Pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension in Cape Town, South Africa

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Background. Pulmonary endarterectomy (PEA) is the only definitive and potentially curative therapy for chronic thromboembolic pulmonary hypertension (CTEPH), associated with impressive improvements in symptoms and haemodynamics. However, it is only offered at a few centres in South Africa. The characteristics and outcomes of patients undergoing PEA in Cape Town have not been reported previously.
Objectives. To assess the difference in World Health Organization functional class (WHO-FC) before and at least 6 weeks after surgery.
Methods. We interrogated the adult cardiothoracic surgery database at the University of Cape Town between December 2005 and April 2021 for patients undergoing PEA at Groote Schuur Hospital and a private hospital.
Results. A total of 32 patients underwent PEA, of whom 8 were excluded from the final analysis owing to incomplete data or a histological diagnosis other than CTEPH. The work-up of these patients for surgery was variable: all had a computed tomography pulmonary angiogram, 7 (29%) had a ventilation/perfusion scan, 5 (21%) underwent right heart catheterisation, and none had a pulmonary angiogram. The perioperative mortality was 4/24 (17%): 1 patient (4%) had a cardiac arrest on induction of anaesthesia, 2 patients (8%) died of postoperative pulmonary haemorrhage, and 1 patient (4%) died of septic complications in the intensive care unit. Among the survivors, the median (interquartile range) improvement in WHO-FC was 2 (1 - 3) classes (p=0.0004); 10/16 patients (63%) returned to a normal baseline (WHO-FC I).
Conclusion. Even in a low-volume centre, PEA is associated with significant improvements in WHO-FC and a return to a normal baseline in survivors.
Keywords. Chronic thromboembolic pulmonary hypertension, pulmonary endarterectomy, pulmonary embolism, pulmonary hypertension.

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Study synopsis
What the study adds. South African patients undergoing pulmonary endarterectomy (PEA) for chronic thromboembolic pulmonary hypertension (CTEPH) have a marked improvement in functional status, with many returning to a normal functional baseline. However, the small number of patients included in this study indicates that PEA is probably underutilised. Pre- and postoperative assessment is inconsistent, despite availability of established guidelines.
Implications of the findings. More patients should be referred to specialist centres for assessment for this potentially curative procedure. Use of guidelines to standardise investigations and monitoring of patients with CTEPH may improve patient selection for surgery.

The natural history of acute pulmonary embolism (PE) in most patients is complete fibrinolysis with near-total resolution of vascular obstruction, a reduction in pulmonary vascular resistance (PVR), and restoration of normal haemodynamics. However, a small minority of patients will have persistent elevations in mean pulmonary arterial pressure (mPAP) and PVR for several months after a precipitating event despite effective anticoagulation, termed chronic thromboembolic pulmonary hypertension (CTEPH).[1,2] CTEPH is not only found in patients after acute PE; ~25% of patients with CTEPH do not have any history of a precipitating PE or deep-vein thrombosis.[3] Staphylococcal infection, endothelial dysfunction, defective fibrinolysis and dysfunctional angiogenesis have been proposed as pathophysiological mechanisms for the failure of clot resolution.[4] Clinical risk

factors for CTEPH include permanent intravascular devices, inflammatory bowel disease, polycythaemia vera, splenectomy, antiphospholipid syndrome, high-dose thyroid replacement therapy and malignancy.[5,6]

The pathological basis for the elevation in mPAP and PVR is unresolved thrombus that has not undergone fibrinolysis but instead has been transformed into hard, hyalinised material. This organised clot becomes incorporated into the pulmonary arterial wall and causes chronic obstruction of the major pulmonary arteries, either completely via total occlusion of blood flow or incompletely by the formation of bands and webs (irregular areas of adherent thromboembolic material).[7] The increase in PVR leads to chronic right ventricular strain and ultimately, over a period of months to years, to right heart failure.[2,7] CTEPH has been assigned its own grouping (group IV) in the World Health Organization (WHO) classification of pulmonary hypertension, owing to unique considerations around its diagnosis and treatment.[8]

