Transplantation and Thromboendarterectomy for Severe Pulmonary Hypertension: Report from the Transplant and Interventions Task Force

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Recent advances in medical and interventional approaches to the management of patients with pulmonary arterial hypertension (PAH) have had a marked effect on the policy toward referring such patients for transplantation and there has been a reduction of 50% in numbers of patients with primary pulmonary hypertension (PPH) undergoing transplantation over the last decade.[1] In practice patients are being referred at a later stage, often in decompensated right heart failure. Such patients present a major challenge to both peri- and postoperative management, with some centers identifying the need for elective ECMO support or at least prolonged ventilatory support. The prognosis of patients presenting with WHO class III and IV symptoms has been improved by both prostaglandin and endothelial antagonist therapy.[2-6] But not all patients show a significant response, so the concept of assessing a patient with advanced disease, listing when appropriate and de-listing if there was a significant response to medical therapy such that the patient improved to WHO class II on symptoms, was supported. The literature supports that transplant centers currently show wide variation in their approach to indications for and timing of lists. It is clear that close communication between PAH centers and transplantation centers is very appropriate.

The results of transplantation for patients with severe pulmonary hypertension (PH) as documented in the International Society for Heart and Lung Transplantation registry data are significantly less good than for patients with respiratory failure due to other causes. It was concluded that transplantation for patients with PH might be best limited to specialist transplant centers with specific interests and skills in treating such patients, rather than being offered by a transplant center, and that such an approach might best fulfill the needs of our patients. It was recognized that the problem of donor lung shortage had led to the need to use marginal lungs from older donors, and that this practice was a particular risk for patients with pulmonary vascular disease.

No true consensus was established with regard to the operation of choice for patients with PH. There was a broad body of literature supporting single lung, bilateral lung, and heart-lung procedures for these patients.[7-10] It was accepted that patients with Eisenmenger syndrome associated with complex congenital heart disease could not be repaired during an isolated lung transplantation procedure and required heart-lung transplantation. There was a trend to supporting the concept of transplanting two lungs rather than one in patients with advanced disease with established right heart failure. However, it was accepted that specialist centers would carry out whichever type of operation they felt was most appropriate for an individual case. It was also accepted that individual differences would occur given differences in thoracic organ allocation and availability.

The recent UNOS guidelines relating to organ allocation to patients with PH in the United States were discussed and it was felt that the proposed walking distance of 160 feet as an arbiter of clinical need and benefit regarding transplantation was too low and incompatible with satisfactory outcomes.

It was recognized that the development in molecular biology offered unrivaled opportunity to help understand underlying mechanisms leading to PPH and associated conditions and that lungs removed at transplantation offered an important resource for research. It was proposed that attempts should be made to ensure that all lungs removed at surgery should be stored in tissue banks and made available to the many individual laboratories worldwide to foster basic research in this area. It was regrettable that lungs from patients transplanted for PH were not systematically being stored. Finally, brief guidelines regarding referral and listing are summarized below.

- WHO class III patients with 6-minute walk distance >332 meters: Treat medically and refer for transplant if no clinical improvement over 3 months.[11]
- WHO class IV patients with 6-minute walk distance <352 meters: Assess and list immediately for transplantation, treat medically, and de-list if improvement over 3 months to class II. Deteriorating patients may be considered for septostomy as a bridge to transplantation.
- Hemodynamic markers of adverse outcome are right atrial pressure >15 mm Hg, cardiac index <2 L/min/m^2, and mixed venous oxygen saturation of ≤63%.

