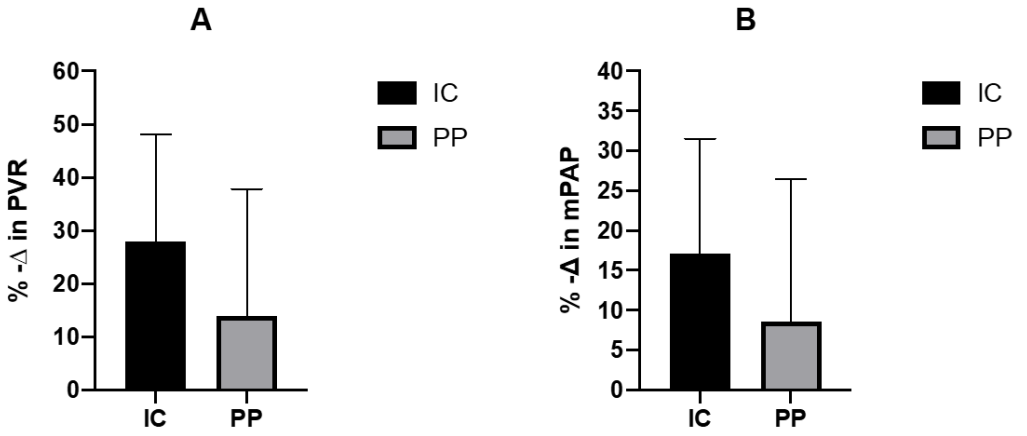
Objective: Pulmonary endarterectomy (PEA), particularly in patients with more distal chronic thromboembolic pulmonary hypertension (CTEPH), may not achieve full clearance. Balloon pulmonary angioplasty (BPA) may be needed to treat residual pulmonary hypertension. We compared whether post-PEA (PP) patients treated by BPA derived similar haemodynamic benefit as those who had inoperable CTEPH (IC).

Methods: We retrospectively compared the haemodynamic effect of BPA in 109 patients – 89 with IC and 20 PP. Serial right heart catheterisation performed at baseline, after each BPA and at 3 months follow-up, compared pulmonary vascular resistance (PVR), mean pulmonary artery pressure (mPAP) and cardiac output (CO). We will also compare WHO functional class, 6-minute walk distance and CAMPHOR QoL.

Results: Preliminary results suggest that PP and IC patients do not differ significantly in terms of baseline disease burden determined by baseline haemodynamics (PVR: 522.25 ± 148.7 vs. 628.47 ± 271.8 dynes.s.cm^{-5}, p = 0.09; mPAP: 39.2 ± 8.8 vs. 42.97 ± 10.6 mmHg, p = 0.14; CO: 4.51 ± 1.0 vs 4.46 ± 0.8, p = 0.82). Neither the total number of BPA procedures undertaken (2.25 ± 0.6 vs. 2.64 ± 1.1, p = 0.12) nor the total number of segments treated (5.40 ± 1.9 vs. 6.08 ± 2.2, p = 0.21) differed. However, IC patients appear to derive greater haemodynamic benefit from BPA; percentage change PVR (-27.9 ± 20.2 % vs. -13.9 ± 23.9 %, p < 0.05) and mPAP (-17.1 ± 14.4 % vs. -8.5 ± 18.0 %, p < 0.05) was greater in IC, as illustrated below. Further analyses will be presented at the conference.

Conclusion: PP and IC patients groups do not differ in haemodynamic or clinical status at baseline. However, IC patients seem to show greater improvement in PVR and mPAP following BPA than do PP patients.



Treatment

ICC2021-36: THE RELATIONSHIP BETWEEN SURGICAL CLEARANCE AND HAEMODYNAMIC RESPONSE IS UNAFFECTED BY BALLOON PULMONARY ANGIOPLASTY

LC Kirkby[1], SP Hoole[2], MS Rodgers[1]

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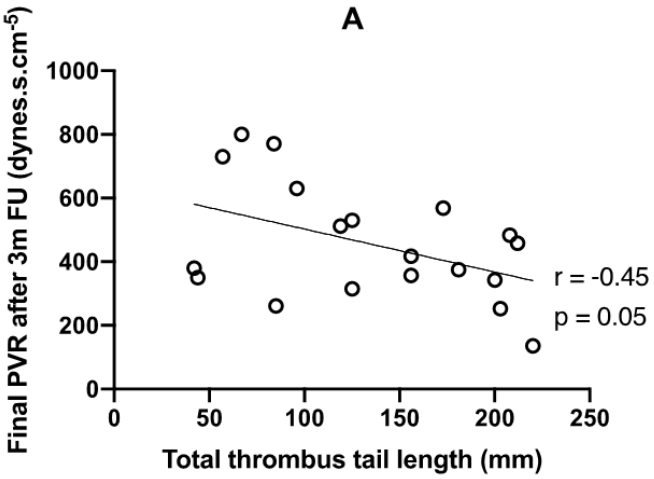
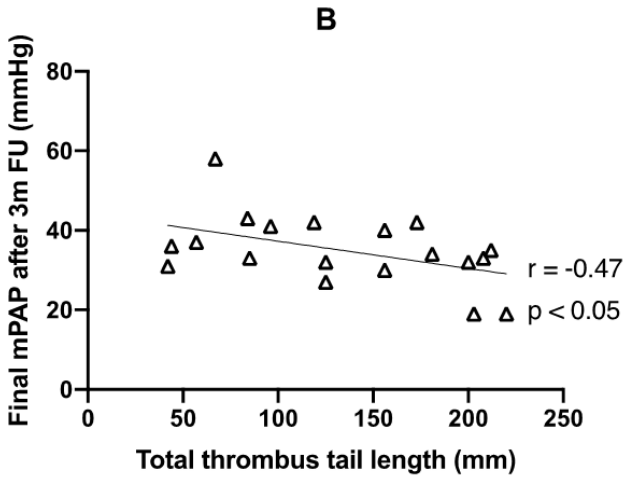
Objective: Pulmonary endarterectomy (PEA) in patients with more distal chronic thromboembolic pulmonary hypertension (CTEPH) may not achieve full clearance and need balloon pulmonary angioplasty (BPA) to treat residual pulmonary hypertension. PEA haemodynamic response is related to total thrombus tail length (TTTL) – a measure of clearance. If BPA is effective in post-PEA patients this association should be abolished.

Methods: We retrospectively compared the haemodynamic effect of BPA in 20 patients with residual CTEPH following PEA. Serial right heart catheterisation was performed at baseline before BPA and at 3 months follow-up after completing BPA. We compared pulmonary vascular resistance (PVR), mean pulmonary artery pressure (mPAP) and cardiac output (CO) with TTTL. Jamieson clearance classification (type I-IV) and haemodynamic effect of BPA will also be presented.

Results: We confirmed that there was a negative correlation between pre-BPA PVR and TTTL ($r = -0.47$, $p < 0.05$) which persisted post-BPA (Figure 1A). Although there was no discernible association between pre-BPA mPAP and TTTL, the association of mPAP and TTTL was strengthened rather than weakened after BPA (Figure 1B). BPA haemodynamic response was not greater in those with lower TTTL compared to higher TTTL tertiles: Δ PVR -47.67 ± 112.8 vs. -64.67 ± 89.8 dynes.s.cm^{-5}, $p = 0.78$; Δ mPAP -1.17 ± 5.31 vs. -4.17 ± 5.71 mmHg, $p = 0.37$.

Conclusion: TTTL correlates with post-surgical haemodynamic response and this relationship is not abolished by BPA, indicating that BPA is ineffective in treating residual CTEPH post-PEA.





Treatment

ICC2021-37: PTE WITH SIMULTANEOUS EXTENDED EN BLOC LEFT ADRENAL-NEPHRECTOMY, RIGHT HEPATECTOMY AND INFERIOR VENA CAVA RECONSTRUCTION FOR CORTICOADRENAL CANCER

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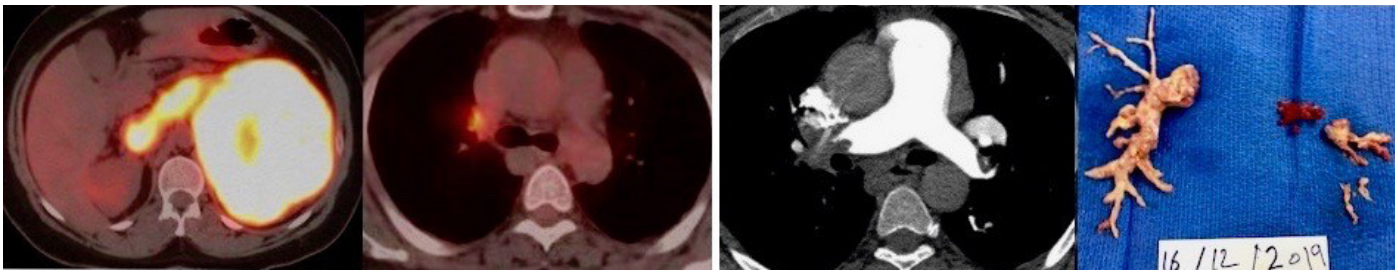
KFSH&RC, Organ Transplant Center and Department of Surgery, Riyadh, Saudi Arabia



Objective: The only curative option for rare adrenocortical carcinoma (ACC) is complete surgical excision. Here, we describe surgical treatment for a patient with initial and persistent symptoms due to tumor embolism to the lungs.