Pulmonary endarterectomy (PEA) is the treatment of choice for patients with CTEPH,[1,4] provided there are no contraindications, and is potentially curative. The procedure involves bilateral complete endarterectomies down to the subsegmental branches of the pulmonary vasculature, performed during periods of deep hypothermic circulatory arrest (DHCA), via a median sternotomy, and on cardiopulmonary bypass.[9,10] PEA has been shown in multiple previous studies to significantly improve PVR and pulmonary arterial pressure to normal or near normal, as well as improving 6-minute walk test (6MWT) distance and WHO functional class (WHO-FC).[10-15]

Cardiothoracic expertise in performing PEA for CTEPH is not widely available in South Africa (SA) in either the public or the private sector. Little is known about outcomes in SA patients who have undergone this potentially life-saving procedure. We aimed to describe the preoperative characteristics of patients who have undergone PEA in Cape Town, SA, as well as to report the in-hospital mortality and functional and haemodynamic outcomes of these patients after surgery.

Methods

Study design and oversight

We conducted a retrospective study of patients who had undergone PEA at Groote Schuur Hospital and a private hospital in Cape Town. Informed consent was waived, as only routine clinical data were used. Ethical approval was granted by the University of Cape Town's Human Research Ethics Committee (HREC) (ref. no. 568/2019). The study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement for observational trials.[16]

Study population

Patients undergoing surgery between December 2005 and April 2021 were enrolled. Determination of candidacy was based on conventional physiological and radiological assessments of operability as determined by a multidisciplinary team (pulmonologists, cardiac surgeons and radiologists). Selection criteria and preoperative work-up were not protocolised, but factors considered were the surgical accessibility of the disease, comorbidities, and adherence to anticoagulation. Patients who were referred for consideration for surgery but not deemed eligible were not captured in the database.

The PEA procedure was performed as outlined above, with the initial strategy used for DHCA being to cool patients to 25°C with 10-minute arrest intervals. Later, with the development of experience necessary to operate on more distal disease, patients were cooled to 20°C for 20-minute arrest intervals, and this became the standard. All patients received standard intensive care unit (ICU) care at both institutions, and postoperative follow-up and investigations were driven by clinician request and patient preference.

Study procedures

Sociodemographic and clinical data on our patients were extracted from the Chris Barnard Division of Cardiothoracic Surgery database (HREC ref. no. R045/2016). Where possible, missing data were obtained by folder review. Demographic and clinical data, data from special investigations, and information regarding the pre-, intra- and postoperative course were captured into a data collection sheet and from there into a password-protected Excel database, version 16.66.1 (Microsoft, USA), accessible only to the specified investigators. The full list of variables can be found in the data collection sheet (Appendix 1, available online at https://www.samedical.org/file/2053).

Outcomes

The primary outcome was the difference in WHO-FC before and at least 6 weeks after PEA (when the patient was deemed to have recovered from the effects of surgery). Anticipated secondary outcomes were changes in 6MWT distance, right ventricular systolic pressure (RVSP, measured by echocardiography), and postoperative haemodynamics (mPAP, PVR, cardiac index and stroke volume index, measured by right heart catheterisation (RHC)).

Statistical analysis

Continuous variables were presented as means with standard deviations (SDs) (for normally distributed data) and medians with interquartile ranges (IQRs) (for non-normally distributed data), and categorical data as frequencies and percentages. Assumption of normality was determined by the Shapiro-Wilk test; normally and non-normally distributed data were compared for pre- and post-surgical values (when available) using Student's *t*-test or the Wilcoxon rank-sum test, respectively. Statistical analyses were performed using Stata version 12.1 (StataCorp, USA).

Results

Study population

Between December 2005 and April 2021, 32 patients underwent PEA and were enrolled in the registry. The median (IQR) number of cases per year was 2 (1 - 3). Eight patients were subsequently excluded from the final analysis: 3 were found to have pulmonary artery sarcoma and not CTEPH on histological examination, 1 was incorrectly captured as a PEA but underwent acute thrombectomy for fresh PE, and patient notes could not be found for the final 4 patients (Fig. 1).

Twenty-four patients with confirmed CTEPH and with available data were included in the final analysis. Their demographic and clinical details are shown in Table 1. Almost 80% were in WHO-FC III or IV, and 11/24 (46%) were in clinical right heart failure. All

were anticoagulated. Only two-thirds (*n*=16/24; 67%) had a history of previous documented venous thromboembolism (VTE). The median (IQR) time from the diagnosis of CTEPH to surgery was 123 (21 - 287) days.