Thromboendarterectomy

There was a clear consensus that patients with PH due to chronic thromboembolic disease should be assessed for thromboendarterectomy and it was proposed that the name of this operation should be changed to pulmonary endarterectomy.[12-14] This suggestion was made because by the time of surgery no true thrombus remained. It was recognized that more experienced centers worldwide were carrying out successful surgery in patients with severe distal disease as well as proximal disease, a technically more challenging procedure.[15] Discussion concerned the presence of vasculopathy similar to that seen in PPH in the vessels of patients with chronic thromboembolic hypertension unaffected by previous thrombi. Mechanisms leading to

this vasculopathy are not understood at present but it did provide a rationale for consideration of medical therapy with prostaglandins and endothelial antagonists in some patients prior to definitive surgery.[16] The worldwide results of thromboendarterectomy are good, and prognosis and health-related quality of life in such patients are much improved by this operation.[14] ■

References

1. Hertz M, Taylor D, Trulock E, et al. The Registry of the International Society for Heart and Lung Transplantation: nineteenth official report – 2002. *J Heart Lung Transplant*. 2002;21:950-970.
2 Barst RJ, Rubin LJ, Long WA, et al. A comparison of continuous intravenous epoprostenol (prostacyclin) with conventional therapy for primary pulmonary hypertension. *N Engl J Med.* 1996;334:296-301.
3. Simonneau G, Barst RJ, Galie N, et al. Continuous subcutaneous infusion of treprostinil, a prostacyclin analogue, in patients with pulmonary arterial hypertension. *Am J Respir Crit Care Med*. 2002;162:800-804.
4. McLaughlin V, Shillington A, Rich S. Survival in primary pulmonary hypertension. The impact of epoprostenol therapy. *Circulation*. 2002; 106:1477-1482.
5. Sitbon O, Humbert M, Nunes H, et al. Long-term intravenous epoprostenol infusion in primary pulmonary hypertension. *J Am Coll Cardiol*. 2002;40:780-788.
6. Barst R, Rich S, Widlitz A, et al. Clinical efficacy of sitaxsentan, an endothelin-A receptor antagonist, in patients with pulmonary arterial hypertension. Open-label pilot study. *Chest*. 2002;121:1860-1868.
7. Pasque MK, Trulock EP, Kaiser LR, Cooper JD. Single-lung transplantation for pulmonary hypertension: three-month hemodynamic follow-up. *Circulation*. 1991;84:2275-2279.
8. Bando K, Armitage JM, Paradis IL, Keenan RJ, Hardesty RL, Konishi H, et al. Indications for and results of single, bilateral, and heart-lung transplantation for pulmonary hypertension. *J Thorac Cardiovasc Surg*. 1994; 108:1056-1065.
9. Gammie JS, Keenan RJ, Pham SM, McGrath MF, Hattler BG, Khosbin E, et al. Single- versus double-lung transplantation in pulmonary hypertension. *J Thorac Cardiovasc Surg*. 1998;115:397-403.
10. Waddell TK, Bennett L, Kennedy R, Todd TRJ, Keshavjee SH. Heart-lung or lung transplantation for Eisenmenger syndrome. *J Heart Lung Transplant*. 2002;21:731-737.
11. Miyamoto S, Nagaya N, Satoh T, Kyotani S, Sakamaki F, Fujita M, et al. Clinical correlates and prognostic significance of six-minute walk test in patients with primary pulmonary hypertension. *Am J Respir Crit Care Med.* 2000;161:487-492.
12. Jamieson SW, Kapelanski DP. Pulmonary endarterectomy. *Curr Probl Surg*. 2000;37:165-252.
13. Fedullo PF, Auger WR, Kerr KM, Rubin LJ. Chronic thromboembolic pulmonary hypertension. *N Engl J Med.* 2001;345:1465-1472.
14. Archibald CJ, Auger WR, Fedullo PF, et al. Long-term outcome after pulmonary thromboendarterectomy. *Am J Respir Crit Care Med*. 1999; 160:523-528.
15. ThistlethwaiteP A, Mo M, Madani MM, et al. Operative classification of thromboembolic disease determines outcome after pulmonary endarterectomy. *J Thorac Cardiovasc Surg*. 2002;124:1203-1211
15. Olschewski H, Simonneau G, Galie N, et al. Inhaled inoprost for severe pulmonary hypertension. *N Engl J Med.* 2002;347:322-329.
16. Kramm T, Mayer E, Dahm M, et al. Long-term results after thromboendarterectomy for chronic pulmonary embolism. *Eur J Cardiothorac Surg*. 1999;15:579-584.