Pediatric Lung Transplantation

PEDİATRİK AKCİĞER TRANSPLANTASYONU

Ömer SOYSAL*

* Department of Thoracic Cardiovascular Surgery, İnönü University, Medical Faculty, MALATYA

SUMMARY

There is limited experience in lung transplantation. The indications of lung transplantation in children are different when compared with adults. There are some special problems in pediatric lung transplantation such as donor shortage, size discrepancy, growth potential of transplanted lung and hemodynamic problems. Although some of these problems have been solved, only 2% of lung and heart-lung transplantation has been done in pediatric age group. Living related organ donation and lobar/segmental pulmonary transplantation may be options for donor shortage and size discrepancy and this area is the new and very promising part of pediatric lung transplantation.

Key Words: Lung transplantation, Lobar, Pediatric

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ÖZET

Akciğer transplantasyonu henüz yaygın kullanımda değildir. Akciğer transplantasyonu endikasyonları çocuklarda erişkinden farklıdır. Pediatrik akciğer transplantasyonunda; donor azlığı, büyüklük uygunsuzluğu, transplante edilen akciğerin büyüme geriliği ve hemodinamik bazı özel sorunlar vardır. Bu sorunların bir kısmı çözülmüş olmasına rağmen, günümüzde akciğer ve kalp-akciğer transplantasyonlarının sadece %2'sinin çocukluk yaş grubunda yapılabildiği de bir gerçektir. Verici azlığı sorunu canlı vericiler ile büyüklük uygunsuzluğu sorunu ise akciğer lob veya segment transplantasyonu ile çözülebilir. Canlıdan akciğer lobu transplantasyonu yeni ve çok ümit verici bir gelişmedir.

Anahtar Kelimeler: Akciğer transplantasyonu, Lob, Pediatrik

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Although heart-lung and lung transplantations have begun 10 years ago, thousands of patients have benefited from these interventions. It has become a clinical reality in adults due to advances in immunosuppression and organ preservation, improved bronchoplastic procedures and strict patient selection criteria (1). Nevertheless, improvement in the results with adult transplantation for end-stage pulmonary disease has led to application of these techniques to the pediatric population. Some forms of end-stage pulmonary vascular diseases in pediatric age group are different than those seen in adult age group, and it is necessary to provide the maintenance of lung function during growth in pediatric patients. Lobar pulmonary transplantation is an option which may solve the size discrepancy and donor shortage problems.

Single lung transplantation provides an attractive option for patients with obstructive lung disease instead of bilateral lung replacement. The method for bilateral sequential lung transplantation using an anterior transverse incision and often avoiding the need for cardiopulmonary bypass reduced the bronchial anastomotic complications (2).

Surgical mortality was only 8% in 130 single and bilateral transplants reported by Patterson (2). Operative mortality for single and double lung transplantation in Toronto group experience were 13 and 21%, respectively. The most important causes of early postoperative mortality in 388 patients reported by St.Louis International Registry were sepsis in 29% of patients, primary organ failure in 17% of patients (2). Overall actua-rial survival among patients registered in St.Louis International Transplant Registry was 60% in two years, 54% in three years. The most common causes of late mortality after one year in 128 patients were bronchiolitis obliterans and sepsis, 23% and 21% respectively (2).

INDICATIONS IN PEDIATRIC LUNG TRANSPLANTATION

The indications for lung transplantation are quite different in children compared with adults. Primary indications for heart-lung transplantation in children are congenital heart disease 46% (including secondary pulmonary hypertension and Eisenmenger's syndrome), pri-

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Correspondence: Ömer SOYSAL
İnönü Universitesi Tıp Fakültesi
Araştırma Hastanesi
Göğüs Kalp Damar Cerrahisi ABD,
MALATYA

Table 1. Heart-lung transplantation: indications

	Pediatric (%)	Adult (%)
Congenital heart disease	46	27.8
Primary pulmonary hypertension	19	28.5
Cystic fibrosis	18	16.7
Other pulmonary disease	7	24.0
Retransplantation	9	3.0

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Table 2. Bilateral lung transplantation: indications

	Pediatric (%)	Adult (%)
Cystic fibrosis	61.2	37.9
Primary pulmonary hypertension	12.2	7.1
Congenital heart disease	6.1	4.2
Idiopathic pulmonary fibrosis	-	6.2
Emphysema	-	30.6
Retransplantation	8.2	4.2

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mary pulmonary hypertension 19%, cystic fibrosis 18%. For bilateral lung transplantation, cystic fibrosis 61.2%, primary pulmonary hypertension 12.2%, congenital heart disease 6.1% are the major indications (3). Table 1 lists the indications for heart-lung and Table 2 for bilateral lung transplantation, and compares these indications with those seen in the adults population. Single lung transplantation has been performed for primary pulmonary hypertension, congenital pulmonary abnormalities and pulmonary fibrosis.

