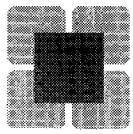

Lung transplantation is here to stay

The clinical development of heart-lung and lung transplantation over the past decade has opened a new era of surgical therapy for end-stage cardiopulmonary and pulmonary diseases which were formerly unresponsive to conventional medical and surgical management. Long-term survival in patients with lung transplants was virtually nonexistent until 1981.[1] The clinical successes of heart-lung, single-lung, and double-lung transplantation during the 1980s, and the recent successful transplantation of lung lobes in infants and young children (Starnes VA et al, unpublished observations) have changed the perception of lung transplantation from one of doubt to one offering real hope as a therapeutic modality. The indications, contraindications, and choice of operative procedures presented by McCarthy et al in this issue of the *Cleveland Clinic Journal of Medicine*[2] reflect the significant advances that have been made in the clinical evolution of lung transplantation over this period.

See McCarthy et al, p. 307

Although a great deal more needs to be learned about the procedure, lung transplantation should no longer be considered primarily as a research exercise or as an act of desperation for use in terminally ill patients. Lung transplantation is a viable therapeutic option for use in carefully selected patients with end-stage disease who have the capacity for full rehabilitation.

Lung transplantation may involve heart-lung, single-lung and double-lung transplants. Transplantation of lung lobes as replacements for a whole lung is the latest innovation and has particular application in children. Experience with this procedure is still quite limited, and, although the early results have been favorable, it is not yet in general use.

The choice of operation is primarily determined by the clinical disorder, but it may also be influenced by the surgeon's preference and by the allografts available for transplantation. In fact, the limited supply of donor organs has led to the development of new applications of lung transplantation that make optimal use of the available allografts.

The increase in heart transplantation limits the supply of heart-lung "blocks" available for transplantation. Thus, although single-lung transplantation is most useful in pulmonary fibrosis with essentially normal cardiac function,[3] newer innovations have seen its successful use in primary pulmonary hypertension,[4,5] in Eisenmenger's syndrome with concurrent repair of atrial septal defects,[4] and emphysema,[6,7] conditions which were previously believed to require replacement of heart and lungs or both lungs.

Conditions associated with chronic bronchial infections, such as cystic fibrosis and bronchiectasis, still require replacement of both lungs, and if the recipient's cardiac function is adequate, the choice of heart-lung or double-lung transplantation then becomes an issue of surgeon preference or allograft availability. In the former case, utilizing the recipient's heart for a "domino" heart transplant in conjunction with the heart-lung transplant permits benefit to two recipients from a single donor source.

When there is more than one transplant option, the patient's overall cardiac status and the functional reserve capacities of the ventricles (particularly the right ventricle) are key factors for determining transplant choice. Cardiac health is the primary determinant for deciding between heart-lung and lung transplantation. In choosing single-lung transplantation, particularly in primary and secondary forms of pulmonary hypertension, the degree of impairment and functional reserve of the right ventricle is critical (provided that left ventricular function and reserve are adequate). As shown by McCarthy et al and reported

by others,[8] right ventricular and overall cardiac function can have the functional reserve to fully recover following single-lung transplantation for pulmonary hypertension. The lower limit of right ventricular function that will allow full recovery has never been clearly defined, although right ventricular ejection fractions of greater than 20%, associated with left ventricular ejection fractions of greater than 35%, are considered to be the lower limits at present.[9] McCarthy et al note that a great deal more research is needed in this regard. In view of the risks associated with multiple cardiac catheterizations in pulmonary hypertension, Doppler echocardiography, radionuclide multiple gated acquisition scans at rest and exercise, and magnetic resonance imaging scans are useful noninvasive techniques for assessing cardiac function. In particular, magnetic resonance imaging techniques show unusual promise for studying cardiac dynamics.

Most of the complications in lung transplantation are similar in principle to those encountered in other forms of organ transplantation. Many of the complications associated with the surgery — rejection, infection, and the consequences of long-term immunosuppression — have been effectively addressed (though not completely resolved); this partly accounts for the recent significant improvements in long-term survival. New and improved surgical techniques, better patient management, improved surveillance for the early detection of rejection and infection (using serial bronchoscopies with transbronchial lung biopsy and pulmonary lavage, serial pulmonary function measurements, and other techniques), improvements in graft procurement and preservation, improved immunosuppression regimens, improved antimicrobial therapy, and better patient selection have all contributed to the improved outcomes.

Despite these advances, the development of severe obstructive airway disease from obliterative bronchiolitis remains an important clinical problem in lung transplantation. Obliterative bronchiolitis was initially described and has been more frequently reported in heart-lung transplantation, but it is also seen in single-lung transplantation. Some evidence suggests that obliterative bronchiolitis is a form of chronic rejection, but its precise cause remains unknown.[10] Early studies reported mean survivals of approximately 12 to 13 months after onset, with a downhill course that was usually resistent to most therapy.[11,12] The introduction of a three-drug immunosuppression regimen of cyclosporine, azathioprine, and prednisone resulted in clinical stabilization and prolonged survival in obliterative bronchiolitis.[13] This appears to be related to preserving adequate oxygenation despite severe mechanical abnormalities of lung function.[14] Recent experience reveals a reduction in the overall incidence of obliterative bronchiolitis and marked improvement in long-term survival in those who acquire it.[10,14,15]

All forms of lung transplantation lead to substantial clinical and functional improvement in long-term survivors. If the allografts remain free of infections and obliterative bronchiolitis, lung function may be maintained at essentially normal levels for years.[14] Even if these complications occur, function is usually adequate for normal activities.

Clinical comparisons of the relative benefits of heart-lung, double-lung, and single-lung transplantations are premature, since the total experience with these procedures is still relatively small. The experience with single- and double-lung transplantation has been significantly less than with heart-lung transplantation, although this will undoubtedly change in the near future. Data from transplant procedures in a variety of clinical conditions is needed to determine which operation is best suited for a given disorder. Since the choice of operations is governed to some extent by allograft availability, and with expanded use of single-lung transplantation in pulmonary hypertension and emphysema, such studies are needed to define the maximum benefits and limitations of each procedure.

Clinicians should no longer consider lung transplantation as a "last ditch" heroic measure, to be reserved exclusively for use in terminally ill patients. In fact, current experience indicates that in most cases such patients are the least desirable for undergoing transplantation. This is apparent from the selection criteria presented by McCarthy et al (which are in keeping with patient selection policies at centers throughout the country[9]). Desperate clinical situations do not in themselves constitute appropriate indications for heart-lung or lung transplantation: candidates for surgery must have the best chances for long-term rehabilitation.

Clinicians must now begin to consider transplantation sooner rather than later in the care of their patients. Long-term management plans should include it among future therapeutic options, if conventional therapy should fail. This will give patients every opportunity to consider transplantation as a viable option before clinical events preclude its use.

Lung transplantation in its various forms has come well beyond the laboratory, as the survival statistics

presented by McCarthy et al indicate. Although more basic and clinical research is needed, lung transplantation has arrived as a therapeutic modality for use in carefully selected patients—and is here to stay.

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