Methods: The patient suffered seven months earlier from massive PE with no response for anticoagulation. She expressed hirsutism, lower limb swelling, and facial puffiness. CT, MRI, and ECHO showed a large left suprarenal mass, with invasion through the left renal vein to IVC with thrombosed right hepatic vein and extension to the right atrium. CT and PET CT suggested neoplastic bilateral pulmonary embolism, with no extravascular findings. The patient consented for palliative surgery. She underwent extended en bloc left adrenal-nephrectomy, including spleen, distal pancreas, with right hepatectomy and resection of inferior vena cava tumor. Perfusion and cooling down were started to complete right hepatectomy and IVC reconstruction. After that, complete PTE under circulatory arrest was done. No macroscopic tumor was left behind. Mean pulmonary pressure normalized from 41 to 18 mmHg, and resistance from 533 to 221 dynes. The patient was initially extubated on the fourth pod. Two re-laparotomies were performed because of postoperative collections.

Results: Pseudomonas and Candida Auris infections complicated her recovery. She is still on hemodialysis. High S-Corsol, S-DHEA and S-Testosterone values normalized. PET CT three months later is negative.

Conclusions: To our knowledge, this is the first macroscopically radical surgery reported for Stage 4 ACC. Three months after her surgery, there is no clear evidence of her disease. Further outcome will be discussed.

Treatment

ICC2021-38: PULMONARY ENDARTERECTOMY AND CONCOMITANT CORRECTION OF CONGENITAL HEART DISEASE – SAFE AND FEASIBLE

R Seetharaman[1], CY Ng[1], J Taghavi1, S Tsui[1], JA Hoschtitzky[2], DP Jenkins[1]

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Objective: Pulmonary endarterectomy (PEA) is the guideline recommended treatment (1C) for Chronic thromboembolic pulmonary hypertension (CTEPH). PEA can be performed safely in conjunction with concomitant coronary artery bypass graft and valvular surgery. However, concomitant surgery for correction of adult congenital heart disease (ACHD) and CTEPH has not been previously reported.

Methods: The prospectively acquired Pulmonary Hypertension database was reviewed retrospectively and 3 cases of PEA and correction of congenital heart defects were identified between 2018 and 2020. Patient management was discussed between the CTEPH and ACHD MDT's at the two centres and operations were performed jointly by a PEA and a congenital cardiac surgeon.

Results: All 3 patients had a successful concomitant surgery. First Case – 45-year-old female who presented with CTEPH predominantly involving both lower lobes and bilateral anomalous pulmonary venous drainage involving the upper lobes with mean Pulmonary Artery (PA) pressure of 38 mmHg and Pulmonary vascular resistance (PVR) of 8WU. Second Case – 76-year-old female who presented with CTEPH and a partial atrio ventricular canal defect with a small atrial and small ventricular component and moderate leak of the left AV valve with mean PA pressure of 46 mmHg and PVR of 12 WU. Third Case – 47-year-old female who had CTEPH primarily involving the right lung and right hemi-anomalous pulmonary venous drainage to Right atrium with mean PA pressure of 35 mmHg and PVR of 10 WU. The mean PVR was reduced from 10 ± 2 WU to 3 ± 1 WU, and all made a satisfactory recovery with improvement in haemodynamics and right heart function.

Conclusion: Careful MDT discussion between CTEPH and ACHD teams is critical to the management of these complex patients and combined surgery is essential to ensure the best outcome. Important to the decision making is estimation that the PH is explained by the thromboembolic burden and that it can be effectively cleared and that the congenital lesion can be repaired.

Treatment

ICC2021-39: UNUSUAL CAUSES OF CTEPH, SUCCESSFULLY TREATED BY SURGERY

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Royal Papworth Hospital, Cambridge, UK

Objective: Two very unusual cases of chronic thromboembolic pulmonary hypertension (CTEPH) are described.

Material and Methods: Retrospective case reports from prospectively collected data to a PH database.
The first case was a 65-year-old female with interstitial lung disease urgently listed for lung transplantation (WHO class IV). The donor had no history of thromboembolic disease. She underwent an uneventful left single lung transplant. Post op she had moderate pulmonary hypertension (mPAP 37 mmHg). She was extubated on post-op day (POD) 1. However, because of high oxygen requirements Computed tomography pulmonary angiogram (CTPA) was performed on POD 7 which showed CTEPH in the donor lung. Due to clinical deterioration with worsening hypoxia, she was readmitted to critical care on POD 9 and underwent pulmonary endarterectomy (PEA) of the allograft left lung on POD 13.
Second case was 5-year-old girl preterm delivery 26 + 1 weeks, with history of right atrial thrombus as a neonate secondary to central line which resolved with anticoagulation and subsequently discharged after 111 days in neonatal ICU with home oxygen. Over the last 2 years, she had 3 episodes of syncope and reduction in physical activity (WHO class III). On further evaluation diagnosed CTEPH with occlusion of the right middle and lower lobes. Her mPAP was 68 mmHg and PVRI of 21.1 WU/m^2. She underwent a successful PEA despite weighing only 16 Kg.

Results: The first patient made steady progress following PEA. Post-operatively her mPAP decreased to 16 mmHg and CTPA showed improved perfusion of the left lung. She was discharged home on POD 42. The second patient had a protracted post-op course and delayed chest closure. However, she made a good recovery and post-op imaging showed improved perfusion to right lung and a reduction in right ventricle volume of more than 50 % on MRI.

Conclusion: PEA is the guideline recommendation for operable CTEPH. However, in the cases described, where previous experience is not available, the key to success is a multi-disciplinary approach.

Figure

Left Pane – Case 1, Right Pane – Case 2

Treatment

ICC2021-41: SEX AND SURVIVAL FOLLOWING PULMONARY ENDARTERECTOMY FOR CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: A SCANDINAVIAN OBSERVATIONAL COHORT STUDY

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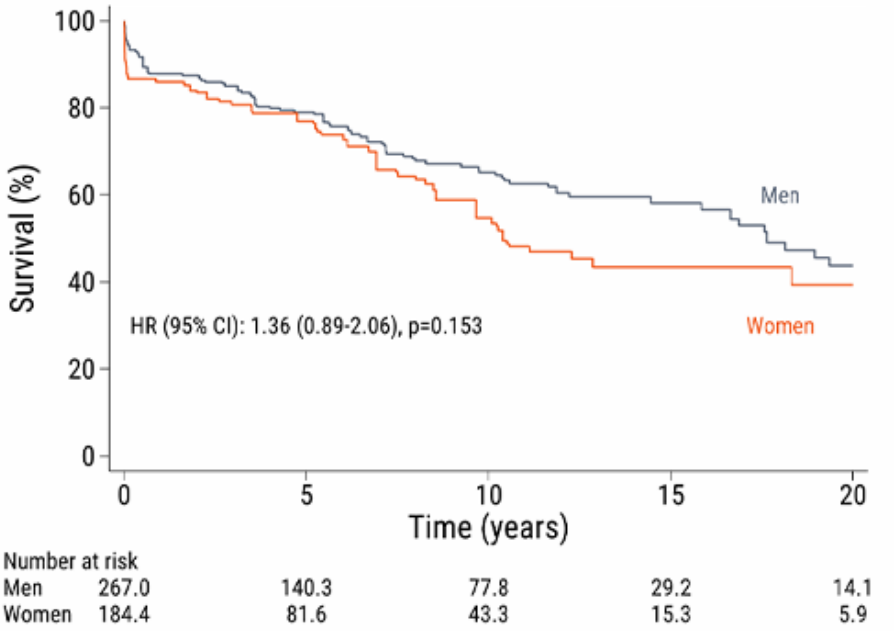
Objective: Studies have suggested sex-related survival differences in chronic thromboembolic pulmonary hypertension (CTEPH). Whether long-term prognosis differs between men and women following pulmonary endarterectomy (PEA) for CTEPH remains unclear. We investigated sex-specific survival after PEA for CTEPH.

Methods: We included all patients who underwent PEA for CTEPH at two Scandinavian centers and obtained baseline characteristics and vital statuses from patient charts and national health-data registers. Propensity scores and weighting were used to account for baseline differences. Flexible parametric survival models were employed to estimate the association between sex and all-cause mortality and the absolute survival differences. The expected survival in a matched general population was obtained and the relative survival was used to estimate cause-specific mortality.