TECHNIQUES IN PEDIATRIC LUNG TRANSPLANTATION

Surgical management of the bronchial anastomosis shows variation in different centers. The very tenuous nature of the omentum in pediatric patients has led to abandonment of its use in bronchial wrapping. According to the physicians in St.Louis Children's Hospital, it is unclear that the technique of bronchial anastomosis alters the incidence or severity of bronchial complications and they have tended to use absorbable suture for the anastomoses in children in hope of encouraging better growth of the suture line (4). Some have reported excellent succes by intussuscepting the donor bronchus into the recipient bronchus (5). As in adults, the technique of double sequential lung transplantation has dramatically decreased the incidence of airway complication (6). The bronchial anastomoses in very small children and infants may have a propensity to develop stenosis or disruption which requires stant placement.

Cardiopulmonary by-pass appears to be more uniformly required to achieve safe transplantation in pediatric age group. Cardiopulmonary support with by-pass has eliminated the need for double-lumen endotracheal tubes or bronchial blockers. Furthermore cardiopulmonary bypass can not be confidently instituted through the femoral route in children, because femoral artery and vein are often small in children and may not provide a-dequate flow. Therefore, it has been elected to use a bilateral transverse thoracotomy incision with take-down of the anterior pericardium as pedicles for bronchial wrapping (4). By means of by-pass, cardiopulmonary depression while clamping the left atrium has been prevented and this approach permits removal of both lungs prior to suturing the donor lungs in place, thus preventing contamination of the transplanted lung in cystic fibrosis patients.

TYPE OF TRANSPLANTATION

It is clear than there is little advantage to heart-lung over lung transplantation for most patients who have a heart that is otherwise normal or correctable. Organ shortage and development of coronary artery disease in the transplanted heart are the handicaps of heart transplantation. Therefore for the patients who do not have significant left ventricular dysfunction, it is possible to expand the use of lung transplantation with cardiac repair to more complicated forms of congenital heart disease.

Bilateral sequential lung transplantation is a preferred technique to single lung transplantation in situations where chronic infection of the lungs is present such as cystic fibrosis. Also in adult respiratory distress syndrome, since there would be a significant ventilation perfusion mismatch after single lung transplantation, bilateral lung transplantation would be required in the majority of these patients.

Controversy remains regarding the use of single lung transplantation for pulmonary hypertension. It is known that pulmonary vascular resistance in the transplanted lung is low enough to receive the entire cardiac output and a rapid drop in pulmonary artery pressure is observed. But these patients may be hemodynamically unstable after transplantation and should be handled very carefully and closely. Although the long-term results of single lung transplantation for pulmonary hypertension is not well-known, the results reported by the International Lung Transplant Registry show similar one year actuarial survival for single or bilateral lung transplantation in pulmonary hypertension (4).

There were totally 54 bilateral single lung, 46 heart-lung, 30 single lung and 3 en bloc bilateral lung transplants in the pediatric age group that surveyed until February 1994 (7).

IMMUNOSUPRESSION

Concerning with organ antigenicity, the skin and the lung are believed to be the two most difficult organs for transplantation (8). Almost every adult lung recipient goes two or three major rejection episode in the first three weeks of transplantation. Most pediatric recipients of lung or heart-lung allografts receive immunosuppressive therapy consisting of cyclosporin A, azathioprine and prednizone. In addition 62% of patients also receive anti-lymphocyte therapy as a part of their immunosuppressive management (7). Concern over growth and devel-

opment has led some centers to try transplant immunosuppression protocols that avoid corticosteroids in children. Since obliterative bronchiolitis which means chronic rejection is an important cause of death in long term outcome after lung transplantation, immunosuppressive management should be balanced to avoid this terrible result but not to cause lymphoproliferative disorders and retardation of growth. The incidence of posttransplant lymphoproliferative disorders is 6.7% among 120 survivors of lung or heart-lung transplants in pediatric age group (7). Lymphoproliferative disease is associated with Epstein-Barr virus infection which often res-ponds to antiviral therapy and reducing immunosuppression (9).

RETRANSPLANTATION

Although the number of patients is small, retransplantation in pediatric heart-lung and lung transplantation is almost twofold of adults (3). In addition, mortality rate of retransplant pulmonary operations is very high (4,10).

