Age should not be a barrier for pulmonary endarterectomy in carefully selected patients

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DOI:
10.1183/13993003.01804-2017

Title

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"Take home" message / Abstract

CTEPH patients over 80 years old undergoing pulmonary endarterectomy have similar outcomes to those under 80.

To the Editor:

Pulmonary endarterectomy (PEA) is the treatment of choice in operable chronic thromboembolic pulmonary hypertension (CTEPH) with excellent long term outcomes [1]. It is a complex surgical procedure requiring cardiopulmonary bypass and removal of obstructive thromboembolic material during periods of deep hypothermic circulatory arrest [1]. We have observed an increase in the number of older CTEPH patients referred for consideration of PEA, which is consistent with other cardiothoracic surgeries. The UK population is aging with a projected 3% increase in those over 85 years in the next 20 years [2]. This may be mirrored by patients with CTEPH getting older, as the incidence of pulmonary embolism, which frequently precedes CTEPH, increases markedly with age [3,4]. Furthermore, an epidemiological analysis by Gall *et al*, has projected that the annual incidence of CTEPH will increase over the next 10 years [5]. Therefore, the management of CTEPH in older patients is a pertinent topic for investigation.

We previously reported that hospital survival in patients over 70 years undergoing PEA was comparable to those under 70, albeit with longer hospital and intensive care unit (ICU) stays [6]. For selected cardiac surgeries (coronary artery bypass and aortic valve surgery) octogenarians have equivalent or improved long-term mortality compared to an age- and sex-matched population [7,8]. Furthermore, patient reported outcomes (PROs) including quality of life improve post-operatively, and are equivalent or better than a matched general population of octogenarians [7,9]. However, increased in-hospital mortality and prolonged hospital / ICU length of stay have also been reported, which may translate to increased health utilisation costs [10,11]. Therefore, in the current study, we aimed to assess the outcomes of CTEPH patients over 80 years old who underwent PEA.

Consecutive CTEPH patients undergoing PEA from June 2006 to August 2016 at the UK National PEA centre (Papworth, UK) were included in a retrospective analysis. The diagnosis of CTEPH was based on international criteria [12]. Suitability for PEA was discussed by a multidisciplinary team comprising pulmonary hypertension physicians, specialist cardiothoracic radiologists and pulmonary endarterectomy surgeons. The cohort was dichotomized into over and under 80 years according to the age at time of surgery. Pre-operative baseline and post-operative 3-6-month follow-up data were recorded, with follow-up data included until 3 months after the end of the census period. PROs were assessed using the Cambridge Pulmonary Hypertension Outcome Review (CAMPHOR) score, a PH specific quality of life measure [13]. Groups were compared using a chi-squared test for categorical data, Wilcoxon rank-sum test for continuous data and log-rank test for survival data. A false discovery rate adjusted p-value was used to account for multiple testing.

1152 individuals underwent PEA (under 80 years: 1115 (97%); over 80: 37 (3%)) during the study period. Baseline and 3-6 month follow-up variables and outcomes are summarised in table 1. Overall survival at 1, 3 and 5 years was 91.8%, 88.2% and 84.4% in the under 80 group, and 83.5%, 76.4% and 69.4% in the over 80 group. Whilst survival was lower in the over 80 group (Log-rank test, p=0.020), it was no different from an age- and sex-matched UK reference population (p=0.500) [15].

There were significant improvements in World Health Organisation (WHO) functional class, 6-minute walk distance (6mwd) and haemodynamics for both under and over 80s post-PEA. Whilst the 6mwd was lower in the over 80s post-PEA (286±164 vs. 360±92; p=0.020) there was an equivalent change from baseline (p=0.676) reflecting the same magnitude of improvement. Furthermore, there was no difference in the median change from baseline for WHO functional class, haemodynamics or PROs between under and over 80s, indicating an equivalent improvement in outcomes.

There were more concomitant cardiac surgical procedures in the over 80 group (11% vs. 27% p= 0.042), predominantly due to more coronary artery bypass grafts (7% vs. 19%). There was a shorter cardiopulmonary bypass time (323±305 minutes vs. 305±65; p=0.020) in the over 80s but no difference in the total deep hypothermic circulatory arrest time or type of surgical disease (Jamieson classification based on location and morphology) (p=0.230 and p=1.000). The hospital length of stay was longer in those over 80 (19±7 vs. 14±10 days; p=0.020) but there was no difference in time spent on the ICU (4±3 vs. 5±5 days; p=0.310). There was also no difference in post-PEA complications (p=1.000) or in hospital mortality (4% vs. 8%; p=0.510).

Despite the study limitations (small group size of over 80s, retrospective single-centre analysis), we found similar outcomes in patients under and over 80 years old undergoing PEA, except for a prolonged hospital length of stay in octogenarians. Whilst survival is reduced in the over 80 group compared to the under 80s, it is no different to a reference age- and sex-matched UK population. The greater number of concomitant cardiac surgeries in octogenarians could indicate that their improvement is multi-factorial. Future research should consider the health utilization and cost implications of older patients undergoing PEA, given they have a prolonged hospital length of stay.