Results: A total of 444 patients were included, comprising 260 (59 %) men and 184 (41 %) women. Unadjusted 30-day mortality was 4.2 % in men versus 9.8 % in women (p = 0.020). In weighted analyses, long-term survival did not differ significantly in women compared with men (HR: 1.36; 95 % CI: 0.89 – 2.06). Relative survival at 15 years conditional on 30-day survival was 94 % (79 % – 107 %) in men versus 75 % (59 % – 88 %) in women.

Conclusions: In patients who underwent PEA for CTEPH, early mortality was higher in women compared with men. After adjustment for differences in baseline characteristics, female sex was not associated with long-term survival. However, relative survival analyses suggested that the observed survival in men was close to the expected survival in the matched general population, whereas survival in women deviated notably from the matched general population.

Figure 1: Kaplan-Meier estimated survival according to sex after pulmonary endarterectomy in the inverse probability of treatment weighted population.



Note that the numbers of patients in the groups are not necessarily integers because of the inverse probability of treatment weighting. HR = hazard ratio; CI = confidence interval.

Treatment

ICC2021-43: CHRONIC THROMBOEMBOLIC DISEASE AMONG PATIENTS UNDERGOING SURGICAL PULMONARY EMBOLECTOMY FOR ACUTE PULMONARY EMBOLISM

D Zieliński[1], A Biederman[1], W Dyk[1], M Zygier[1], R Wojdyga[1], E Pirsztuk[2], K Szostakiewicz[2], B Błaszczyk[2,3], P Szatkowski[2,4], K Wróbel[1]

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Objective: Some patients undergoing pulmonary embolectomy are found to have undiagnosed chronic thromboembolic disease during the procedure. The purpose of this study is to evaluate the prevalence of chronic thromboembolic disease among patients undergoing pulmonary embolectomy and its impact on the patient outcomes.

Methods: Between 2013 and 2021, 33 patients underwent pulmonary embolectomy for acute pulmonary embolism. 5 patients with a known history of acute pulmonary embolism. None of the patients were diagnosed with chronic thromboembolic hypertension or chronic thromboembolic disease. All procedures were performed by surgeons experienced in performing pulmonary artery endarterectomy. Depending on the intraoperative identification of chronic lesions, patients were classified into two groups Acute/Chronic and Acute group.

Results: Intraoperatively, 39 % (13) of patients were identified to have chronic thromboembolic disease (Acute/Chronic group). There were no significant relationship in laboratory tests between groups. Patients in the Acute/Chronic group presented significantly longer duration of respiratory symptoms. All patients with a history of acute pulmonary embolism were found to have chronic disease intraoperatively. In the Acute/Chronic group, longer extracorporeal circulation and total circulatory arrest times were required and extracorporeal membrane oxygenation was significantly more frequently used. There was no death in the Acute group and 2 deaths in the Acute/Chronic group (0 % vs. 15 %; p = 0.148). Patients' characteristics and outcomes are shown in Table 1.

Conclusion: Chronic thromboembolic disease is not uncommon among patients undergoing pulmonary embolectomy. These patients require particular attention both during the qualification for the surgery and further management and a team with extensive treatment experience.

	All (n-33)	Acute (n-20)	Acute/Chronic (n-13)	p value
Age	51.88 ± 15.96	55.79 ± 17.42	46.57 ± 12.44	NS (0.102)
Sex	51.52 % (17)	45.00 % (9)	61.54 % (8)	NS (0.481)
DVT	69.70 % (23)	70.00 % (14)	69.23 % (9)	NS (> 0.999)
History of PE	15.15 % (5)	0	38.46 % (5)	**0.005**
Respiratory symptoms duration	7.00 (3.00; 21.00)	4.00 (3.00; 7.00)	17.5 (8.50; 60.00)	**0.004**
> 1 week	54.55 % (18)	30.00 % (6)	92.31 % (12)	**0.001**
> 2 weeks	42.42 % (14)	25.00 % (5)	69.23 % (9)	**0.029**
> 3 weeks	24.24 % (8)	5.00 % (1)	53.85 % (7)	**0.002**
Malignancy	21.21 % (7)	20.00 % (4)	23.08 % (3)	NS (> 0.999)
Major surgery/trauma < 3 weeks	15.15 % (5)	20.00 % (4)	7.69 % (1)	NS (0.625)
Troponin (pg/mL)	68.50 (31.20; 254.80)	96.94 (42.40; 254.80)	56.95 (31.00; 114.00)	NS (0.873)
NT-proBNP (pg/mL)	7766 (2937; 11362)	7896 (2937; 11362)	7354 (3754; 11764)	NS (> 0.999)
D-dimer (ng/mL)	15166 (2090; 20722)	18130 (7964; 25922)	4772 (2090; 10000)	NS (0.083)
RV/LV ratio	1.90 ± 0.42	1.93 ± 0.40	1.87 ± 0.45	NS (0.830)
PESI score	108.12 ± 40.83	112.89 ± 40.51	101.64 ± 41.87	NS (0.221)
Operative data				
ECC time (m)	166.00 (144.00; 189.00)	151.00 (142.00; 169.00)	182.00 (153.00; 219.00)	**0.029**
Cross-clamp time (m)	78.00 ± 18.00	73.00 ± 19.00	85.00 ± 19.50	NS (0.059)
DHCA (m)	18.00 (13.00; 26.00)	16.00 ± 9.00	26.00 ± 13.00	**0.022**
ECMO	12.12 % (4)	0	30.77 % (4)	**0.017**
Postoperative haemodynamic				
mPAP (mmHg)	21.50 ± 5.62	19.11 ± 3.76	24.85 ± 6.19	**0.003**
PVR (dyn×s/cm^5)	185.38 ± 98.49	136.67 ± 65.57	252.85 ± 98.35	**0.002**
CI (l/min/m^2)	2.80 ± 0.64	2.77 ± 0.66	2.85 ± 0.64	NS (0.440)
Postoperative outcomes				
Ventilation time (h)	23.00 (20.00; 37.00)	21.00 (20.00; 37.00)	24.00 (17.00; 31.00)	NS (0.660)
ICU stay (d)	6.00 (4.00; 10.00)	6.00 (4.00; 9.00)	6.00 (4.00; 13.00)	NS (0.865)
Renal failure	21.21 % (7)	20.00 % (4)	23.08 % (3)	NS (> 0.999)
New dialysis at discharge	0	0	0	
Neurology	0	0	0	
In-hospital stay (d)	16.00 (13.00; 27.00)	14.00 (12.00; 20.00)	27.00 (14.00; 38.00)	**0.046**
In-hospital mortality	6.06 % (2)	0	15.38 % (2)	NS (0.148)
Follow up mortality	12.12 % (4)	5.00 % (1)	23.08 % (3)	NS (0.276)

Given values are: median (interquartile range) for quantitative variables without normal distribution, mean and standard deviation for quantitative variables with normal distribution and percent (number) for qualitative variables.
DVT – deep vein thrombosis; PE – pulmonary embolism; RV – right ventricle; LV – left ventricle; PESI – pulmonary embolism severity index; ECC – extracorporeal circulation; DHCA – deep hypothermic circulatory arrest; ECMO – extracorporeal membrane oxygenation; mPAP – mean pulmonary artery pressure; PVR – pulmonary vascular resistance; CI – cardiac index; ICU – intensive care unit.

Treatment

ICC2021-45: THE UNUSUAL CASE OF CTEPH TREATED BY BPA IN PATIENT WITH SINGLE-LUNG AFTER CANCER SURGERY

S Darocha[1], P Kurzyna[2], M Banaszkiewicz-Cyganek[1], P Kędzierski[1], M Florczyk[1], A Pietrasik[2], D Zieliński[3], A Biderman[3], A Torbicki[1], M Kurzyna[1]

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Objective: To evaluate the efficacy and safety of BPA in single-lung patient with proximal CTEPH.

