Survival after pulmonary thromboendarterectomy: Effect of residual pulmonary hypertension

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Objective: Pulmonary endarterectomy is the treatment of choice for chronic thromboembolic pulmonary hypertension. In many patients hemodynamics are normalized early after surgical intervention. However, the effect of residual pulmonary hypertension on postoperative clinical status and survival is unknown.

Methods: Data were collected prospectively on all patients who underwent pulmonary endarterectomy in a continuous national series between 1997 and December 2007. Postoperatively, patients underwent scheduled reinvestigation, including functional testing and right heart catheterization, at 3 months after the operation. They were divided into 2 groups based on mean pulmonary artery pressure: group 1, less than 30 mm Hg; group 2, 30 mm Hg or greater.

Results: Three hundred fourteen patients underwent pulmonary endarterectomy, survived to hospital discharge, and completed the 3-month follow-up period. At 3 months after pulmonary endarterectomy, there was a significant reduction in mean pulmonary artery pressure for the whole cohort (48 ± 12 to 26 ± 10 mm Hg, $P < .001$). However, 31% of the patients had residual pulmonary hypertension. Group 1 patients enjoyed significantly better exercise capacity and improved symptoms compared with group 2 patients. In addition, there were significantly fewer patients receiving targeted medical therapy in group 1 versus group 2 (0% vs 25%, $P < .001$). Conditional survival after discharge from the hospital for the whole cohort was 90.0% at 5 years and was not different between groups (90.3% for group 1 vs 89.9% for group 2, $P = .36$).

Conclusions: For patients undergoing pulmonary endarterectomy, survival after hospital discharge is excellent. Residual pulmonary hypertension significantly compromised symptom status and functional capacity but did not appear to adversely affect medium-term survival. The effect of targeted medical therapy in patients with residual pulmonary hypertension after pulmonary endarterectomy needs to be evaluated further. (J Thorac Cardiovasc Surg 2011;141:383-7)

Chronic thromboembolic pulmonary hypertension (CTEPH) is a serious condition. Historically before the development of surgical treatment, survival was very poor.[1] In a recent cohort of patients comprehensively followed in the modern era, outcomes had improved.[2] Pulmonary endarterectomy is the treatment of choice to relieve pulmonary artery obstruction in patients with CTEPH and has been remarkably successful.[3] The largest and most comprehensive series to date demonstrates that in the postoperative period patients enjoy a reduction in pulmonary pressure and an improvement in cardiac function with few complications and a low risk of mortality.[4]

However, not all patients are suitable for surgical intervention, and it is increasingly recognized that some patients have residual pulmonary hypertension (PH) after pulmonary endarterectomy.[5-7] Estimates of the number of patients with residual PH after pulmonary endarterectomy have varied from 5% to 35% depending on the definition, and few units have evaluated these patients comprehensively. One other center has reported post–pulmonary endarterectomy persistent PH, with an incidence of 35% (33/93 patients) at 1 year.[5] Another center recently reported a 24% incidence of increased pulmonary vascular resistance (PVR) after pulmonary endarterectomy and showed that advanced New York Heart Association (NYHA) class was associated with poorer survival.[8] When we reported all incident cases of CTEPH in the United Kingdom between 2001 and 2006, we found that in 198 patients investigated at 3 months after pulmonary endarterectomy, using the formal definition of PH (mean pulmonary artery pressure [mPAP] >25 mm Hg and PVR >240 dynes $\cdot$ sec^{-1} $\cdot$ cm^{-5} at rest), residual PH was present in 35%.[2] To our surprise, survival at 3 years remained excellent and was not different from that of the larger group with no residual PH. In the past, medical management of patients with CTEPH has proved disappointing,

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Abbreviations and Acronyms

CTEPH = chronic thromboembolic pulmonary hypertension
mPAP = mean pulmonary artery pressure
NYHA = New York Heart Association
PH = pulmonary hypertension
PVR = pulmonary vascular resistance

with little response to vasodilator therapy.[9,10] However, newer targeted medical therapies might provide some advantage, and therefore it is important to identify patients who could benefit from medical treatment even after pulmonary endarterectomy surgery.[11-16]

Many units have now reported in-hospital results after pulmonary endarterectomy surgery. Outcome after discharge from the hospital has been more difficult to quantify and less frequently reported. We have recently published the results of pulmonary endarterectomy surgery after hospital discharge for all United Kingdom patients.[2,17] Even though this series included patients from the beginning of our pulmonary endarterectomy program, we found remarkable improvement in functional and hemodynamic parameters at 3 months and 1 year, with excellent medium-term survival at 5 years.

