Lobar Pulmonary Transplantation

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There is limited experience in lung transplantation. The indications of lung transplantation in children are different 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 hearth-lung transplantation has been done in pediatric patients. 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. [Journal of Turgut Özal Medical Center 1996;3(2):137-142]

Key Words: *Lung transplantation, lobar, pediatric*

Pulmoner lob transplantasyonu

Akciğer transplantasyonunda deneyim birikimi azdır. Çocuklarda akciğer transplantasyonu endikasyonları erişkinlerden farklıdır. Verici azlığı, büyüklük uyumsuzluğu, transplante edilen akciğerin büyüme potansiyeli ve hemodinamik sorunlar gibi bazı özel sorunlar pediatrik akciğer tranplantasyonunun zorluklarıdır. Bu sorunların bir kısmının çözülmüş olmasına rağmen, hala ancak akciğer ve kalp-akciğer transplantasyonlarının sadece % 2'si çocuklarda yapılmış bulunmaktadır. Canlı organ vericisi ve lobar/segmental akciğer transplantasyonu pediatrik akciğer transplantasyonlarında verici azlığı ve büyüklük uyumsuzluğu sorunları için seçenek olabilir. Canlıdan pulmoner lob transpantasyonu pediatrik akciğer transplantasyonu sahasında yeni ve çok ümit verici bir gelişmedir. [Turgut Özal Tıp Merkezi Dergisi 1996;3(2):137-142]

Anahtar Kelimeler: *Akciğer transplantasyonu, lob, pediatrik*

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. Nevertheless, improvement in the results with adult transplantation for end-stage pulmonary disease has led to application of these techniques to the pediatric population. Children have different forms of end-stage pulmonary vascular disease than adults, and it is necessary to provide maintenance of adequate lung function during growth in pediatric patients. Indications for pediatric lung transplantation are shown in Table 1. Lobar pulmonary transplantation is an option which may solve the size discrepancy and donor shortage problems.

As recipient lists for patients needing lung transplantation continue to grow, available donors remain static. 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 (1). Only 10% to 15% of donors have lungs suitable for transplantation (2). The average waiting period in

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adult series for lung transplantation ranged from 90 to 150 days (3). 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 (4). Third option is living related lobar transplantation. Pediatric lung transplant patients have not yet survived long enough to make a decision on the best transplant method.

Table 1. Indications for pediatric lung transplantation

Pulmonary fibrosis
Unusual interstitial fibrosis
Desquamative interstitial fibrosis
Pulmonary alveolar proteinosis
Idiopathic pulmonary alveolar microlithiasis
Cystic fibrosis
Radiation-induced pulmonary fibrosis
Obliterative bronchiolitis
Bronchopulmonary dysplasia
Pulmonary vascular disease
Primary pulmonary hypertension
Pulmonary hypertension after corrected congenital heart disease
Pulmonary hypertension and correctable congenital heart disease (Eisenmenger's syndrome)
Inadequate pulmonary vascular bed
Pulmonary atresia
Ventricular septal defect
No central pulmonary arteries
Congenital diaphragmatic hernia

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 (4). 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.

Which lobe is appropriate?

Each lobe of lung has been used in both animals and human beings. Concerning the appropriate lobe or segment, it must be small enough to fill into the neonatal (the child's) hemithorax, arterial supply should be from one or at the most two, venous outflow must have adequate length and width, the bronchus must be suitable for anastomosis. From the cadaveric dissections, right middle lobe was found as the most appropriate lobe. Since two segments of middle lobe have separately useable artery, vein and bronchus, each segment of middle lobe can be transplanted by itself. It is reported that either the right middle lobe or its anterior segment provides the most favorable size and hilar anatomy and is technically feasible both in the pig and human neonates (5).

Neonatal lambs underwent successful left lung transplantation from unrelated adult sheep donors. The left upper lobe was used in two recipients, and the right upper lobe in six. Implantation of upper lobes to the left chest was performed by left thoracotomy. Preservation of maximal pulmonary artery and venous length during the native pneumonectomy was important to allow matching of the vascular cuffs. The donor lobar bronchial cuff was also kept short to permit collateral circulation from the lung parenchyma. The lobes were contoured to the dimensions of the recipient hemithorax using a linear stapler. At postmortem examination, all bronchial anastomoses, arterial and venous anastomoses were patent (6).

Another important group of pediatric patients waiting for lung transplantation is cystic fibrosis. Bilateral single lung transplantation is now the most commonly used type of transplantation in infected end-stage pulmonary disease (7). Nowadays, 65% to 80% of patients suffering from cystic fibrosis survive for more than 15 years and reach a normal height with current medical treatment. Complication rate of bronchial anastomosis is lower than tracheal anastomosis, and in a canine model, bronchial healing is better with two lobar anastomoses than with a single anastomosis performed on the left main stem bronchus (8). Because of these reasons, bilateral lobar transplantations were performed (left lower lobe plus right middle for the first and lower lobes for the second) in two patients with cystic fibrosis

successfully (9). The lobes can be selected on the basis of size match of the lobe to the child's chest on computed tomographic calculations (10).