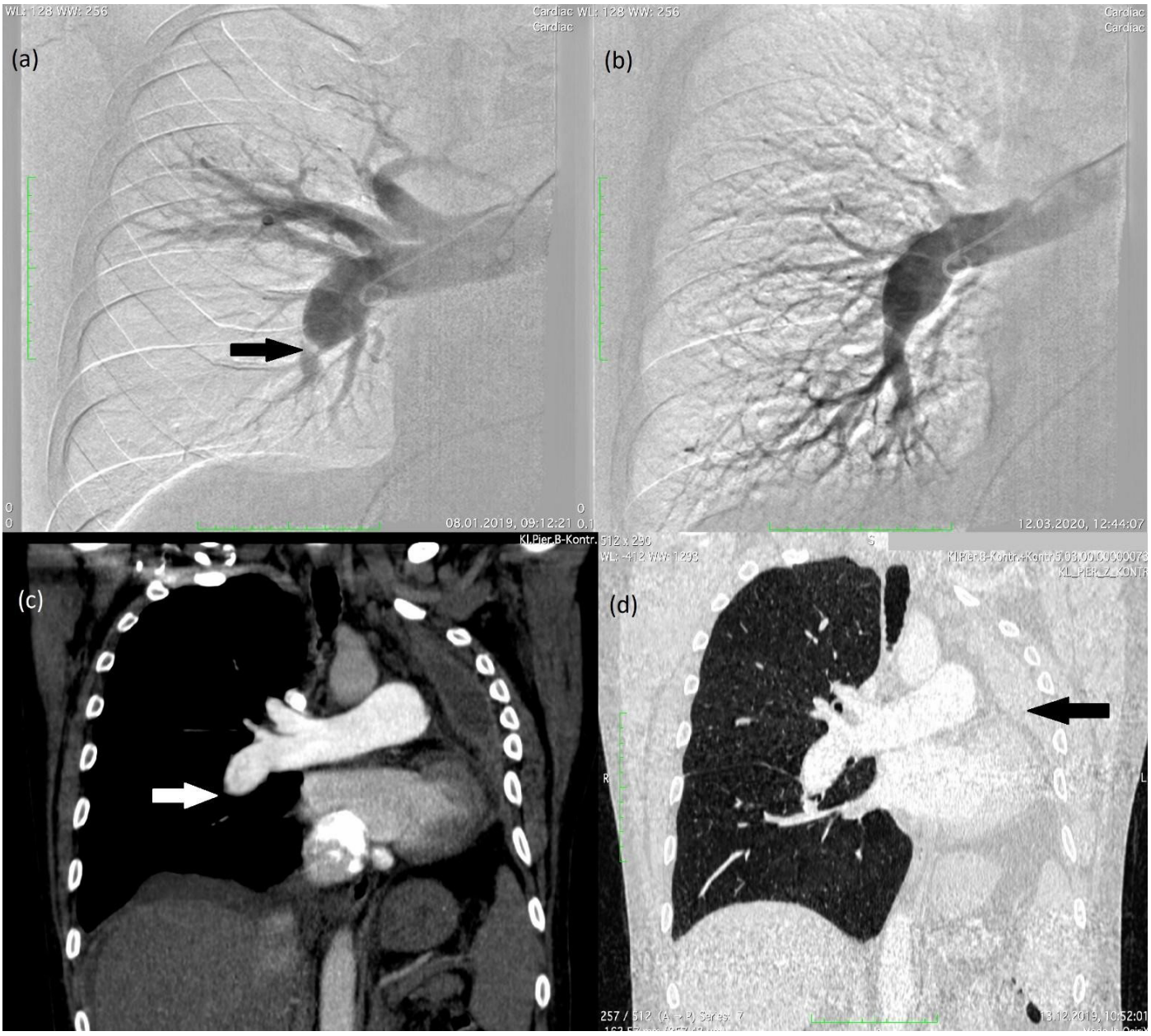
Methods: We present the case of a 46-year-old man with pulmonary hypertension, one year after left-sided pneumonectomy for squamous cell lung cancer. On admission, he presented severely limited exercise tolerance and dyspnea corresponding to WHO functional class IV. After RHC (mPAP 43 mmHg, PVR 10.17 WU) and pulmonary angiography, CTEPH was diagnosed with organised clots located at the proximal level of right pulmonary artery. CTEPH-team disqualified the patient from surgical treatment due to high perioperative risk and referred him for balloon pulmonary angioplasty (BPA) together with specific pharmacotherapy. Sildenafil 3 x 25 mg was started and the patient underwent a cycle of 9 sessions of BPA without complications. In total, 26 vascular lesions were treated. Because of heparin-induced thrombocytopenia, bivalirudin was used as antithrombotic therapy in the perioperative period.

Results: Four months after the last BPA we noted hemodynamic improvement (mPAP 23 mmHg, PVR 2.56 WU), significant improvement in physical capacity (improvement in 6 MWT from 126 m to 450 m) and decrease of NT-proBNP level (2112 to 203 pg/ml). There was no recurrence of the neoplastic process at oncological surveillance. To our knowledge, we present the first case of BPA in a single-lung patient with a good hemodynamic response (75 % decrease in PVR) and satisfactory clinical outcome.

Conclusion: Treatment of proximal CTEPH with BPA may result in significant clinical improvement and is a safe technique when surgery has excessively high perioperative risks.

Abbreviations: WHO – World Health Organization, RHC – right heart catheterization, mPAP – mean pulmonary artery pressure, PVR – pulmonary vascular resistance, WU – Wood unit, CTEPH – chronic thromboembolic pulmonary hypertension, BPA – balloon pulmonary angioplasty, 6 MWT – 6-minute walk test, NT-proBNP – N-terminal pro b-type natriuretic peptide, CT – computed tomography.

Figure 1



Pulmonary angiography performed before the first BPA session (panel A) showing an amputated right lower lobe artery (arrow). Angiography performed after the last BPA session (panel B) with improvement of distal perfusion. Computed tomography performed before the first session (panel C) presenting proximal occlusion of the right pulmonary artery (arrow). CT scan (panel D) presenting reduced chest capacity due to left-sided pneumonectomy (arrow).

Treatment

ICC2021-46: SELEXIPAG FOR THE TREATMENT OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: OUTCOME FROM THE PHASE 3 STUDY

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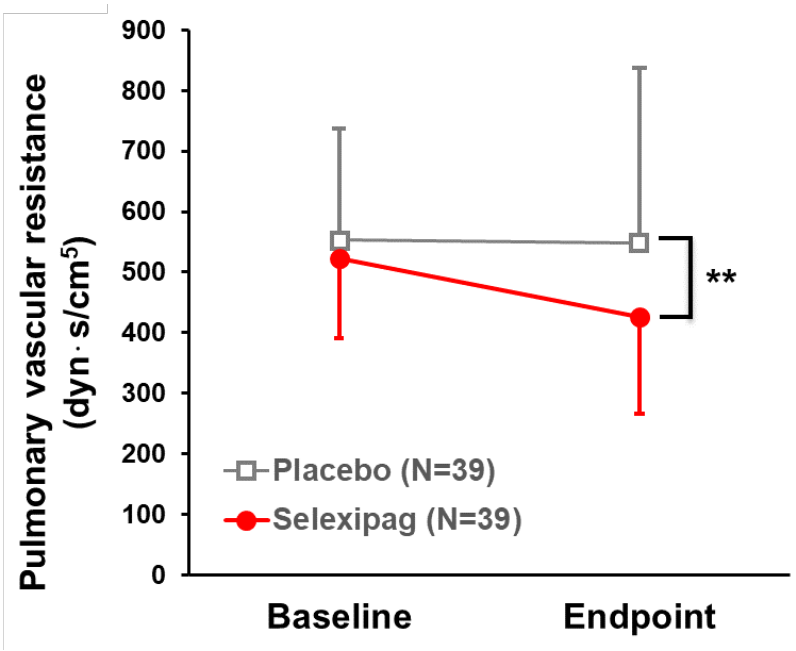
Objective: In order to investigate the usefulness of selexipag for the treatment of CTEPH, a phase 3 clinical trial was performed.

Methods: In the multicentre, randomised, double-blind, placebo-controlled study, 78 Japanese patients with inoperable CTEPH or persistent/recurrent pulmonary hypertension after pulmonary endarterectomy and/or balloon pulmonary angioplasty were randomly assigned to receive placebo or selexipag. The primary endpoint was the change in pulmonary vascular resistance (PVR) from baseline to week 20. The secondary endpoints were changes in PVR index, mean pulmonary arterial pressure, cardiac index, mean right atrial pressure, total pulmonary resistance, mixed venous oxygen saturation, Euro QOL 5 dimensions 5-level, 6-min walk distance, Borg Dyspnoea Scale score, N-terminal pro-brain natriuretic peptide, and World Health Organization functional class.

Results: The change in PVR in the selexipag group was -98.2 ± 111.3 dyn·s/cm^5, whereas that in the placebo group was -4.6 ± 163.6 dyn·s/cm^5 (mean difference, -93.5 dyn·s/cm^5; 95 % confidence interval, -156.8, -30.3; P = 0.006). Furthermore, the PVR index (P = 0.004), cardiac index (P < 0.001), total pulmonary resistance (P = 0.002), mixed venous oxygen saturation (P = 0.029), and Borg Dyspnoea Scale score (P = 0.036) improved significantly. The most common adverse events in the selexipag group were the same as those generally observed when prostacyclin analogue is administered, including headache.

Conclusion: The study revealed significant improvement of PVR and other pulmonary haemodynamics with selexipag in patients with CTEPH and showed a favourable benefit-risk profile in the current standard CTEPH treatment.

Figure: Change in pulmonary vascular resistance from baseline to week 20.



Treatment

ICC2021-47: SURGICAL OUTCOMES OF PULMONARY THROMBOENDARTERECTOMY IN THE TREATMENT OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: A SINGLE-CENTER EXPERIENCE

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Objectives: The present study aims to review a single-center experience of pulmonary thromboendarterectomy (PTE) and analyze the clinical outcomes.