However, the CTEPH disease process is complex, and it is known that patients with operable (so-called proximal) disease in the segmental pulmonary artery branches can also have a distal small-vessel vasculopathy in the nonobstructed vascular beds with histologic changes similar to those seen in idiopathic PH.[18,19] Indeed, this 2-compartment model was proposed many years ago by Moser and Braunwald[20] after their early experience of treating this condition. This fact explains why some patients have a degree of persisting PH even after apparently successful surgical clearance of all visible disease. Persistently increased PVR in the immediate postoperative period is known to be a significant risk factor for in-hospital death, especially if greater than 500 dynes · s^{-1} · cm^{-5}.[2,4] The effect of residual PH in the longer term is not completely understood. The objective of this study was to determine the effect of residual PH on symptom status and survival after pulmonary endarterectomy in the largest cohort followed to date.

MATERIALS AND METHODS

All patients with CTEPH were discussed preoperatively at a weekly multidisciplinary team meeting with PH physicians, specialist radiologists, and pulmonary endarterectomy surgeons. All data were entered prospectively into a dedicated surgical and PH database, as previously reported.[17] An inferior vena caval filter was inserted in all patients preoperatively. Pulmonary endarterectomy was performed by using principles similar to those used by the University of California, San Diego group.[4,21] All patients underwent surgical intervention with deep hypothermia, but complete arrest of the circulation was not used in every case.[17,22] Anticoagulation was continued postoperatively in all cases.

At 3 months after pulmonary endarterectomy, all patients were invited to return to Papworth Hospital for full review by the pulmonary vascular disease physicians. NYHA class, 6-minute walk test, and right heart catheterization data were recorded. These variables were again examined at 12 months after pulmonary endarterectomy, although right heart catheterization was not repeated unless there was residual PH at 3 months or changes in symptom status, echocardiographic estimates of pulmonary artery pressure, or both. Patients continued follow-up at their local PH specialist center after 1 year.

Based on the mPAP at 3 months, patients were divided into 2 groups: those with mPAPs of less than 30 mm Hg (group 1) and those with potentially prognostically important post–pulmonary endarterectomy PH mPAPs of 30 mm Hg or greater (group 2). Thirty millimeters of mercury was chosen as the division because pressures of greater than and less than this level at baseline appeared to correlate with impaired or normal survival in Riedel and colleagues' original account of survival in patients with CTEPH.[1] It was also a more useful practical definition of residual PH in patients after pulmonary endarterectomy because it coincided with the pressure criteria accepted in our hospital above which to consider use of advanced medical therapies in suitable patients with class III symptoms.[2]

Survival after discharge from the hospital was calculated with a censor date of December 31, 2008. For patients from England and Wales, the National Health Service spine summary care record-tracking system was used based on the patient's individual National Health Service number. For patients from Scotland and Ireland, survival status was checked with the general practitioner during the first 2 weeks of January 2009 by 2 independent researchers from the Papworth research and development department.

Statistics

Analysis was performed with the SPSS version 13.0 statistical software package (SPSS, Inc, Chicago, Ill). Continuous variables are described as the mean ± standard deviation or median ± interquartile range and compared by using Student's t test or the Mann–Whitney U test, as appropriate. Categorical data are expressed as proportions and compared by using the χ^2 test. Follow-up over time was assessed by using repeated-measures analysis of variance or the Friedman test, as appropriate. Estimation of cumulative survival was performed by using the Kaplan–Meier method and compared with the log-rank test.

RESULTS

During the period from the start of the program in 1997 and December 2007, 314 patients underwent pulmonary endarterectomy at Papworth hospital, survived to hospital discharge, and completed follow-up. Full hemodynamic data were available for 306 patients at 3 months (97.4% complete). The mean age of the study population was 55 years (range, 17–81 years), and 54.3% were male. Thirty-one percent of patients had an mPAP of 30 mm Hg or greater at 3 months after pulmonary endarterectomy.

The NYHA class for the whole cohort at baseline and follow-up is shown in Figure 1, A, and the hemodynamic data are shown in Table 1. As expected, by 3 months after pulmonary endarterectomy, there was a significant reduction in mPAP (48 ± 12 to 26 ± 10 mm Hg, $P < .001$) and PVR (805 ± 365 to 301 ± 232 dynes · s^{-1} · cm^{-5}, $P < .001$). Cardiac index was increased significantly for the whole group (2.0 ± 0.7 to 2.5 ± 0.5 L · min^{-1} · m^{-2}, $P < .001$).

Patients in group 1 enjoyed significantly better exercise capacity and improved symptoms compared with those in group 2 (Table 2 and Figure 1, B). The postoperative 6-minute walk distance was significantly greater in group