Bronchiolitis obliterans remains a significant complication of single and bilateral sequential lung transplantation, affecting nearly 40% of surviving patients (11). Spirometry has been used to screen for bronchiolitis obliterans. If FEV_1 drops under 15% of predicted value permanently, the patients should be evaluated with computed tomography, bronchoscopy and transbronchial biopsy. If histological findings are not conclusive, an open lung biopsy should be performed (24).

CARDIOPULMONARY BYPASS DURING LUNG TRANSPLANTATION

It is essential to have cardiopulmonary bypass capability on a standby basis in all operations for lung transplantation. Generally, other than recipients with pulmonary hypertension, single lung recipients seldomly require by-pass, in adults (12). By-pass should be used for all patients with end-stage pulmonary hypertension to protect the right ventricle from the abrupt increase in afterload resulting from pulmonary artery clamping (12). In more than half of these patients, the reason for by-pass was donor lung dysfunction which was the tissue damage from the reperfusion of the lung after ischemia (13). To avoid the use of double-lumen endotracheal tubes or bronchial blockers and insufficiency of one lung anesthesia in small children have led the use of cardiopulmonary by-pass more often in pediatric lung transplantation than adults.

EXTRACORPOREAL MEMBRANE OXIGENATOR (ECMO)

Recently, ECMO has achieved remarkable success in treating reversible forms of neonatal respiratory failure such as meconium aspiration and severe pneumonia (14). A potentially large group of patients who might benefit from lobar transplantation are infants who have congenital diaphragnatic hernia. ECMO can provide temporary neonatal cardiopulmonary support and serves as a bridge to lung transplantation in very sick diaphragmatic hernia babies. It permits time to find a donor. ECMO can provide temporary support to the transplanted lung during the transient postoperative period of pulmonary dysfunction due to reimplantation response. If the baby is hemodynamically stable, ECMO can also be used to give a period of lung rest which would permit adequate bronchial healing (15). Although ECMO has significant neurological and bleeding complications, successful transplantations were performed in babies with congenital diaphragmatic hernia (16) and also in adults on ECMO (17).

LOBAR TRANSPLANTATION

As recipient lists for patients needing lung transplantation continue to grow, available donors remain static (18). The lack of donor organs is the major limitation preventing wide spread application of this life-saving therapy. As many as 87% of patients accepted for lung transplantation die while waiting for an appropriate lung donor (19). Only 10% to 15% of donors have lungs suitable for transplantation (20). The average waiting period in adult series for lung transplantation ranged from 90 to 150 days (21). So, donor shortage is one of the important obstacle of pediatric lung transplantation. Three options now exist for the pediatric patient in need of lung transplantation. The use of size-matched immature organs is the technique most commonly employed for pediatric lung transplantation as the first option. The alternative to the use of pediatric cadaveric lung allografts is the use of reduced-size cadaveric lung transplants in which a lobe or segment of an adult lung is sculpted to fit the recipient's chest (22). Pediatric lung transplant patients have not yet survived long enough to make a decision on the best transplant method. Third option is living-related lobar transplantation.

Cadaveric or living-related donation of a reduced size lung (lobe or segment) may solve the donor shortage problem for pediatric lung transplantation. The use of a pulmonary lobe may also improve the size discrepancy problem and probably permit multiple lung transplants from a single donor. Finally, living-related lobar transplantation has the potential immunological and preservation advantages (22). The use of living donor lungs has many appealing features: increased donor pool, elective timing, short ischemic time, a normal lung, available anytime, daytime operation, more favorable tissue matching. But there have been many anatomic, technical, physiological and immunological problems in pulmonary lobar transplantation.

RESULTS OF PEDIATRIC LUNG TRANSPLANTATION

Five year actuarial survival after heart-lung transplantation is approximately 40% in pediatric group, 45% in adults (23). One year survival rate has been 70% with a two year survival rate of approximately 40% to 50% when either transplantation technique is used (24). Although these results are encouraging, they are slightly lower than adults. In an adult series of lung transplantation with 15 patients who had emphysema and under-

went lung transplantation (one bilateral, 14 single), one year actuarial survival rate was 93.3%. Survival rates are actually influenced by the primary disease requiring transplantation as well as the transplantation technique. The procedures more often require the employment of cardiopulmonary by-pass for safe extubation. The results are better in fibrosis and emphysema groups, and also in bilateral single lung transplantation group. Actual one year survival in en bloc bilateral lung transplantation is 57% but it is 84% in bilateral single lung transplantation (23). Infection and obliterative bronchiolitis are the major life-threatening complications following transplantation in this patient group.

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