Methods: We identified consecutive 76 patients (aged 50.0 ± 4.0 years) who underwent PTE to treat chronic thromboembolic pulmonary hypertension (CTEPH) between 2000 and 2021. Perioperative and mid-term clinical outcomes including follow-up 6-minute walk test and echocardiographic results were analyzed.

Results: Among the study cohort, 20 (26.3 %) patients had history of deep vein thrombosis and 10 (13.2 %) presented antiphospholipid syndrome or hematological disorders. Preoperative mean pulmonary artery pressure was 46.0 ± 12.8 mmHg and pulmonary vascular resistance was 9.8 ± 5.6 WU. All surgeries were performed under total circulatory arrest with mean time of 22.0 ± 19.7 minutes. Early mortality occurred in 5 (6.6 %) and perioperative complication included: low cardiac output syndrome (n = 9, 11.8 %), bleeding requiring surgical intervention (n = 2, 2.6 %) and new-onset dialysis (n = 7, 9.2 %). During follow-up (285.7 patient-years [PY]), 11 patients (3.9 %/PY) died and 8 patients (2.8 %/PY) underwent re-intervention. Overall survival at 3- and 5-year was 90.8 ± 3.3 % and 84.9 ± 4.5 %, respectively. Follow-up 6-minute walk test-distance was improved from 386.0 ± 98.6 meters to 471.0 ± 61.5 meters, and the RA-RV pressure gradient was alleviated from 81.0 ± 26.3 mmHg to 27.0 ± 19.1 mmgHg. At the latest follow-up, 53 (74.6 %) had warfarin therapy whereas 11 (15.5 %) used new oral anticoagulants.

Conclusions: PTE poses a relatively high perioperative risk; however, overall survival rate was respectable with improvement in functional status and echocardiographic parameters. Thus, PTE may be positively considered in CTEPH patients standing at the borderline of surgical eligibility.

Other

ICC2021-14: INCIDENCE OF RENAL FAILURE REQUIRING RENAL REPLACEMENT THERAPY POST PULMONARY THROMBO-ENDARTERECTOMY

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Objectives: Immediate post operative care of patients undergoing pulmonary thrombo endarterectomy (PEA) is guided by a protocol that emphasizes the need for achieving a negative fluid balance and maintaining a cardiac index around 2 to prevent reperfusion injury to the lungs. Depleting intravascular volume might cause post-operative renal impairment. We sought to study the incidence of renal failure requiring renal replacement theraphy (RRT) in the immediate post-operative period post PEA.

Methods: We conducted a retrospective analysis of the electronic records of the patients who underwent a PEA, in the calendar year of 2019. Data pertaining to demographics, intraoperative events, length of stay on ITU, renal function parameters, fluid balance details were extracted for the initial three post- operative days.

Results:

Outcomes				
	PTE	**PTE+**	**Post op ECMO**	**Mortality**
Elective	160.00	37.00	9	4
Urgent	0.00	2.00	0	0
Demographics				
	Mean	**SD**		
Age	57.83	15.61	years	
Sex	106.00	93.00		
BMI	31.08	7.44		
Bypass time	304.30	52.08	minutes	
X clamp time	39.71	15.52	minutes	
Length of stay on ITU	5.51	7.15	days	
Renal indices				
				% change/day
Pre-op creatinine	90.88	47.87	micromol/L	
Creatinine day 1	124.82	46.99	micromol/L	27.19 %
Creatinine day 2	124.21	54.23	micromol/L	-0.49 %
Creatinine day 3	100.23	47.36	micromol/L	-23.92 %
Fluid balance day 1	-890.69	1135.92	millilitre	
Fluid balance day 2	-830.14	716.44	millilitre	
Fluid balance day 3	-638.81	1653.17	millilitre	
				Percentage
Post op RRT	14.00			7.04 %
Pre op dialysis	3.00			1.51 %
New RRT in post op period	11.00			5.53 %

Conclusions: The incidence of new onset renal failure requiring renal replacement theraphy in the immediate post operative period after PEA is 5.53 %.
Despite achieving a significant negative fluid balance in the post operative period, the rate of rise in serum creatinine plateaus and returns to approximately pre-operative levels by Day 3.
This might explain the reduced requirement of post operative respiratory ECMO and relatively shorter length of stays in the intensive care post-operatively.

Other

ICC2021-22: BILATERAL LUNG TRANSPLANTATION FOLLOWING PULMONARY THROMBENDARTERECTOMY: CASE REPORT

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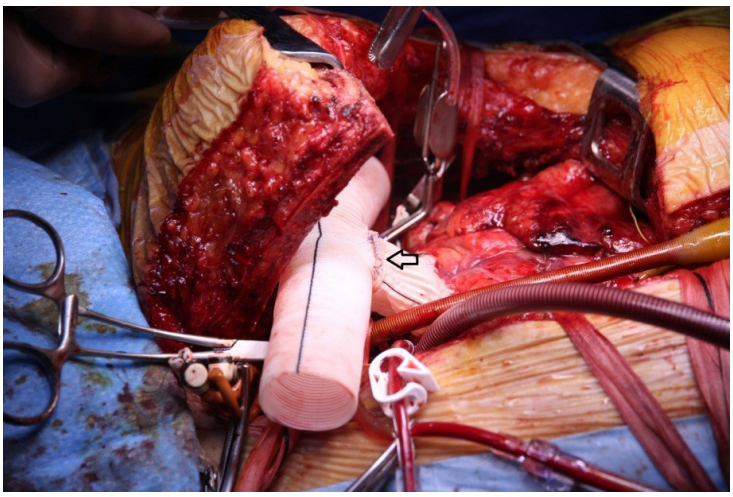
Objectives: To present the first case in Kazakhstan of bilateral lung transplantation (LTx) with neopulmonary artery trunk and its main branches formation due to donor-recipient pulmonary artery mismatch after previous pulmonary thrombendarterectomy (PTE) as an option in such cases.

Methods: A 55-years-old male presented CTEPH with concomitant secondary ASD (5.0 cm) and coronary artery disease. In this case CTEPH developed on the background of long-existing congenital heart disease with hypervolemia of the pulmonary circulation and dilatation of vessels due to the above. Hemodynamic parameters: pulmonary artery pressure 84/36 (mean 53) mmHg, PVR 7,3 Wood Units, PVR (I) 14,2 Wood Units, PVR/SVR – 0,26, RA – 14/5 – 9 mm.Hg, Qp/Qs – 1,7 by right heart catheterization. Pulmonary artery trunk was 5.2 cm, LPA 4.1 cm, RPA 6.0 cm by CT angiopulmonography.

Results: The patient underwent PTE with no reflow condition with subsequent central V-A ECMO as a bridge to LTx. In 12 days bilateral LTx with neopulmonary trunk and its main brunches formation was performed. Unfortunately, in 130 days after LTx patient died due to septic shock.



Conclusion: This is the first case of bilateral LTx following PTE in Kazakhstan. Neo synthetic bifurcated pulmonary trunk can be used as an option to adapt donor-recipient vessels mismatch.
PTE should be performed in high-level centers permitting all surgical methods and requires a multidisciplinary approach.

Other

ICC2021-30: EXERCISE HYPERVENTILATION AND PULMONARY GAS EXCHANGE IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION: EFFECTS OF BALLOON PULMONARY ANGIOPLASTY

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Objectives: In patients with chronic thromboembolic pulmonary hypertension (CTEPH), balloon pulmonary angioplasty (BPA) improves symptoms and exercise capacity. We aimed at studying how BPA affects exercise hyperventilation and gas exchange.

Methods: Symptom-limited cardio-pulmonary exercise tests (CPET) and carbon monoxide lung transfer (TLCO) measurements were performed before and after BPA (interval: 3.3±2.3 months) in 22 CTEPH patients without significant cardiac and/or pulmonary comorbidities.

Results: Peak work rate improved by 22% after BPA whilst $\dot{V}E$ at peak did not change despite improved ventilatory efficiency (lower $\dot{V}E$ with respect to CO_2 output). At the highest identical work rate pre- and post-BPA (81±27 watts), $\dot{V}E$ and the alveolar-arterial oxygen gradient ($P(A\text{-}a)O_2$) decreased by 25% and 30% after BPA, respectively. The physiological dead space fraction of tidal volume (VD/VT), calculated from arterial and mixed expired CO_2, decreased by 25%. In the meantime, TLCO did not change. The best correlates of $P(A\text{-}a)O_2$ measured at peak exercise were physiological VD/VT before BPA and TLCO after BPA.

Conclusions: The fact that TLCO did not change suggests that the pulmonary capillary blood volume was unaffected by BPA. Thus, improvement of physiological VD/VT was likely to be a consequence of reduced alveolar ventilation/perfusion ($\dot{V}A/Q$) ratio heterogeneity and of reduced hyperventilation rather than an improvement of true alveolar dead space. In addition, the correlation between TLCO (measured either before or after BPA) and $P(A\text{-}a)O_2$ measured after BPA suggests that TLCO may provide an easily accessible marker to predict the response to BPA in terms of pulmonary gas exchange.