Preoperative work-up and PEA procedure

The preoperative work-up (Table 2) was highly variable. All patients had a preoperative computed tomography pulmonary angiogram showing proximal obstructive burden, while only 7/24 (29%) had a ventilation/perfusion scan. Only 5/24 patients (21%) had preoperative RHC, and none had a pulmonary angiogram. Relevant haemodynamic parameters from the 5 RHCs are presented in Table 3. All patients had a preoperative echocardiogram: in 2 cases there was no tricuspid regurgitation, and the RVSP could not be measured; in the remainder, the median (IQR) RVSP was 82 (64 - 89) mmHg. Only 13/24 patients managed a preoperative 6MWT, for which the mean (SD) distance was 322 (140) m. Details of the median cardiopulmonary bypass time, aortic cross-clamp time and circulatory arrest time during deep hypothermia are given in Table 4. Three patients (13%) had concomitant procedures performed during the operation; 2 patients had a tricuspid valve annuloplasty, and 1 had a mitral valve annuloplasty.

Treatment outcomes

In-hospital mortality was 4/24 (17%): 1 patient (4%) had a cardiac arrest on induction of anaesthesia, and was placed on bypass with the surgery performed as a salvage procedure but could not be weaned off bypass; 2 patients (8%) died of postoperative pulmonary haemorrhage; and 1 patient (4%) died in the ICU of septic complications 9 days after surgery. The median (IQR) length of stay in the ICU for survivors was 4 (2 - 5) days, with a median (IQR) length of mechanical ventilation of 1 (1 - 1) day. The median (IQR) length of hospital stay was 9 (8 - 20) days. Of the 24 PEAs, 17 (71%) were performed after the extracorporeal membrane oxygenation (ECMO) programme was established, with 1 patient (4%) requiring ECMO in the postoperative period. Sixteen patients (67%) experienced one or more intra- or postoperative complications: bleeding requiring transfusion (*n*=5/24; 21%), arrhythmias (*n*=3/24; 13%), sternal wound sepsis (*n*=3/24; 13%), anaesthetic complications (*n*=2/24; 8%), need for re-look surgery (*n*=2/24; 8%), acute renal failure (*n*=3/24; 13%), pericardial effusion/cardiac tamponade (*n*=2/24; 8%), pleural effusion requiring repeat draining (*n*=1/24; 1%), haemothorax (*n*=1/24; 1%) and pneumonia with septic shock and multiorgan failure (1/24; 1%).

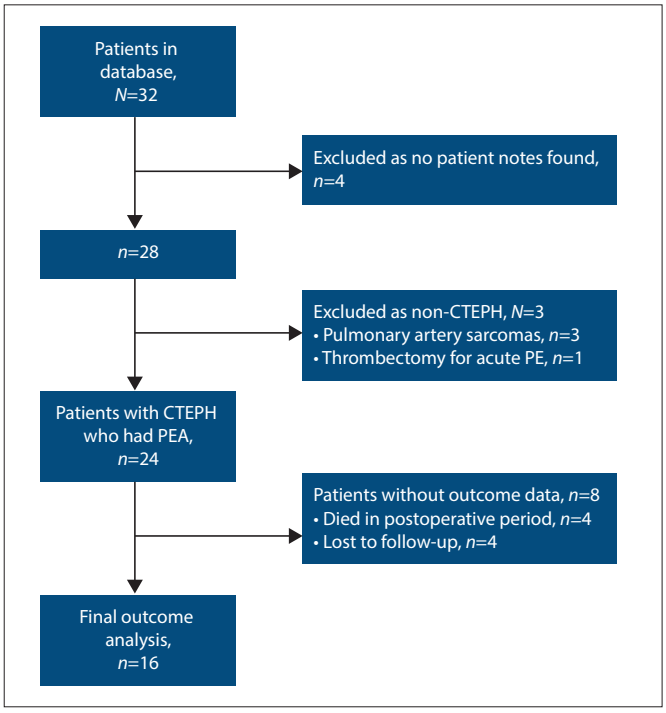

Fig. 1. CONSORT flow diagram. (CTEPH = chronic thromboembolic pulmonary hypertension; PE = pulmonary embolism; PEA = pulmonary endarterectomy.

