

Bilateral sequential lung transplantation for end stage septic lung disease

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Abstract

Background - Bilateral sequential lung transplantation (BSLT) has been widely adopted as an alternative to combined heart and lung transplantation for the management of end stage septic lung disease in many transplant centres.

Methods - A retrospective review was undertaken of the first 32 consecutive patients with septic lung disease to undergo BSLT at the Freeman Hospital.

Results - Between April 1988 and October 1994 32 patients underwent BSLT. Survival at 30 days was 85% and actuarial survival at one year was 70%. Improved pulmonary function was seen in all surviving patients.

Conclusion - BSLT for septic lung disease offers comparable survival to heart-lung transplantation, with excellent functional results. Long term results may be superior because the disadvantages of transplanting the heart are avoided.

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Keywords: lung transplantation, cystic fibrosis.

Heart-lung transplantation, originally introduced for Eisenmenger's syndrome,¹ has been successfully used for the treatment of septic lung disease with one year survival exceeding 70% and good functional results.² This technique results in the unnecessary placing of a denervated donor heart in a patient with no cardiac dysfunction and who, as a result, is exposed to the risks of accelerated coronary artery disease, the incidence of which can be as high as 12%.³ Bilateral sequential lung transplantation (BSLT), with hilar anastomoses, retains the innervated heart and reduces the risks of vagal damage and excessive mediastinal bleeding, and has been successfully used in patients with septic lung disease.^{4,5}

Methods

PATIENT SELECTION

150 patients with septic lung disease (119 with cystic fibrosis and 31 with other forms of bronchiectasis) were assessed for pulmonary transplantation between April 1988 and October 1994 at our institution. Patients were accepted for transplantation if they showed evidence of progressive respiratory failure with significant hypoxaemia and reduced exercise tolerance. The presence of multiresistant organisms (e.g. *Pseudomonas cepacia*) or bronchopulmonary aspergillosis did not preclude acceptance.

OPERATIVE TECHNIQUE

In our current technique the access is through

a "clam shell" incision. Cardiopulmonary bypass is routinely used during implantation of the second lung and often during implantation of both lungs. The donor bronchus is kept very short and the suture line is covered with donor and recipient peribronchial tissues.

Standard triple immunosuppression therapy consisting of cyclosporin, azathioprine, and steroids is used, together with equine antihuman thymocyte globulin for the first three days.

Results

Between April 1988 and October 1994 32 patients (19 women) of mean age 29 years (range 15-49) with end stage septic lung disease underwent BSLT.

The 30 day survival was 85% (figure). The causes of early death were donor organ failure in one patient, bronchial dehiscence in one patient, and sepsis in three patients. Two of these patients developed mediastinitis and grew *Staphylococcus aureus* and *Pseudomonas aeruginosa* respectively; the third sepsis-related death was due to uncontrollable *Pseudomonas cepacia* infection in the lung and pleural spaces. Actuarial survival at six months and one year were 78% and 70%, respectively. At two years the survival was 66%. There have been seven late deaths. In five patients death followed the development of obliterative bronchiolitis and, in another two, sepsis led to multiorgan failure and death.

There were 25 episodes of infection that required treatment within six months of transplantation. Major infective complications were mediastinitis in two patients, septicaemia in four patients, and disseminated nocardial infection in one patient.

Lymphoproliferative disease was seen in one patient. Histological appearances were of high grade non-Hodgkin's lymphoma of B cell type consistent with an Epstein-Barr virus driven lymphoproliferative disorder.

There were 23 episodes of rejection (grade A2 and above) treated in 27 patients within six months of transplantation. Obliterative bronchiolitis was diagnosed by transbronchial biopsy in five patients. There was relentless deterioration in all these patients and death within six months of diagnosis despite treatment.

Airway complications were seen in only two patients; ischaemic stenosis of the intermediate bronchus was successfully treated with serial dilatation and stenting in one, and bronchial dehiscence occurred in another patient who subsequently died.

