American Journal of Transplantation 2004; 4: 1283–1288
Blackwell Munksgaard

doi: 10.1111/j.1600-6143.2004.00514.x

A Decade of Living Lobar Lung Transplantation: Perioperative Complications after 253 Donor Lobectomies†

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Living lobar lung transplantation places two donors at risk for each recipient. We examined the perioperative outcomes associated with the 253 donor lobectomies performed at our institution during our first decade of living lobar lung transplantation. There have been no perioperative or long-term deaths. 80.2% of donors (n = 203) had no perioperative complications, while fifty (19.8%) had one or more complication. The incidence of intraoperative complications was 3.6%. Complications requiring reoperation occurred in 3.2% of donors. 15.0% of donors had other perioperative complications; the most serious were two donors who developed pulmonary artery thrombosis, while the most common was the need for an additional thoracostomy tube or a thoracostomy tube for $\geq$14 d for persistent air leaks and/or drainage. Right-sided donors were more likely to have a perioperative complication than left-sided donors (odd ratio 2.02, p = 0.04), probably secondary to right lower and middle lobe anatomy. This experience has shown donor lobectomy to be associated with a relatively low morbidity and no mortality, and is important if this procedure is to be considered an option at more pulmonary transplant centers, given continued organ shortages and differences in philosophical and ethical acceptance of live organ donors.

Key words: Donor lobectomy, living donor, lung transplantation, outcomes

†Read at the 29th Annual Meeting of The Western Thoracic Surgical Association, Carlsbad, CA, USA June 18–21, 2003.

Received 17 November 2003, revised and accepted for publication 31 March 2004

Introduction

Continued and increasing organ shortages and long waiting times have led to the development of live organ donor programs for end-stage kidney, liver, and pulmonary disease (1–4). The use of living donors for kidney transplantation continues to increase, due to superior graft and patient survival as compared with cadaveric donors and now accounts for more than 50% of kidney transplants performed each year (2,5). The use of living donors for liver transplantation has also increased dramatically – with 35% growth in the most recent year, and 42% growth from 1996 to 2001 (2). Although the use of live organ donors is considered ethically acceptable at most transplant centers, it creates the unique situation whereby the treatment approach affects not only the patient with end-stage organ disease, but also the live organ donor (1). The recent deaths of both liver and kidney donors has highlighted this issue and brought increased public attention to live organ donation (6).

Living lobar lung transplantation was developed in response to the mismatch between supply and demand for those individuals awaiting lung transplantation (7). While accounting for only a small fraction of lung transplants, this technique has proven itself to be beneficial to a select group of patients who would have either become unsuitable for transplantation or succumbed to disease while awaiting a cadaveric organ (7–11). The need for donor safety is accentuated with this technique due to the necessity of placing two donors at risk for each recipient. Although a small series of complications associated with donor lobectomies has been reported, no large series have been published (12). In this report, we examined the perioperative outcomes and complications after 253 donor lobectomies during our first decade of living lobar lung transplantation.

Patients and Methods

Between January 1993 and December 2002, inclusive, a total of 253 donor lobectomies were performed at the University of Southern California University Hospital for use in 128 living lobar lung transplants in 123 recipients.

The 253 donors constitute the cohort of patients for this outcomes analysis. This study was approved by the Institutional Review Board of the University of Southern California Keck School of Medicine (#029026).

Donor selection

Appropriate donor selection is vital to success in living lobar lung transplantation. The donor selection process is designed to identify donors with excellent health, adequate pulmonary reserve (minimum forced vital capacity and forced expiratory volume in 1 s greater than 85% predicted and arterial oxygen content greater than 80 mmHg on room air), an emotional attachment to the recipient, and a willingness to accept the risks of donation without coercion.

The details of donor selection have been described previously (13,14). Absolute criteria include an age between 18 and 55, no history of thoracic procedures on the side to be donated, and excellent general health. Briefly, the process begins with an initial screening of potential donors for these criteria, as well as a psychosocial evaluation of their desire to donate. Suitable potential donors then undergo blood typing, chest radiography, and spirometry to assess lung size and function. Preference is given to donors larger than the recipient. A more complete medical evaluation is then conducted if this preliminary screening is found to be acceptable which include transplant serologies (HIV, RPR, CMV, EBV, hepatitis), electrocardiogram, echocardiography, stress test if over 40 years of age, formal pulmonary function testing, high-resolution chest computed tomography, and a quantitative ventilation-perfusion scan with differential split and segmental analysis. The right lower lobe is usually selected from the larger donor, while, if the donors are of the same height, the donor with the more complete fissure on the left is chosen to donate that side. HLA matching is not required for donor selection; however, a prospective cross-match to rule-out the presence of anti-HLA antibodies is performed.