Postoperative outcomes

Of the 20 patients (83%) who survived to hospital discharge, 16 were seen for clinical follow-up between 6 weeks and 11 months after

Table 1. Patient characteristics (*N*=24)

	n (%)*
Age (years), mean (SD)	41 (10)
Female	18 (75)
Medical comorbidities	
Hypertension	7 (29)
HIV	6 (25)
Asthma/COPD	3 (13)
CKD	3 (13)
Obesity	2 (8)
Valvular heart disease	2 (8)
Thrombophilia	2 (8)
Diabetes mellitus	1 (4)
History of previous VTE (all)	16 (67)
Pulmonary embolism	13 (54)
Deep-vein thrombosis	3 (13)
Days from diagnosis to surgery, median (IQR)	123 (21 - 302)
WHO-FC	
I	0
II	5 (21)
III	14 (58)
IV	5 (21)
Signs of right heart failure	11 (46)
Type of anticoagulation	
Warfarin	19 (79)
DOAC	4 (17)
LMWH	1 (4)
Diuretic therapy	17 (71)
PH-specific therapy (sildenafil)	2 (8)
Preoperative IVC filter	9 (38)
Preoperative mechanical ventilation	0
Preoperative inotropes	0

SD = standard deviation; COPD = chronic obstructive pulmonary disease; CKD = chronic kidney disease; VTE = venous thromboembolism; IQR = interquartile range; WHO-FC = World Health Organization functional class; DOAC = direct oral anticoagulant; LMWH = low-molecular-weight heparin; PH = pulmonary hypertension; IVC = inferior vena cava.
*Except where otherwise indicated.

surgery (median (IQR) follow-up period 4 (2 - 5) months). Their postoperative outcomes are shown in Table 5. Of the 4 patients lost to follow-up, 3 were still alive at 4 months after surgery (based on National Health Laboratory Service data), making the 4-month mortality 4/23 (17%). The median (IQR) improvement in WHO-FC was 2 (1 - 3) classes (p=0.0004); 10/16 patients (63%) returned to a normal baseline (WHO-FC I). A 6MWT was performed for 9 patients, with a mean (SD) distance of 445 (108) m attained. No patients underwent postoperative RHC; those who had a postoperative echocardiogram with measurable RVSP (n=6 patients) had a median (IQR) RVSP of 33 (30 - 52) mmHg.

Discussion

This study, which is to our knowledge the only report of outcomes of CTEPH surgery in SA, has four main findings: (*i*) that PEA results in significant improvement in functional class for patients with CTEPH; (*ii*) that PEA is underutilised in our setting for the treatment of CTEPH; (*iii*) that our post-surgical outcomes are worse than those reported in other large international cohorts; and (*iv*) that diagnostic approaches, preoperative work-up and postoperative follow-up of CTEPH at our two hospitals are not standardised and require strengthening.

CTEPH is a potentially surgically curative form of pulmonary hypertension, with PEA resulting in significant overall improvements in exercise capacity (median decrease in severity of 2 functional classes) and a return to a normal baseline (WHO-FC I) for almost two-thirds of survivors. Median time at assessment in our study was 4 months; improvement in functional class and exercise capacity may take 3 - 12 months while the right heart undergoes remodelling,[4] so this improvement might have been even greater if assessed at a later time point.

