Preoperative Partitioning of Pulmonary Vascular Resistance Correlates With Early Outcome After Thromboendarterectomy for Chronic Thromboembolic Pulmonary Hypertension

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Background—Pulmonary thromboendarterectomy (PTE) is the preferred treatment for chronic thromboembolic pulmonary hypertension (CTEPH), but persistent pulmonary hypertension after PTE, as a result of either inaccessible distal thrombotic material or coexistent intrinsic small-vessel disease, remains a major determinant of poor outcome. Conventional preoperative evaluation is unreliable in identifying patients at risk for persistent pulmonary hypertension or predicting postoperative hemodynamic outcome. We postulated that pulmonary arterial occlusion pressure waveform analysis, a technique that has been used for partitioning pulmonary vascular resistance, might identify CTEPH patients with significant distal, small-vessel disease.

Methods and Results—Twenty-six patients underwent preoperative right heart catheterization before PTE. Pulmonary artery occlusion waveform recordings were performed in triplicate. Postoperative hemodynamics after PTE were compared with preoperative partitioning of pulmonary vascular resistance derived from the occlusion data. Preoperative assessment of upstream resistance ($R_{up}$) correlated with both postoperative total pulmonary resistance index ($R_{2}$/$H_{11005}$ $0.79, P<0.001$) and postoperative mean pulmonary artery pressure ($R_{320}$=$0.75, P<0.001$). All 4 postoperative deaths occurred in patients with a preoperative $R_{up}$ <60%.

Conclusions—Pulmonary arterial occlusion pressure waveform analysis may identify CTEPH patients at risk for persistent pulmonary hypertension and poor outcome after PTE. Patients with CTEPH and $R_{up}$ value <60% appear to be at highest risk. (Circulation. 2004;109:18-22.)

Key Words: pulmonary heart disease ■ hypertension, pulmonary ■ endarterectomy ■ occlusion

Chronic thromboembolic pulmonary hypertension (CTEPH) is a life-threatening complication of venous thromboembolism that is caused by incomplete resolution of pulmonary emboli. It has been estimated that there are 2500 new cases of CTEPH each year in the United States. As in other forms of severe pulmonary hypertension, untreated patients with CTEPH eventually progress to right heart failure and death. Although pulmonary arterial hypertension (PAH) tends to involve the small muscular vessels, the primary site of vasculopathy in CTEPH is the large elastic pulmonary arteries. This proximal location in CTEPH renders it accessible to surgical intervention with removal of the obstructing lesions. Accordingly, pulmonary thromboendarterectomy (PTE) is considered the treatment of choice for CTEPH.

Concomitant small vessel arteriopathy is also often present to varying degrees in CTEPH. In these patients, pulmonary hypertension persists despite removal of proximal material. Persistent pulmonary hypertension after PTE remains a significant problem and is associated with increased morbidity and mortality: More than a third of perioperative deaths and nearly half of long-term deaths have been attributed to persistent pulmonary hypertension. The current standard preoperative evaluation does not accurately detect the presence or assess the degree of small vessel involvement in patients with CTEPH, nor does it reliably predict postoperative hemodynamic outcome.

The pulmonary artery occlusion technique was developed to estimate pulmonary capillary pressure and most likely approximates pressure in the precapillary small pulmonary arteries (occlusion pressure; Pocl). With Pocl, the pulmonary arterial resistance can be partitioned into larger arterial (upstream) and small arterial plus venous (downstream) components. We postulated that a higher upstream resistance ($R_{up}$) would be expected in patients with CTEPH who have predominantly proximal (large-vessel) disease, whereas CTEPH patients with lower $R_{up}$ are likely to have significant concomitant small-vessel disease and are, there-
fore, at risk for persistent pulmonary hypertension after PTE. To test this hypothesis, we performed measurements of Poccl during the preoperative evaluation in a series of CTEPH patients referred to our center for PTE, and we correlated the preoperative distribution of resistance with surgical outcome.