All survivors showed marked improvement in pulmonary function. Mean (SD) PaO₂ measured on room air was 10.80 (0.92) kPa at one month after transplantation (p<0.01) compared

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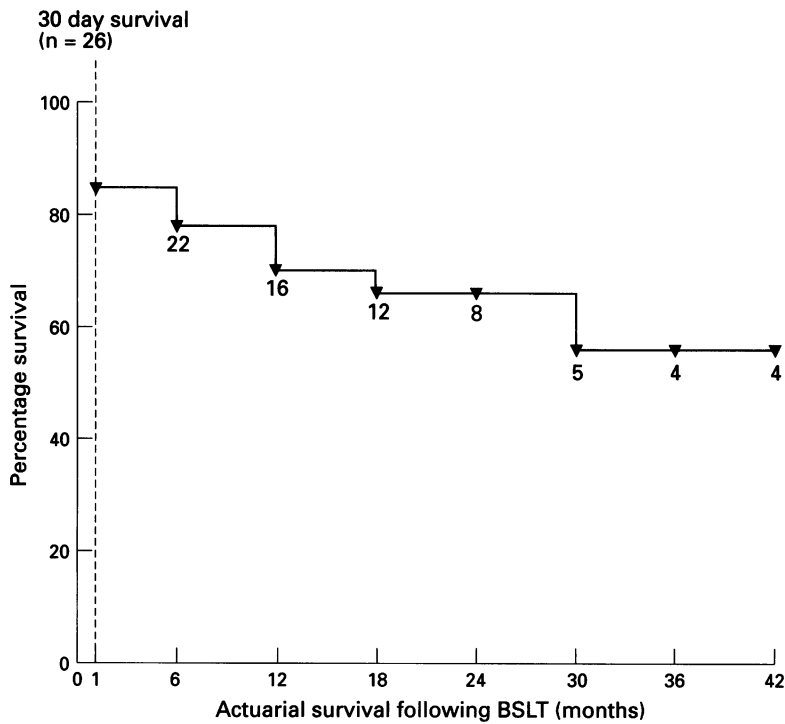
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Actuarial survival of patients undergoing bilateral sequential lung transplantation (BSLT) for end stage septic lung disease.

with a preoperative value of 7.40 kPa. Mean (SD) P_{CO_2} was 5.33 (0.77) kPa, a significant reduction from the preoperative value of 6.03 (1.05) ($p < 0.05$). There was similar improvement in the forced expiratory volume in one second (FEV_1) to 76 (13.7)% predicted at three months and 78 (18)% at six months following transplantation ($p < 0.01$) (preoperative value 22%). Exercise tolerance assessed by the six minute walking test also improved significantly from a preoperative value of 403 m to 620 (86) m at three months and 631 (107) m at six months ($p < 0.01$) with no desaturation.

Discussion

The choice of operative procedure for septic lung disease is limited. We have successfully used single lung transplantation with elective contemporaneous contralateral pneumonectomy in one patient whose anatomy precluded BSLT.⁶ However, the danger of recurrent or residual infective complications means that in most circumstances both lungs should be transplanted. Our current technique of BSLT, although similar to that of the Toronto and St Louis groups,⁷ has several novel aspects. Firstly, we routinely use cardiopulmonary bypass for implantation of the second lung and often during implantation of both lungs. Secondly, we have abandoned the routine use of omentopexy. This follows our experience with single lung transplantation where we encountered a low incidence of anastomotic complications in patients where omental wrap was not used. In only two patients did excessive bleeding result in re-exploration which compares favourably with results of heart-lung transplantation where incidence of re-exploration for bleeding can be as high as 28%.⁸

Airway complications have been remarkably low compared with other published series.^{4,5} We

attribute this low incidence of airway complications to the routine use of high dose steroids early in the perioperative period with possible resultant increased bronchial blood flow.⁹

Rejection and infection occurred frequently during the first month after transplantation and gradually decreased over six months. Infective complications were a major cause of mortality and morbidity during the first six months. Obliterative bronchiolitis remains a major problem in long term survivors following pulmonary transplantation.¹⁰ Five of our long term survivors have developed the condition and subsequently died due to progressive respiratory failure. Although some groups consider retransplantation for patients with end stage obliterative bronchiolitis, we believe the present results of this procedure do not justify such a course of action.¹¹

One potential advantage of BSLT over heart-lung transplantation is the preservation of autonomic cardiac innervation and possible functional consequences of cardiac denervation. Although Schaeffers *et al* concluded that cardiac denervation occurs after double lung transplantation,¹² we have shown that autonomic pathways remain intact after BSLT.¹³ This is due to minimal mediastinal dissection inherent in the technique of BSLT.

In conclusion, BSLT has evolved to become the operation of choice for patients with end stage septic lung disease. It provides a good early and intermediate survival with excellent functional results. Future challenges include the reduction of early morbidity and mortality from septic complications and prevention of the development of obliterative bronchiolitis.

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