The small number of patients operated on over a 15-year period shows that PEA is severely underutilised in our setting, in both the public and private sectors. A recent prospective observational study (the FOCUS study) that followed up patients after acute PE showed a cumulative incidence of 2.3% for CTEPH at 2 years;[17] estimates from other smaller studies range between 0.1% and 9.1%.[4] Studies from two secondary-level hospitals in our drainage area (which includes three secondary-level hospitals as well as the tertiary referral centre) showed the number of patients with confirmed PE at each institution over a 2-year period to be 41[18] and 43.[19] Although we cannot say for certain what the total annual incidence of PE in our drainage area (which includes the public institutions as noted, as well as numerous private facilities) would be, we can assume it to be a significant number of cases. Therefore, even using conservative estimates for CTEPH after PE for our population (which would already underestimate the true incidence, as there is not always a history of prior VTE), a diagnostic and treatment gap is apparent. Potential factors accounting for the low number of CTEPH diagnoses and PEAs performed affect every part of the referral and treatment pathway. Under-recognition and underdiagnosis (including access to diagnostic imaging) and the paucity of specialist pulmonary hypertension services are important obstacles in resource-limited countries.[20] In addition, lack of awareness of the surgical options for management, resource constraints on cardiothoracic and ICU capacity (which limit centre volume), competing priorities, and a conservative institutional approach to addressing pulmonary arterial obstruction beyond level 1 (involving one of the main pulmonary arteries) and level 2 (starting at the level of the lobar branches or past the origin of the upper lobe artery)[21] disease may play a role.

The post-surgical outcomes reported in this study are considerably worse than in previous reports of PEA from other settings and eras. PEA outcomes in high-volume centres approach those of routine cardiac surgery owing to improved management of the cardiac and pulmonary complications of PEA and the well-established use of ECMO. The latest in-hospital mortality rate reported by the centre with the greatest experience globally with PEA (University of California San Diego) is 2.2%,[10] with mortality in the international CTEPH registry (which includes centres in Canada and Europe) reported as 4.7%.[12] The inverse association between centre volume and outcome that has been described for other complex cardiothoracic procedures, including heart and lung transplantation,[22-25] undoubtedly also applies to our low-volume

Table 2. Preoperative investigations (N=24 unless otherwise shown)

	n (%)*
CTPA performed	24 (100)
V/Q scan performed	7 (29)
Echocardiogram performed	24 (100)
RVSP (mmHg), median (IQR) (n=22†)	82 (64 - 89)
6MWT performed	13 (54)
6MWT distance (m), mean (SD) (n=13)	322 (140)
RHC performed	5 (21)
mPAP (mmHg,) mean (SD) (n=5)	49 (3.5)
PVR (Wood units), median (IQR) (n=5)	7.9 (6.3 - 13.7)
Cardiac output (L/min), mean (SD) (n=5)	4.0 (0.7)

CTPA = computed tomography pulmonary angiogram; V/Q = ventilation/perfusion; RVSP = right ventricular systolic pressure; IQR = interquartile range; 6MWT = 6-minute walk test; SD = standard deviation; RHC = right heart catheterisation; mPAP = mean pulmonary artery pressure; PVR = pulmonary vascular resistance.
*Except where otherwise indicated.
†Unable to assess RVSP for 2 patients as no tricuspid regurgitation.

Table 3. Right heart catheterisation (N=5)

Patient	Age (years)	Mean PAP (mmHg)	PVR (Wood units)	Average CO (L/min)
1	33	52	13.5	3.4
2	59	53	13.7	3.7
3	42	45	6.3	5.1
4	48	49	7.9	3.5
5	64	46	6	4.4

PAP = pulmonary artery pressure; PVR = pulmonary vascular resistance; CO = cardiac output.

Table 4. PEA procedure (*N*=24 unless otherwise shown)

	n (%)*
Cardiopulmonary bypass time (minutes), median (IQR) (*n*=23)	155 (137 - 174)
Cross-clamp time (minutes), median (IQR) (*n*=23)	80 (46 - 91)
Circulatory arrest time (minutes), median (IQR)	25 (14 - 35)
Lowest core temperature (°C), median (IQR)	24 (22 - 25)
Concomitant procedures performed (all)	3 (13)
Tricuspid valve annuloplasty	2 (8)
Mitral valve annuloplasty	1 (4)
ECMO	1 (4)
Days in ICU, median (IQR)	4 (2 - 5)
Days in hospital, median (IQR)	9 (8 - 20)
Days ventilated, median (IQR)	1 (1 - 1)
Patients with complications (all)	16 (67)
Bleeding (requiring transfusion)	5 (21)
Sternal wound sepsis	3 (13)
Acute renal failure	3 (13)
Arrhythmia	3 (13)
Need for re-look surgery	2 (8)
Anaesthetic complication	2 (8)
Pleural effusion	1 (4)
Haemothorax	1 (4)
Pericardial effusion/cardiac tamponade	2 (8)
Pneumonia	1 (4)
In-hospital mortality	4 (17)

PEA = pulmonary endarterectomy; IQR = interquartile range; ECMO = extracorporeal membrane oxygenation; ICU = intensive care unit.
*Except where otherwise indicated.