We acknowledge that CTEPH patients over 80 were highly selected to undergo PEA and therefore our results may not apply to “all comers”. However, it reinforces the effectiveness of the PEA selection process at expert centres. Age alone should not be a contraindication for PEA and individuals with suspected CTEPH should be referred for specialist evaluation.

Acknowledgements: The National Pulmonary Hypertension Centres UK and Ireland for referring patients that were considered for PEA.

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TABLE 1
Baseline variables and post-PEA outcomes subdivided by age cohorts.

	Baseline			Follow-up		
	Under 80	**Over 80**	**p-value**	**Under 80**	**Over 80**	**p-value**
Subjects (n)	1115	37				
Age at PEA [years]	61 (22)	81 (2)				
Gender [female]	517 (46)	17 (46)	1.000			
Comorbidities						
COPD	78 (7)	2 (5)	1.000			
Diabetes	94 (9)	2 (6)	0.950			
Atrial fibrillation/flutter	91 (9)	5 (14)	0.810			
Ischaemic heart disease	124 (12)	7 (19)	0.560			
Malignancy	85 (8)	4 (11)	1.000			
Systemic hypertension	307 (30)	10 (28)	1.000			
CAMPHOR score[a]:						
Symptoms	13 ± 10	12 ± 9	1.000	4 ± 8	4 ± 7	0.860
Activity	11 ± 9	14 ± 8	0.260	6 ± 9	9 ± 6	0.300
Quality of life	11 ± 11	11 ± 11	0.870	4 ± 10	6 ± 8	1.000
WHO functional class [1/2/3/4 (%)][b]	0 / 14/ 73/ 13	0/ 3/ 70/ 26	0.046	28/ 47/ 23/ 1	22/ 40/ 33/ 4	0.450
6mwd [metres]	290 ± 216	227 ± 210	0.051	360 ± 164	286 ± 92	0.020
mPAP [mmHg]	45 ± 15	42 ± 12	0.560	25 ± 13	28 ± 12	0.560
PVR [dynes.s.cm^{-5}]	666 ± 479	743 ± 462	0.310	235 ± 212	297 ± 294	0.081
CI [L/min/m^2]	2.2 ± 0.8	1.9 ± 0.8	0.020	2.3 ± 0.7	2.3 ± 0.8	0.810
Type of surgical disease[c] [1/2/3/4 (%)]	14/ 58/ 26/ 3	14/ 59/ 27/ 0	1.000			
Bypass time [mins]	323 ± 65	305 ± 51	0.020			
Arrest time [mins]	37 ± 15	33 ± 13	0.230			
Concomitant surgery: Total	123 (11)	10 (27)	0.042			
CABG	76 (7)	7 (19)				
PFO/ASD closure	34 (3)	1 (3)				
MVR	12 (2)	0 (0)				
AVR	8 (1)	2 (5)				
Complications: Total[d]	277 (32)	12 (35)	1.000			
ECMO	60 (6)	2 (6)				
Pneumonia	110 (12)	6 (18)				
Re-intubation	91 (10)	3 (9)				
Renal replacement therapy	52 (6)	0 (0)				
Return to theatre	80 (9)	2 (6)				
Tracheotomy	61 (6)	1 (3)				
Length of stay [days]						
Intensive care unit	4 ± 3	5 ± 5	0.310			
Total hospital	14 ± 10	19 ± 7	0.020			
In-hospital mortality [%]	4	8	0.510			
Residual PH[e]						
mPAP≥25mmHg				463 (51)	18 (62)	1.000
mPAP≥30mmHg				309 (34)	13 (44)	0.560
mPAP≥38mmHg and PVR≥425dynes.s.cm^{-5}				101 (11)	2 (7)	0.930
Survival [%]						
1 year				91.8	83.5	0.020
3 years				88.2	76.4	
5 years				84.4	69.4	

Data presented as median ± Interquartile range or number of patients (%) unless otherwise stated. 6mwt: 6-minute walk distance; AVR: aortic valve replacement; CABG: coronary artery bypass graft; CAMPHOR: Cambridge Pulmonary Hypertension Outcome Review score; CI: cardiac index; ECMO: Extracorporeal membrane oxygenation; mPAP: mean pulmonary arterial pressure; MVR: mitral valve replacement; PFO/ASD: patent foramen ovale / atrial septal defect; PH: pulmonary hypertension; PVR: pulmonary vascular resistance; WHO: World Health Organisation.

[a] CAMPHOR score: a higher score denotes a worse patient reported outcome
[b] Total percentage may not add up to 100 due to rounding
[c] Jamieson classification
[d] Total: any of the listed complications
[e] The higher residual PH thresholds have been associated with post-PEA outcomes [14]