Hemodynamic changes after lobar transplantation

The effects of chronic denervation of pulmonary vasculature are not well understood. After denervation (left pneumonectomy plus reimplantation of left lower lobe) no changes in baseline pulmonary artery pressure, pulmonary capillary wedge pressure, cardiac output and pulmonary vascular resistance were observed. But after clamping the right hilum, significantly higher pulmonary artery pressure and pulmonary vascular resistance were measured in the group with reimplanted left lower lobe than the other groups who had innervated lung or lobe. This may be the result of chronic denervation and receptor upregulation (11).

In a study that compared the relationship between segmental blood flow and segmental vascular resistance of the pulmonary lobe with that of the transplanted lung, segmental blood flow of the lung decreased in the early postoperative period but returned to the pretransplantation level in two postoperative weeks in both lobar and whole lung transplant groups. The same result was also obtained for segmental vascular resistance. There was no significant difference in the segmental vascular resistance in any segmental flow between pulmonary lobe and single lung before and after transplantation (12).

Unilateral pulmonary artery occlusion in adult animals characteristically results in a marked fall in the pulmonary vascular resistance secondary to vasodilatation (13). But in neonatal swine this manipulation resulted in a dramatic rise in pulmonary vascular resistance and pulmonary artery pressure with a fall in cardiac output (14). The response of the left lower lobe transplant to conditions simulating congenital diaphragmatic hernia , by occlusion of the right pulmonary artery was similar and demonstrated a dramatic rise in pulmonary vascular resistance and pulmonary artery pressure with decreased cardiac output. This response explains the inability of the denervated lobar graft to modulate pulmonary vascular resistance to accommodate increased blood flow (15). This event is reversible and rarely clinically significant (16).

Harvesting a lobar graft from a mature donor and transplantation into a neonatal swine recipient is technically feasible. Use of the recipient's left atrial appendage for venous anastomosis is technically easier and hemodynamically well tolerated. After implantation of mature lobe to the place of neonatal left lung, there was no increase in pulmonary arterial pressure and left atrial pressure, but only a 15% increase in pulmonary vascular resistance and a 23% decrease in cardiac output (4).

Unlike adult transplant recipients, pediatric transplant patients will undergo significant growth and development after transplantation. So transplanted lung function must be sufficient to support the growing recipient. The development of mature lobes has been completed in adult lungs but this is not the case in immature lobes. Dynamic airway resistance which reflects small airway obstruction is normal in transplanted mature lobes when compared with immature whole lung (17). This is likely due to the more developed pulmonary vascular bed in the lobar graft.

Pulmonary function studies demonstrate a decrease in lung volumes that result in a restrictive ventilatory defect after lung transplantation (18). The most common late finding has been that of bronchiolitis obliterans with the imposition of a progressive restrictive ventilatory defect (19). Bronchiolitis obliterans may be due to small airway obstruction related to denervation (20).

Living-related lobar lung transplantation from an adult beagle into a pneumonectomized puppy is technically feasible and the gas exchange of the transplanted lobe could provide complete respiratory support. But at follow-up study, when right hilum was clamped, an increase in pulmonary vascular resistance was observed (21). Many authors report a high pulmonary vascular resistance in transplanted or reimplanted lungs , probably due to an inability of the denervated lung to vasodilate appropriately (11,13). In clinical single lung or lobar transplantation, contralateral lung will always be abnormal. Functional differences that exist after denervation of the immature as compared with the mature lung are related to the degree of pulmonary maturation at

the time of denervation or transplantation (22). In the normally innervated, healthy pulmonary vascular bed, an increase in flow results in capillary recruitment with a resultant decrease in pulmonary vascular resistance and maintenance of pulmonary pressure (23). Denervated immature pulmonary vasculature seems not to have this physiologic response, whereas denervated mature pulmonary vasculature has. So, transplantation of mature lung tissue may be functionally superior to immature allografts (22).

Growth potential of transplanted lobe

Immature rat lung will continue to grow after being transplanted. That growth includes new alveolar formation, increase in size of existing ones, increase of diameter of bronchie (24). The difficulties of extrapolating from one species to another are fully recognized, but one might hope that this would be also true for an immature transplanted human lung. Denervation alone led to generally normal growth in transplanted lung (24). These results are very important for neonates as well as children under the age three, because alveolar multiplication continues until at least four years of age (25), and alveoli and airways continue to increase in size until adulthood while the thoracic cage grows (26).