Methods

Twenty-six patients (18 women and 8 men) referred to our center with symptoms and signs consistent with pulmonary hypertension due to CTEPH were studied. Informed consent, approved by institutional review board, was obtained from all patients. All patients met diagnostic criteria for CTEPH, as determined by an independent clinician, on the basis of standard preoperative evaluations.

All patients underwent right heart catheterization as part of the standard PTE evaluation protocol at our institution. A 7F, flow-directed, balloon-tipped Swan-Ganz catheter (131HF7; Baxter Healthcare Corp) was inserted in an internal jugular vein after administration of local anesthetic. Under fluoroscopic and continuous pressure monitoring, the catheter was positioned into a pulmonary artery. Hemodynamic measurements were obtained at end-expiration after zeroing the transducer at mid-chest. The pressure data were collected using a disposable transducer (Namic; Boston Scientific) connected to a hemodynamic and electrocardiographic monitoring system (Mac-Laboratory 7000, General Electric Medical Systems). The vascular pressure signals were sampled at 200 Hz with the use of an analogue-to-digital converter (DAQCard-AI16XE-50, National Instruments) and displayed and stored on a personal computer. Cardiac output was recorded by using thermodilution technique as an average of at least 3 measurements.

After single inflation of the pulmonary artery catheter, occlusion waveforms were recorded during breath-holding for ~8 seconds at end-expiration. Measurements were performed in triplicate. The pulmo-

![Figure 1. Sample pulmonary artery pressure occlusion waveforms from 2 patients with (A) primarily upstream resistance (note the relatively rapid drop in pressure to Ppao) and (B) significant downstream resistance (longer time is needed for the pressure to reach Ppao).](http://circ.ahajournals.org/doi/abs/10.1161/CIRCULATIONAHA.119.046361)
nary vascular pressure signals were filtered using a 2-pole digital low-pass filter with a cutoff at 18 Hz. A biexponential fitting of the pressure decay curve between the moment of occlusion and the pulmonary artery occluded pressure (Ppao), with normalization to the mean pulmonary artery pressure (mPpa), has been previously described and is used here to derive Poccl (Figure 1).8,10,11 The Rup was calculated as follows: Rup % = 100 × (mPpa − Poccl) / (mPpa − Ppao).

Postoperative hemodynamic measurements were obtained in all patients between postoperative days 1 and 3 (mean, 1.4 ± 0.6 days). All patients returned from the operating room with a new 7F Swan-Ganz catheter terminating in a proximal pulmonary artery. When possible, the postoperative hemodynamics were recorded after extubation and while patients were receiving the least amount of pharmacological vasoactive therapy. For patients who had rapid and uneventful early postoperative course, the last set of hemodynamics before discontinuation of the Swan-Ganz catheter was recorded and used for analysis. Eleven patients remained intubated, and 7 patients were receiving vasoactive therapy (4 on dopamine alone, 2 on dopamine and epinephrine, and 1 on dopamine and vasopressin) during postoperative hemodynamic recording. Because Ppao is not routinely measured postoperatively because of concern about mechanical vascular injury immediately after PTE, total pulmonary resistance index (TPRi), rather than pulmonary vascular resistance index, was calculated according to the standard formula.

Relationships between hemodynamic variables and preoperative Rup values were analyzed using linear regression and calculation of the Spearman’s correlation coefficient ($R^2$). Results are presented as mean ± SD unless otherwise stated.

### Results

Twenty-six patients underwent PTE and postoperative hemodynamic measurements. There were no adverse events related to performing occlusion measurements. The demographics and baseline hemodynamics are shown in the Table. With the exception of patients 8 and 24, who had bilateral intraoperative type 4 disease, the remainder of the patients had primarily types 1 and 2 disease.12

Preoperative Rup values correlated inversely with both postoperative TPRi and mPpa ($R^2$ of 0.79 and 0.75, respectively; Figure 2). TPRi and mPpa values before and after PTE correlated poorly ($R^2$ of 0.10 and 0.09, respectively). Also, Rup correlated poorly with preoperative TPRi and mPpa ($R^2$ of 0.11 and 0.15, respectively) and with the degree of change in TPRi and mPpa after PTE ($R^2$ of less than 0.01 and =0.16, respectively).