Table 5. Postoperative outcomes (*N*=16 unless otherwise shown)

	n (%)*
4-month mortality (*n*=23)	4 (17)
Time to follow-up post surgery (months), median (IQR)	4 (2 - 5)
WHO-FC at follow-up	
I	10 (63)
II	5 (31)
III	1 (6)
IV	0
Signs of right heart failure	2 (13)
Postoperative echocardiogram performed	8 (50)
RVSP (mmHg), median (IQR) (*n*=6†)	33 (30 - 58)
Postoperative 6MWT performed	9 (56)
Postoperative 6MWT distance (m), mean (SD) (*n*=9)	445 (108)
Postoperative RHC performed	0

IQR = interquartile range; WHO-FC = World Health Organization functional class; RVSP = right ventricular systolic pressure; 6MWT = 6-minute walk test; SD = standard deviation; RHC = right heart catheterisation.
*Except where otherwise indicated.
†Unable to assess RVSP for 2 patients as no tricuspid regurgitation.

centre. In addition, we have evolving institutional experience with extracorporeal support during the study period, having only established a nascent programme towards the end of 2015. However, despite most of the cases being performed after the service was established, the use of rescue ECMO in our study was rare, similar to the ~5% incidence reported in other large surgical series.[4] It is more likely that the numerically higher mortality is a function of small patient numbers that include some high-risk cases, with over a fifth of patients (21%) in WHO-FC IV prior to surgery. In comparison, only 10% of operated patients from the University of California San Diego series[10] and 13% of operated patients from the international CTEPH registry[12] were in WHO-FC IV prior to surgery.

Finally, our study demonstrates that diagnostic approaches, preoperative work-up and postoperative follow-up of CTEPH at our institution are not standardised and are probably suboptimal. Preoperative RHC was performed sparingly despite being mandated in all pulmonary hypertension guidelines to confirm the diagnosis, as well as to establish the severity of the haemodynamic impairment. Pulmonary angiography, the gold standard for depicting the pulmonary vasculature and which can be performed at the same time as the RHC, was not done on any patient, probably because there has been a lack of institutional expertise in both the performance and interpretation of this modality. The finding on histological examination of pulmonary artery sarcomas (a rare and aggressive malignant tumour, often mistaken for PE based on similar clinical and radiological features[26]) in almost 10% of patients reinforces the importance of thorough preoperative imaging and evaluation. Postoperative non-invasive follow-up was also inconsistent, with even echocardiographic assessments generally lacking. Guidelines for the diagnosis of CTEPH and for follow-up after PEA have been outlined in a recent consensus statement from the International Society for Heart and Lung Transplantation[4] and should be a reference document for centres going forward. At our institution, we have subsequently taken measures to aim towards a standardised practice falling in line with these recommendations, including mandating ventilation/perfusion scans and pulmonary angiograms.

Several limitations of this study deserve emphasis. First, while the number of patients undergoing PEA was already small, a quarter had to be excluded from the initial analysis and there were ultimately only outcome data for half of the operated patients. These exclusions may affect the conclusions that can be drawn from these data, and the small numbers prevented analyses of risk factors for mortality. Second, we only included patients who actually underwent PEA; the number of patients referred with CTEPH but not considered operable could not be established owing to the retrospective nature of the study. This is important, as up to a quarter of patients deemed inoperable are in fact candidates after additional imaging such as pulmonary angiography, which as mentioned was not performed in this study. Up to 90% of patients are surgical candidates in expert centres,[27,28] and it would have been interesting if we could have reported our denominator of referrals for PEA. Lastly, the preoperative assessment and postoperative follow-up were not standardised, and there was a dearth of data on haemodynamics or even echocardiographic measures of right ventricular function postoperatively. However, functional class remains an easy-to-record and patient-centred outcome measure for this group.