After domestic pig single lung transplantation, the growth is retarded. The animals in study group doubled their body weight in 11 weeks compared with only six weeks for control pigs without transplantation. This is assumed to be the effect of immunosuppression used after transplantation (27). There was not any differences in the growth of the bronchial tree and pulmonary artery system between controls and the recipients of pulmonary allografts. Lung growth was suggested by an increase in the pulmonary arterial and bronchial dimensions as measured by angiography and bronchography. The same study also showed that absorbable suture material can be safely used when transplanting pulmonary allografts in growing animals (27). It is very important for children to allow adequate growth of the airway anastomosis and vascular suture lines.

Autotransplantation of left lung in baboons was performed. Denervation was the issue but not the immunosuppression and rejection in this model. Lung volume measurements were done by nitrogen washout, computed tomography and at autopsy, by volume displacement in the five weeks and seven months of transplantation. It has been demonstrated that, normal volume growth is possible in infant primate lung after the transplantation, in the absence of such factors as chronic immunosuppression and rejection (28).

Transplanted mature lobes increased in size as determined by gross weight and fixed lung volume, but no increase in functional residual capacity in a porcine model. This indicated that transplanted mature lobes most likely grew through an increase in connective tissue and cellular components of the lung parenchyma and not through an increase in alveolar number (29).

Living-related lobar lung transplantation

Donor evaluation and selection for living related transplantation involves careful assessment of both psychosocial and physiologic factors. Donors must be in an excellent health condition without factors that might increase the risk of donor operation. Anatomically, left lower lobe is favorable, while considering living related lobar transplantation. Left lower for left side, right lower lobe alone or right lower lobe and middle lobe together for the right chest were used in seven patients with cystic fibrosis. Each transplant patient received one lobe from first donor, one lobe from the second donor. Most of the donors were the patients' parents. Standard lobectomy techniques were modified to facilitate implantation and optimize preservation of the donor lobes. Donor left and right lower lobectomies for living-related bilateral lobar transplantation provide a source of donor lungs for selected patients in need of bilateral lung transplantation (30).

Unilateral lung transplantation has provided effective short-term therapy in adults with end-stage pulmonary disease. In need of single lung transplantation, living-related lobar transplantation from an adult into a pneumonectomized child is technically feasible, as demonstrated in dogs (21).

The respiratory function of the implanted lobe was studied by angiography. After pulmonary arteriogram was performed, the catheter was advanced into the right pulmonary artery and inflated. That dog survived for two days with all respiratory function provided by the left lower lobe transplant. This was shown in two animals that the

gas exchange of the transplanted lobe was sufficient to provide complete respiratory support of the animal (21).

Lung transplantation has become an effective therapy in the adults with end-stage pulmonary disease in last decade. Recent experience with lung transplantation in the pediatric age group offers new hope for neonates, infants and children. Lung transplantation can be performed with acceptable early results. Due to the critical donor shortage, living-related lobar transplantations should be put in progress in both animals and humans. Lower lobes are favored because of the more constant relations and favorable anatomy of the structures at the pedicle. Hemodynamic variables are not changed significantly after lobar transplantation. Lobar graft, since it is always denervated, is not able to modulate pulmonary vascular resistance to accommodate increased blood flow, but this reversible and not significant clinically.

Dynamic airway resistance which reflects small airway obstruction is higher in immature lobar transplants, that may be the reason of bronchiolitis obliterans. Immature pulmonary vasculature does not have the ability to vasodilate to accommodate increased blood flow, whereas mature pulmonary vasculature has. Therefore transplantation of mature lobe tissue may be functionally superior to immature allografts.

Growth potential of transplanted lobe is controversial, and needs to be examined in new experimental studies. Cardiopulmonary bypass may be required in any pulmonary transplant procedure. ECMO can be used as a bridge to lung transplantation, and in posttransplant period, to restore hemodynamic stability and to permit adequate bronchial healing. These are specially the case in children. 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 area of pediatric lung transplantation.