Other

ICC2021-40: CLINICAL PRACTICES AND UNMET NEEDS IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH) – A GLOBAL CROSS-SECTIONAL SCIENTIFIC SURVEY (CLARITY)

G Kopeć[1], K Abe[2], P Forfia[3], G Heresi[4], M Jevnikar[5], O Moiseeva[6], N Skoro-Sajer[7], M Terra-Filho[8], H Whitford[9], Z Zhai[10], A Beaudet[11], V Gressin[12], C Meijer[13], K Sheares[14]

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Objective: Diagnosis and treatment advances have led to a rapid evolution of CTEPH management. Recent international guidelines and recommendations describe best practices, but there is limited real-world evidence in CTEPH. The objective of this international survey is to gain insights into current clinical practices from hospital-based physicians and identify unmet needs in CTEPH.

Methods: CLinical prActices and unmet needs in chRonIc Thromboembolic pulmonarY hypertension (CLARITY) is a global, descriptive, observational, cross-sectional scientific survey developed by an independent committee of international CTEPH experts using the Delphi method. The 30-minute online survey will be disseminated in 2021 to a diverse group of specialists (cardiologists, pulmonologists, thoracic/cardiac surgeons, radiologists, internists) across the globe via scientific societies and healthcare practitioners' organizations (international/regional/local). The questionnaire is divided into sections covering awareness, diagnosis and treatment of CTEPH (operability assessment; surgical, interventional and medical treatment; multimodal treatment approach), and anticoagulation use. Skip and branch logic were built into the survey to optimize the response rate. The survey will be available in English, French, German, Italian, Japanese, Korean, Polish, Portuguese, Russian, simplified Chinese, Spanish, and Turkish. The survey tool (Qualtrics) is compliant with GDPR and data will be reported in aggregate form.

Conclusions: CLARITY will provide quantitative and qualitative insights on the contemporary management of CTEPH and identify differences in care delivery and barriers to optimal care from the physicians' perspective. The findings may help to improve patient pathways, such as access to or use of resources, and contribute to future research programs in CTEPH.

Other

ICC2021-44: CTEPH IN PATIENTS WITH ANTI-PHOSPHOLIPID SYNDROME: RISK FACTORS AND MANAGEMENT

K Rosen[1,6], E Raanani[2,6], A Kogan[2,6], G Kenet[3,6], M Misgav[3,6], A Lubetsky[3,6], S Niznik[1], H-J Schäfers[5], N Agmon-Levin[1,6,a], **MJ Segel[4,6,a]**

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Objective: Antiphospholipid syndrome (APS) may cause chronic thromboembolic pulmonary hypertension (CTEPH). Current knowledge regarding prevalence and risk factors for CTEPH among APS patients is limited. We sought to determine clinical features and biomarkers that could identify APS subjects suffering from CTEPH, and describe the prevalence, course and treatment outcomes of patients with APS-CTEPH.

Methods: 504 APS patients were treated in our center from 2008 – 2019. We studied clinical and laboratory features of 69 APS patients, comparing 19 patients diagnosed with CTEPH (APS-CTEPH) and treated accordingly, with 50 consecutive age and gender matched patients with no evidence of pulmonary hypertension (APS-No-CTEPH).

Results: CTEPH prevalence was 3.8 % in our APS cohort and was associated with the following: primary APS ($p < 0.05$); prior pulmonary embolism ($p < 0.001$); recurrent venous thromboembolism (VTE) ($p < 0.001$); lower platelet counts ($p < 0.001$); triple anti-phospholipid antibodies positivity ($p < 0.001$); higher titers of anti-cardiolipin IgG ($p < 0.001$) and anti-B2GPI IgG ($p < 0.001$), and high Russell viper venom time ratio (RVVT-ratio) ($p < 0.05$). Additionally, history of catastrophic APS was more prevalent in APS-CTEPH vs. APS-No-CTEPH ($p < 0.05$). Of APS-CTEPH patients, 15/19 underwent pulmonary endarterectomy (PEA): In 12/15 the procedure was elective and resulted in good perioperative and long-term outcomes, while only 1 of 3 patients that underwent urgent PEA survived.

Conclusions: CTEPH is relatively common in APS. Primary APS, prior PE, recurrent VTE, thrombocytopenia and specific anti-phospholipid antibodies predict CTEPH in APS. Active assessment for CTEPH in APS patients should be considered, as PEA was found to be effective and relatively safe, especially if electively performed.

Other

ICC2021-48: RELATIONSHIP BETWEEN EXERCISE-INDUCED INTRAPULMONARY SHUNT AND VENTRICULAR FUNCTION IN PATIENTS WITH CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION

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Objective: To evaluate the relationship between exercise-induced intrapulmonary shunt and clinical, hemodynamic, laboratory, echocardiographic and exercise data of patients with chronic thromboembolic pulmonary hypertension (CTEPH).

Methods: Seventeen patients (10 women, 49 ± 13 yrs) with CTEPH underwent transthoracic echocardiography, six-minute walk test and incremental cardiopulmonary exercise test. After undergoing right heart catheterization, patients received 100 % oxygen with a face mask from a Douglas bag and performed a 50 % maximal workload steady-state exercise. Arterial and mixed venous blood samples were obtained for gas analysis and calculation of intrapulmonary shunt using the following equation: $QS/QT = [(PAO_2 - PaO_2) \times 0.0031]/\{CavO_2 + [(PAO_2 - PaO_2) \times 0.0031]\}$.

Results: All participants showed an increased shunt volume/fraction detected by 100 % oxygen breathing during exercise (0.71 ± 0.31 mL; 9.81 ± 2.75 %). Most of them had inoperable disease (n = 11), were not using pulmonary vasodilator therapy (n = 11) and were in functional NYHA class II (n = 12). Mean pulmonary artery pressure was 54 ± 17 mmHg, pulmonary artery occlusion pressure was 11 ± 3 mmHg and pulmonary vascular resistance was 816 ± 406 dinas.s.cm^5. The average 6-minute walk distance was 447 ± 80 m, VO_2 at peak was 14.84 ± 3.11 mL/kg/min and peak SpO_2 was 90 ± 5 %. Shunt volume was negatively correlated to hemodynamic severity, NT-proBNP and troponin levels, echocardiogram PASP, VO_2/W slope, VE/VCO_2 slope and VE/VCO_2 at anaerobic threshold (Table 1).

Conclusion: Intrapulmonary shunt seems to be a protective mechanism to decrease potential damaging effects of high perfusion pressure during exercise.

Table 1: Correlations between hemodynamic, laboratory, echocardiographic, exercise data and shunt volume.

Data	Spearman's rank correlation coefficient
PAP (mmHg)	- 0.625 (p = 0.007)
POAP (mmHg)	- 0.193 (p = 0.458)
PVR (dynes.s.cm^5)	- 0.620 (p = 0.008)
RAP (mmHg)	- 0.673 (p = 0.003)
CO (L/min)	0.593 (p = 0.012)
CI (L/min/m^2)	0.713 (p = 0.001)
SVI (mL/m^2/beat)	0.502 (p = 0.040)
PVC (mL/mmHg)	0.701 (p = 0.002)
SvO_2 (%)	0.534 (p = 0.027)
NT-pro BNP (pg/mL)	- 0.757 (p < 0.001)
Troponin (ng/mL)	- 0.521 (p = 0.039)
Echo TAPSE	0.895 (p < 0.001)
Echo PASP	- 0.528 (p = 0.043)
6-minute walk distance (m)	0.391 (p = 0.134)
$VO_{2\ PEAK}$ (mL/kg/min)	0.451 (p = 0.069)
VO_2/W slope (mL/min/W)	- 0.644 (p = 0.007)
FC/VO_2 slope (beat/L)	- 0.155 (p = 0.567)
VE/$VCO_{2\ PEAK}$ slope	- 0.588 (p = 0.013)
O_2 pulse (%)	0.298 (p = 0.245)
VE/$VCO_{2\ AT}$	- 0.680 (p = 0.010)
$PETCO_{2\ PEAK}$ (mmHg)	0.403 (p = 0.109)
SpO_2 (%)	0.358 (p = 0.158)
$PaCO_{2\ SS}$ (mmHg)	0.685 (p = 0.002)

Other

ICC2021-49: RATIONALE AND DESIGN OF THE SELEXIPAG IN INOPERABLE OR PERSISTENT/ RECURRENT CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (SELECT) TRIAL