All 4 postoperative deaths occurred in patients with a preoperative Rup of <60% (Table). The nonsurvivors had the highest postoperative TPRi and mPpa values. Right heart failure from persistent pulmonary hypertension was the leading cause of all 4 deaths. Two patients had concomitant reperfusion pulmonary edema, which contributed to their deaths. These 4 nonsurvivors had higher preoperative pulmonary vascular resistance compared with survivors (1269 ± 263
Our study demonstrates that preoperative assessment of pulmonary Poccl may provide useful information about operative risk and outcome in CTEPH. Developed as a method of estimating pulmonary capillary pressure, the pulmonary artery occlusion technique appears to estimate pre-capillary pressure.\(^5\)\(^{-}\)\(^7\) Animal studies suggested that the site of pressure measurement may be in pulmonary arterial vessels between 50 and 900 \(\mu\)m in diameter—vessels inaccessible to PTE. This information about distal pulmonary artery pressure allows for partitioning of pulmonary vascular resistance into large arterial (upstream) and small arterial plus venous (downstream) components. Patients with higher downstream resistance appear to be at risk for persistent pulmonary hypertension and death after PTE.

In addition to redefining the traditional risk assessment before PTE, the occlusion technique may also help identify patients who should be considered for medical therapy as an alternative to PTE.\(^13\)\(^{-}\)\(^18\) In our series, all postoperative deaths occurred in patients with Rup of \(<60\%\). The mortality rate for this cohort was 15\%, significantly higher than the institution’s mean after PTE.\(^1\) This may have been related to an equally higher rate of postoperative persistent pulmonary hypertension seen in this cohort. Whether these nonsurvivors would have benefited from medical therapy, either in lieu of PTE or before PTE,\(^16\) is unknown. The role of medical
therapy in CTEPH—including efficacy, choice of drug(s), and patient selection—remains unclear and in need of further exploration. By helping to identify those patients least likely to benefit from PTE, the occlusion technique may expand the number of available candidates for trials of medical therapy.

There are several limitations and questions raised by this study. Although the pulmonary artery occlusion technique has been used in animal studies for many years, clinical experience, particularly in patients with pulmonary hypertension, is limited.7,8 Multiple versions of the occlusion technique have been investigated, all for estimating pulmonary capillary pressure on the basis of the application of electrical circuit models to the pulmonary circulation.7,19 It is unclear if other models of the occlusion technique will be superior to the current one for partitioning vascular resistance in CTEPH. It is also unknown if the correlation after PTE will be similar in centers with less experience.2 Although multiple measurements were obtained in each patient, occlusions were not repeated in multiple segments or in the contralateral lung. The use of flow-directed occlusion may be the important factor accounting for our findings, despite the known anatomic heterogeneity of CTEPH. None of the patients in the study had either exercise-related pulmonary hypertension or unilateral chronic thromboembolic disease; occlusion technique data in these 2 unique patient groups are currently unavailable. Lastly, it is unclear if patients with seemingly distal CTEPH by conventional evaluation and high Rap values should be considered for PTE. Lesions that are upstream (proximal) according to the occlusion technique may still be too distal for successful PTE.

Conclusions

Pulmonary artery occlusion waveform analysis seems to be a safe and promising technique for assessing the degree of small-vessel disease and the risk of persistent pulmonary hypertension after PTE in select patients with CTEPH. Patients with Rap values <60% appear to have the highest postoperative risk.

References

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_Circulation_. 2004;109:18-22; originally published online December 29, 2003; doi: 10.1161/01.CIR.0000111841.28126.D4

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2003 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/109/1/18

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