REFERENCES

1. Veith FJ. Lung transplantation in perspective (editorial). N Engl J Med 1987; 314: 1186-7.
2. Harjula A, Baldwin JC, Starns VA. Proper donor selection for heart-lung transplantation. J Thorac Cardiovasc Surg 1987; 94: 874-80.
3. Bolman RM, Shumway SJ, Estrin JA. Lung and heart-lung transplantation. Ann Thorac Surg 1991; 43: 585-90.
4. Crombleholme TM, Adzick NS, Longaker MT. Reduced-size lung transplantation in neonatel swine: technique and short-term physiological response. Ann Thorac Surg 1990; 49: 55-60.
5. Jennings RW, Lorenz HP, Duncan BW, Bradley SM. Adult-to-neonate lung transplantation: anatomic considerations. J Pediatr Surg 1992; 27: 1285-90.
6. Lillehei CW, Everts E, Shamberger, RC. Reduced-size lung transplantation from adult to neonatal sheep. J Pediatr Surg 1992; 27: 1153-6.
7. Bisson A, Bonnette P. A new technique for double-lung transplantation: bilateral single lung transplantation. J Thorac Cardiovasc Surg 1992; 103: 40-6.
8. Pinsker KL, Koerner SK, Kamholz SL, Hagstrom JWC. Effect of donor bronchial length on healing. A canine model to evaluate bronchial anastomotic problems in lung transplantation. J Thorac Cardiovasc Surg 1979; 77: 669-73.
9. Bisson A, Bonnette P, Kadi NBE, Leroy M, Colchen A. Ann Thorac Surg 1994; 57: 219-21.
10. Starns VA, Lewiston NJ, Likart H, Theodore J. Current trends in lung transplantation: lobar transplantation and expanded use of single lungs. J Thorac Cardiovasc Surg 1992;104: 1060-6.
11. Johnson AM, Teague WG, Flanagan TL, MgGahren ED. Decreased vascular compliance after reimplantation of the lower lobe in young pigs. Ann Thorac Surg 1990; 50: 277-80.
12. Kitamura M, Starns VA, Tagusari O, Akimoto T. Segmental flow-resistance relationship in pulmonary lobar tranplantation: possibility for donor lobe evaluation in pediatric lung transplantation. J Heart Lung Transplant 1994; 13: 319-24.
13. Allgood RJ, Ebert PA, Sabiston DC. Immediate changes in pulmonary hemodynamics following lung autotransplantation. Ann Surg 1968; 167: 352-8.
14. Crombleholme TM, Adzick S, Hardy K Pulmonary lobar transplantation in neonatel swine: a model for treatment of congenital diaphragmatic hernia. J Pediatr Surg 1990;25:11-8.
15. Ebert PA, Allgood RJ, Jones HW III. Hemodynamics during pulmonary artery occlusion. Surgery 1969; 62: 18-24.
16. Daikoff GR, Allen PD, Streck CJ. Pulmonary vascular resistance following lung reimplantation and transplantation. Ann Thorac Surg 1970; 9: 569-79.
17. Kern JA, Tribble CG, Zografakis JG, Cassada DC. Analysis of airway function of immature whole lung transplants versus mature lobar transplants. Ann Thorac Surg 1994; 57: 1089-94.
18. Copeland JG. Heart-lung transplantation: current status. Ann Thorac Surg 1987; 43: 2-3.
19. Burke CM, Theodore J, Dawkins KD. Posttransplant obliterative brochiolitis and other late lung sequelae in human heart-lung transplantation. Chest 1984; 86: 824-9.

20. McGahren E, Teague WG, Flanagan TL. Airway obstruction after autologous reimplantation of the porcine lobe. J Thorac Cardiovasc Surg 1989; 97: 587-92.

21. Backer CL, Ohtake S, Zales VR, LoCicero III. Living-related lobar lung transplantation in beagle puppies. J Pediatr Surg 1991; 26: 429-33.

22. Kern JA, Tribble CG, Chan BBK, Flanagan TL. Reduced-size porcine lung transplantation: long-term studies of pulmonary vascular resistance. Ann Thorac Surg 1992; 53: 583-9.

23. Fishman AP. Dynamics of the pulmonary circulation, In: Dow P (ed.), Handbook of physiology, circulation. Vol. 2. Washington, DC, American Physiologic Society, 1963: 1667-743.

24. Hislop AA, Odom NJ, McGregor CGA, Haworth SG. Growth potential of the immature transplanted lung: an experimental study. J Thorac Cardiovasc Surg 1990; 100: 360-70.

25. Thurlbeck WM. Postnatal human lung growth. Thorax 1982; 37: 564-71.

26. Davies G, Reid L. Growth of the alveoli and pulmonary arteries in childhood. Thorax 1970; 35: 669-81.

27. Haverich A, Dammenhayn L, Demertzis S, Kemnitz J, Reimers P. Lung growth after experimental transplantation. J Heart Lung Transplant 1991; 10: 288-95.

28. Thomas DD, Standaert TA, Anton WR. Growth potential of the transplanted lung in the infant primate. Ann Thorac Surg 1993; 56: 1274-8.

29. Kern JA, Tribble CG, Flanagan TL. Growth potential of the porcine reduced-size mature pulmonary lobar transplants. J Thorac Cardiovasc Surg 1992; 104: 1329-32.

30. Cohen RG, Barr ML, Schenkel FA, DeMeester TR. Living-related donor lobectomy for bilateral lobar transplantation in patients with cystic fibrosis. Ann Thorac Surg 1994; 57: 1423-8.

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