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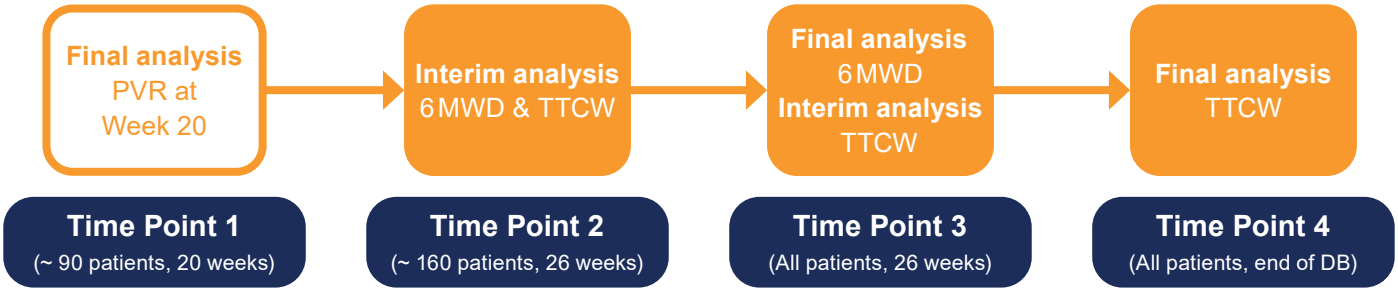
Objective: SELECT (NCT03689244) is an ongoing multicentre, randomised, double-blind (DB), placebo-controlled, group-sequential, Phase 3 study with an open-label extension (OLE) to assess the efficacy and safety of selexipag as an add-on to standard-of-care in patients with inoperable or persistent/ recurrent chronic thromboembolic pulmonary hypertension (CTEPH) after surgical pulmonary endarterectomy (PEA) and/or interventional balloon pulmonary angioplasty (BPA). Selexipag is an oral selective prostacyclin receptor agonist approved for the treatment of pulmonary arterial hypertension.

Methods: Up to 280 patients will be randomised 1:1 to selexipag or placebo in the DB period, which will end when 148 clinical worsening events have been recorded. Patients completing the DB treatment period may enter the OLE. The primary endpoint (PEP) is the effect of selexipag on pulmonary vascular resistance (PVR) at Week 20. Key secondary endpoints include change in 6-minute walk distance at Week 26 and time to clinical worsening up to end of the DB period. When ~90 patients complete their Week 20 PVR assessment, the final analysis on the PEP will be performed. If the PEP is significant, the study will continue per protocol, the two key secondary endpoints will be analysed, and the study deemed a success if at least one is significant (Figure).

Conclusions: Treatment options for patients with inoperable or persistent/recurrent chronic CTEPH are limited. SELECT is the first randomised controlled trial to investigate the safety and efficacy of an oral prostacyclin pathway agent in these patients, including after BPA, those on riociguat and other PH therapies.

Figure: SELECT study design.



6MWD: 6-minute walk distance; DB: double-blind; PVR: pulmonary vascular resistance; TTCW: time to clinical worsening.

Funding statement
Funded by Actelion Pharmaceuticals Ltd, a Janssen Pharmaceutical Company of Johnson & Johnson.

Other

ICC2021-50: DESIGN AND RATIONALE FOR THE MACITENTAN IN INOPERABLE OR PERSISTENT/ RECURRENT CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (MACITEPH) TRIAL

G Heresi[1], HA Ghofrani[2], M Humbert[3], D Jenkins[4], H Matsubara[5], G Hernandez[6], G Lack[7], E McGuire[6], G Thomas[7], **NH Kim[8]**

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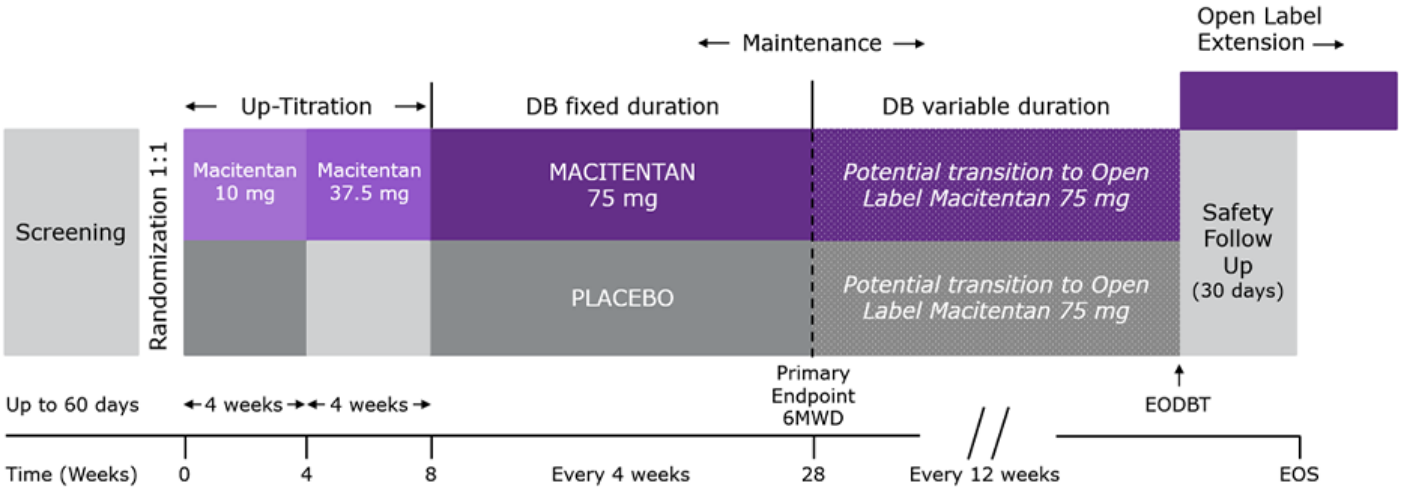
Objective: MACiTEPH (NCT04271475) is an ongoing randomised, double-blind, multicentre, placebo-controlled, adaptive, Phase 3 study evaluating efficacy and safety of macitentan 75 mg once daily, in adults with inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH). Macitentan, an oral dual endothelin receptor antagonist (ERA), could provide benefit in CTEPH by inhibiting the endothelin pathway involved in secondary microvasculopathy.

Methods: Up to 230 participants will be randomised 1:1 to macitentan 75 mg or placebo, with treatment allocation stratified by inoperable (± balloon pulmonary angioplasty; BPA) vs. persistent/recurrent after pulmonary endarterectomy (± BPA), and by use of PH therapies at baseline. Patient eligibility is verified by an adjudication committee. An interim analysis will be conducted for futility/sample size reassessment.
The primary endpoint is change from baseline to Week 28 in 6-minute walk distance. Secondary endpoints include time to clinical worsening and change from baseline to Week 28 in quality of life, CTEPH symptoms, WHO functional class, and accelerometer-assessed daily physical activity. Safety will be evaluated throughout the study.
The double-blind period consists of an up-titration and a variable maintenance phase (Figure). Patients who completed the double-blind study may enter the open-label extension (OLE) for at least 2 years. Earlier entry is possible after Week 28 if a clinical worsening event has occurred.

Conclusions: Currently no ERAs are approved to treat CTEPH. MACiTEPH is the first randomised controlled trial designed to investigate the safety and efficacy of macitentan 75mg in patients with inoperable or persistent/recurrent CTEPH, including after BPA, those on riociguat and other PH therapies.

Figure: MACiTEPH study design.



For each participant, the duration of the double-blind period is based on their timepoint of entry into the study, as they remain on DB treatment until all participants have completed Week 28 (i.e., the primary endpoint assessment). Upon entering the open-label extension, participants will go through an 8-week double-dummy up-titration phase.
6MWD: 6-minute walk distance; DB: double blind; EODBT: end of double-blind treatment; EOS: end of study.

Disclosures
NH Kim received consulting fees from Janssen Pharmaceutical Companies of Johnson & Johnson, Bayer Healthcare and Merck, and speaker's fees from Janssen Pharmaceutical Companies of Johnson & Johnson and Bayer Healthcare.

Funding statement
Funded by Actelion Pharmaceuticals Ltd, a Janssen Pharmaceutical Company of Johnson & Johnson.

Previous work of ICA Executive Board members

ICC2021-P1: IMPACT OF CURRENT MANAGEMENT STRATEGIES FOR CTEPH ON PATIENT OUTCOME

M Delcroix[1], J Pepke-Zaba[2], E Fadel[3], D Jenkins[2], N Kim[4], M Madani[5], H Matsubara[6], G Simonneau[7], E Mayer[8], I Lang[9]

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Objective: The effect of pulmonary endarterectomy (PEA) on long-term outcomes of patients with chronic thromboembolic pulmonary hypertension (CTEPH) was assessed in the European CTEPH registry (Pepke-Zaba et al., Circulation 2011; Delcroix et al., Circulation 2016). In the meantime, additional treatment options have become available, namely balloon pulmonary angioplasty (BPA) and riociguat, a soluble guanylate cyclase stimulator. Our new CTEPH registry aimed to evaluate current treatment strategies at expert centres worldwide.