Conclusion

In summary, this study gives insight into current practices and outcomes at our institution regarding PEA for CTEPH. Surviving patients experienced significant functional improvement, although haemodynamic outcomes could not be assessed. Prolonged ICU stay was not required, and the need for ECMO was minimal. Preoperative work-up was variable, and this may have influenced patient selection for surgery. In addition, consideration should be given to longer-term specialist follow-up for those presenting with acute PE, as the diagnosis of CTEPH in our setting is almost certainly often missed or significantly delayed.

Declaration. The research for this study was done in partial fulfilment of the requirements for SADvE's MMed (Internal Medicine) degree at the University of Cape Town. TCP an GC are members of the *AJTCCM* editorial board. Another editor was given responsibility for overseeing the peer review of this submission.

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Author contributions. SADvE, TCP, JB, GJS and GLC were involved in conceptualising and designing the study. JB and TCP assisted with access to the database, data collection and review of the surgical aspects of the paper. SADvE did all other data collection. SADvE, GLC and GJS interpreted the data and wrote the first draft. All authors read and commented on the final manuscript.

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1. Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: The Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): Endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). Eur Heart J 2016;37(1):67-119. https://doi.org/10.1093/eurheartj/ehv317
2. Wilkens H, Konstantinides S, Lang IM, et al. Chronic thromboembolic pulmonary hypertension (CTEPH): Updated recommendations from the Cologne Consensus Conference 2018. Int J Cardiol 2018;272S:69-78. https://doi.org/10.1016/j.ijcard.2018.08.079
3. Pepke-Zaba J, Delcroix M, Lang I, et al. Chronic thromboembolic pulmonary hypertension (CTEPH): Results from an international prospective registry. Circulation 2011;124(18):1973-1981. https://doi.org/10.1161/circulationaha.110.015008
4. De Perrot M, Gopalan D, Jenkins D, et al. Evaluation and management of patients with chronic thromboembolic pulmonary hypertension – consensus statement from the ISHLT. J Heart Lung Transplant 2021;40(11):1301-1326. https://doi.org/10.1016/j.healun.2021.07.020
5. Delcroix M, Kerr K, Fedullo P. Chronic thromboembolic pulmonary hypertension: Epidemiology and risk factors. Ann Am Thorac Soc 2016;13(Suppl 3):S201-S206. https://doi.org/10.1513/AnnalsATS.201509-621AS
6. Kim NH, Lang IM. Risk factors for chronic thromboembolic pulmonary hypertension. Eur Respir Rev 2012;21(123):27-31. https://doi.org/10.1183/09059180.00009111
7. Lang IM, Dorfmüller P, Vonk Noordegraaf A. The pathobiology of chronic thromboembolic pulmonary hypertension. Ann Am Thorac Soc 2016;13(Suppl 3):S215-S221. https://doi.org/10.1513/AnnalsATS.201509-620AS
8. Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J 2022;43(38):3618-731. https://doi.org/10.55788/c838601b
9. Jamieson SW, Kapelanski DP, Sakakibara N, et al. Pulmonary endarterectomy: Experience and lessons learned in 1,500 cases. Ann Thorac Surg 2003;76(5):1457-1462. https://doi.org/10.1016/s0003-4975(03)00828-2
10. Madani MM, Auger WR, Pretorius V, et al. Pulmonary endarterectomy: Recent changes in a single institution's experience of more than 2,700 patients. Ann Thorac Surg 2012;94(1):97-103. https://doi.org/10.1016/j.athoracsur.2012.04.004
11. Condliffe R, Kiely DG, Gibbs JS, et al. Improved outcomes in medically and surgically treated chronic thromboembolic pulmonary hypertension. Am J Respir Crit Care Med 2008;177(10):1122-1127. https://doi.org/10.1164/rccm.200712-1841OC
12. Mayer E, Jenkins D, Lindner J, et al. Surgical management and outcome of patients with chronic thromboembolic pulmonary hypertension: Results from an international prospective registry. J Thorac Cardiovasc Surg 2011;141(3):702-710. https://doi.org/10.1016/j.jtcvs.2010.11.024