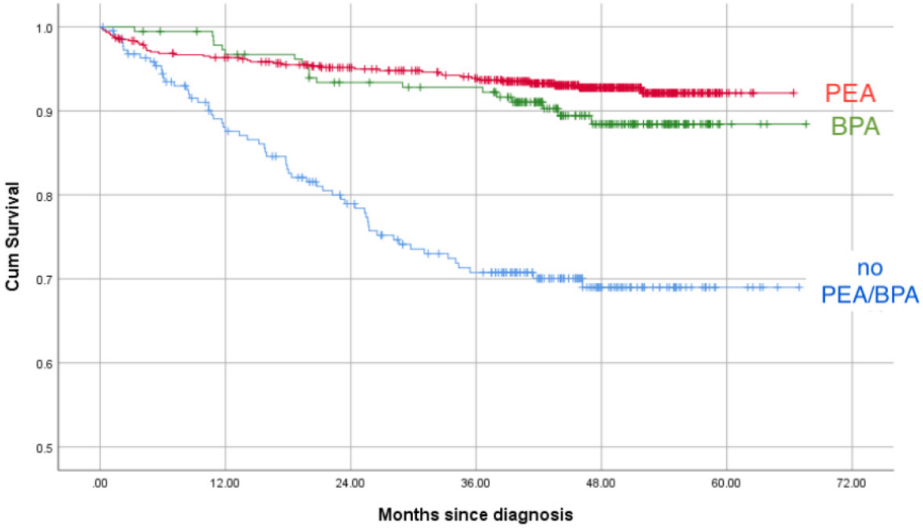
Methods: Newly diagnosed, consecutive CTEPH patients were included at 34 centres between February 2015 and September 2016; follow-up continued until September 2019.

Results: Of 1009 patients enrolled, 605 (60 %) and 185 (18 %) underwent PEA and BPA, respectively. Among the 219 patients not undergoing interventional treatment, 76 % were treated with pulmonary hypertension-specific drugs; proportions were 38 % and 78 % for patients undergoing PEA and BPA, respectively. Median age at diagnosis was lower for patients undergoing PEA vs those undergoing BPA and no interventional treatment (60 years vs 66 and 69 years; $p < 0.001$), while pulmonary vascular resistance was similar across groups (mean 638 dyn·s·cm^{-5}). During follow-up (minimum 3 years, maximum 5.6 years), 7 %, 10 % and 27 % of the patients undergoing PEA, BPA and no intervention, respectively, died ($p < 0.001$). Three-year survival was over 90 % in patients undergoing interventional treatments (Figure 1). For patients not undergoing interventional treatment, 3-year survival was 70 %, reaching 85 % for patients specifically receiving riociguat ($n = 92$).

Conclusions: Data from this new registry reveal considerable differences in patient outcome between current therapeutic approaches.

Presented as an oral presentation at the European Respiratory Society (ERS) International Congress 2021

Figure 1: Time to death (all causes) since diagnosis by intervention.



Previous work of ICA Executive Board members

ICC2021-P2: IMPLICATIONS OF NEW PH DEFINITION FOR CTEPD

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Introduction: In light of the change in diagnostic threshold for pulmonary hypertension (PH) we wished to determine demographic and clinical differences between patients with mPAP < 20 mmHg and those with mPAP 20 – 25 mmHg at baseline and at 1-year follow-up.

Method: We studied patients diagnosed with chronic thromboembolic pulmonary disease (CTEPD) with mPAP < 25 mmHg on right heart catheterisation (RHC) between 1/1/2015 and 31/12/2019. Baseline demographics and haemodynamics were compared between those with mPAP < 20 and mPAP 20 – 24 mmHg. Pairwise analysis was carried out to determine changes in clinical endpoints at 1-year from baseline. Patients who underwent pulmonary endarterectomy (PEA) in this time were excluded from longitudinal analysis. Mortality was assessed over the entire study period.

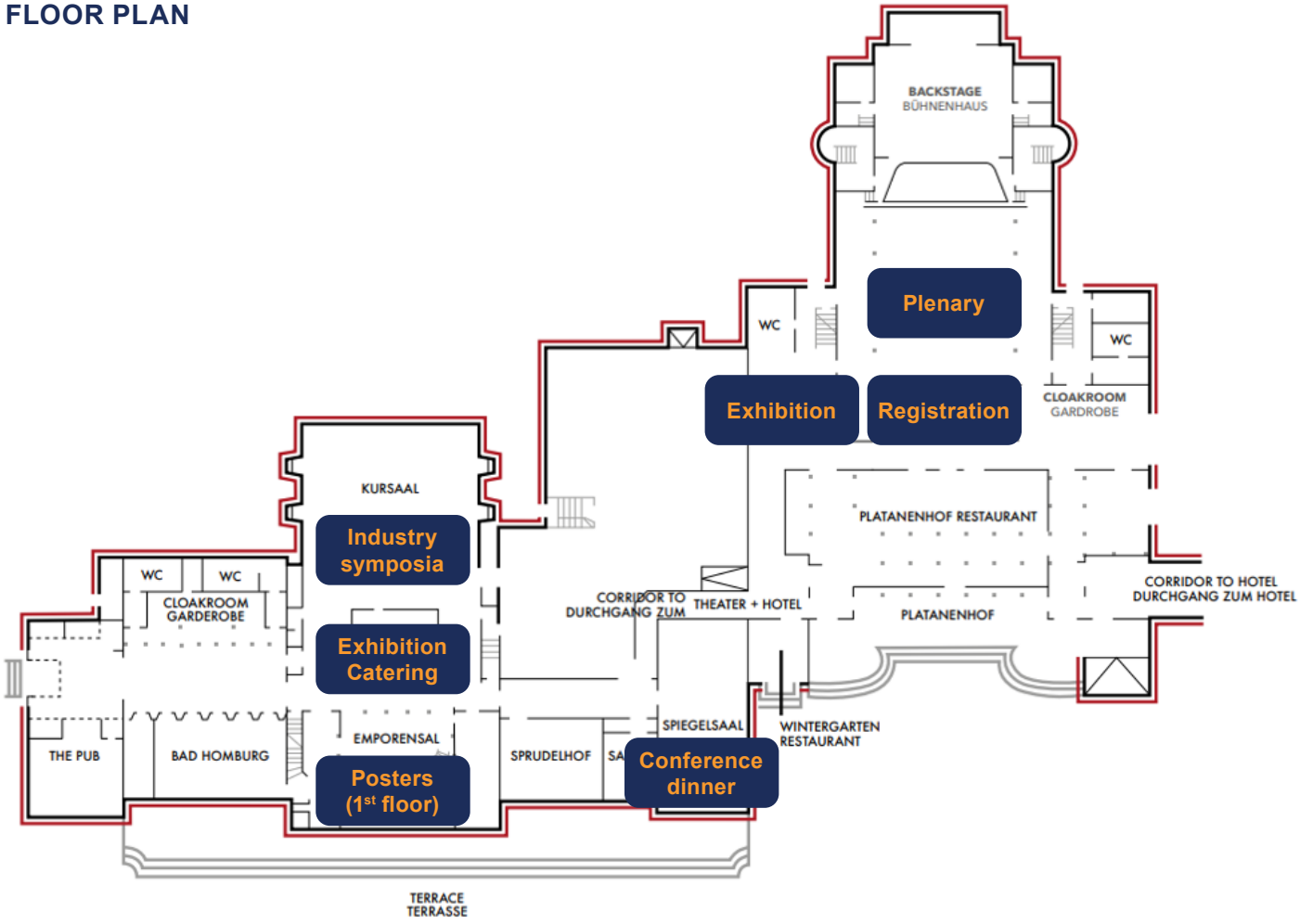
Results: 112 patients were recruited; 57 had mPAP < 20, 56 had mPAP 20 – 24. Baseline demographics were similar in both groups with no significant differences noted in echocardiography, 6 minute walk distance (6 MWD), NT-pro BNP level and quality of life. Patients with mPAP < 20 had lower PVR (127 ± 45 vs 197 ± 75 dynes, $p < 0.01$) and RVEDP (5.9 ± 2.4 vs 7.8 ± 3.4 mmHg, $p < 0.01$). At 1 year no major deterioration was seen in either group. No patients were treated with PH-specific therapy; 8 had undergone PEA. Over median of 38 months follow-up, mortality was 4/57 in the mPAP < 20 group and 4/56 in the mPAP 20 – 24 group. Cause of death was malignancy in 62.5 % of cases.

Conclusion: There is no statistical difference in baseline clinical features between CTEPD patients with mPAP < 20 and 20 – 24 mmHg, except for PVR and RVEDP. Neither group displayed disease progression at 1 year. However, mortality over 38 months is significant and mainly attributable to malignancy.

Presented as a poster at the European Respiratory Society (ERS) International Congress 2021

GENERAL INFORMATION

FLOOR PLAN



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Departure times will be 14:20 and 14:30. This service is free of charge.