13. Thistlethwaite PA, Kaneko K, Madani MM, Jamieson SW. Technique and outcomes of pulmonary endarterectomy surgery. Ann Thorac Cardiovasc Surg 2008;14(5):274-282.
14. Matsuda H, Ogino H, Minatoya K, et al. Long-term recovery of exercise ability after pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension. Ann Thorac Surg 2006;82(4):1338-1343. https://doi.org/10.1016/j.athoracsur.2006.03.105
15. Skoro-Sajer N, Marta G, Gerges C, et al. Surgical specimens, haemodynamics and long-term outcomes after pulmonary endarterectomy. Thorax 2014;69(2):116-122. https://doi.org/10.1136/thoraxjnl-2013-203746
16. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. Lancet 2007;370(9596):1453-1457. https://doi.org/10.1016/s0140-6736(07)61602-x
17. Valerio L, Mavromanoli AC, Barco S, et al. Chronic thromboembolic pulmonary hypertension and impairment after pulmonary embolism: The FOCUS study. Eur Heart J 2022;43(36):3387-3398. https://doi.org/10.1093/eurheartj/ehac206
18. Bulajic B, Welzel T, Vallabh K. Clinical presentation and diagnostic work up of suspected pulmonary embolism in a district hospital emergency centre serving a high HIV/TB burden population. Afr J Emerg Med 2019;9(3):134-139. https://doi.org/10.1016/j.afjem.2019.05.003
19. Ramlakhan R, Andronikou S, Rajkumar A. The prevalence and radiological findings of pulmonary embolism in HIV-positive patients referred for computed tomography pulmonary angiography in the Western Cape of South Africa. Cardiovasc J Afr 2017;28(4):221-228. https://doi.org/10.5830/cvja-2016-083
20. Davies-van Es S, Calligaro G, Manning K, Williams H, Dheda K, Symons G. The aetiology, clinical presentation and treatment of patients with pulmonary hypertension in Cape Town: A preliminary report from the Groote Schuur Hospital Pulmonary Hypertension Registry. Afr J Thorac Crit Care Med 2018;24(4):133-138. https://doi.org/10.7196/ajtccm.2018.v24i4.218
21. Madani MM. Surgical treatment of chronic thromboembolic pulmonary hypertension: Pulmonary thromboendarterectomy. Methodist DeBakey Cardiovasc J 2016;12(4):213-218. https://doi.org/10.14797/mdcj-12-4-213
22. Shudo Y, Wang H, Lingala B, et al. Evaluation of risk factors for heart-lung transplant recipient outcome: An analysis of the United Network for Organ Sharing Database. Circulation 2019;140(15):1261-1272. https://doi.org/10.1161/circulationaha.119.040682
23. Thourani VH, Brennan JM, Edelman JJ, et al. Association of volume and outcomes in 234 556 patients undergoing surgical aortic valve replacement. Ann Thorac Surg 2022;114(4):1299-1306. https://doi.org/10.1016/j.athoracsur.2021.06.095
24. Russo MJ, Iribarne A, Easterwood R, et al. Post-heart transplant survival is inferior at low-volume centers across all risk strata. Circulation 2010;122(11 Suppl):S85-S91. https://doi.org/10.1161/circulationaha.109.926659
25. Tie HT, Shi R, Zhou Q, Wang K, Zheng XQ, Wu QC. Annual case volume on mortality after coronary artery bypass grafting: A dose-response meta-analysis. Interact Cardiovasc Thorac Surg 2019;29(4):568-575. https://doi.org/10.1093/icvts/ivz151
26. Cervilla-Munoz E, Galeano-Valle F, Del-Toro-Cervera J, Calleja-Carton E, Demelo-Rodriguez P. Differential diagnosis and treatment approach to pulmonary artery sarcoma: A case report and literature review. ERJ Open Res 2020;6(3):00124-2020. https://doi.org/10.1183/23120541.00124-2020
27. D'Armini AM, Morsolini M, Mattiucci G, et al. Pulmonary endarterectomy for distal chronic thromboembolic pulmonary hypertension. J Thorac Cardiovascular Surg 2014;148(3):1005-1011. https://doi.org/10.1016/j.jtcvs.2014.06.05224
28. Jenkins DP, Biederman A, D'Armini AM, et al. Operability assessment in CTEPH: Lessons from the CHEST-1 study. J Thoracic Cardiovasc Surg 2016;152(3):669-674.e3. https://doi.org/10.1016/j.jtcvs.2016.02.062

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