Donor lobectomy

The important difference in performing a lobectomy for lobar transplantation, as opposed to a lobectomy for cancer or infection, is that the lobe must be removed with adequate margins of bronchus, pulmonary artery, and pulmonary vein to allow successful re-implantation in the recipient, while allowing closure of these structures in the donor without compromise.

The procedure of donor lobectomy has been described previously (14). Briefly, the donor lobectomy is performed through a muscle-sparing posterolateral thoracotomy through the fourth or fifth intercostal space. The lobar vasculature is first dissected and anatomic variants identified. For the right lobectomy the relationship of the superior segmental artery of the lower lobe and the middle lobe pulmonary artery is defined, while on the left, the relationship between the superior segmental artery to the lower lobe and the lingular artery is defined. This dissection allows vascular clamps to be placed just distal to the middle lobe artery and proximal to the superior segmental artery of the lower lobes. Next the inferior pulmonary veins and right middle lobe vein (for a right lobectomy) are defined. Fissures are completed with stapling devices to minimize potential air leaks in the donor and recipient after transplantation. After the vascular dissection is completed, the lungs are ventilated for 5–10 min and heparin (300 units/kg) and methylprednisolone (500 mg) are administered. The pulmonary artery is clamped and divided first, followed by the pulmonary vein to avoid injury to the allograft by venous congestion. In the right lobectomy, the right middle lobe bronchus is identified and the bronchus to the lower lobe tangentially transected, while on the left, the tangential transection begins at the base of the upper lobe bronchus and ends superior to the bronchus to the superior segment of the left lower lobe.

In vivo flushing and cooling of the graft is not possible in living donors therefore the lobe is taken to a separate sterile table for preservation with a cold pulmonoplegic solution. The pulmonary vessels and bronchus are then repaired. The bronchus is closed with interrupted polypropylene suture and then covered with a pleural flap. Chest tubes are placed, and the chest closed. The donors are transported to the recovery room with epidural catheters in place for pain control. Chest tubes are required until any air leak has stopped, output is acceptable, and the remaining lung tissue fills the hemithorax with minimal to no pneumothorax. Donors currently receive low-dose enoxaparin postoperatively to prevent thromboembolic complications. Oral analgesics are administered upon removal of the chest tubes and epidural catheter. Perioperative antibiotics consisted of cefazolin, or vancomycin if penicillin allergic, preoperatively and continued until chest tube removal.

Statistical analysis definition of variables

Data are presented as the mean value ± standard deviation. Continuous variables between right- and left-sided donors were compared using an unpaired Student's *t*-test with equal variance. Dichotomous variables for the following donor subgroups were compared to evaluate the risk of perioperative complication using a two-tailed Fisher's exact test and 95% confidence intervals: male or female, age less than or greater than 40 years, relationship of donor to recipient, smoking history, right- or left-sided lobectomy, estimated blood loss (EBL) less than or greater than 300 mL, and donation in first (1993–97) or last 5 years of our experience (1998–2003). GraphPad version 3.03 for Windows (GraphPad Software, Inc., San Diego, CA, USA) was used for all statistical analyses.

Results

Donor demographics and preoperative characteristics

Demographics and preoperative characteristics are presented for the overall cohort of 253 lobar donors in Table 1. One hundred and twenty-seven donors underwent right lobectomy, while 126 underwent left-sided lobectomy. Mean age of the donors was 36.5 ± 9.8 years (range 18–56 years) and did not differ between right- and left-sided donors ($p = 0.23$). Sixty-three percent of donors were male while 37% were female. A larger proportion of right-sided donors were males, while left-sided donors were more likely to be female ($p < 0.0001$). Similarly, right-sided donors were slightly taller and heavier than left-sided donors ($p = 0.0001$ and 0.0002, respectively). Seventy percent of donors had some relationship to the recipient, while 30% were not related (i.e. friends or spouses). Mean preoperative percent predicted FVC, FEV_1, and FEF_{25-75} were greater than 95% for all parameters, and there were no differences between right-and left-sided donors. Right-sided donors had slightly lower PaO_2 on room air; however, this difference is unlikely to have been clinically relevant as both were quite adequate ($p = 0.03$). Thirteen percent of donors did have a smoking history; however, the mean number of pack-years was low (5.3 ± 5.9 years).

Perioperative characteristics

Perioperative characteristics are presented for the overall cohort of 253 lobar donors in Table 2. Mean EBL was 216 ± 174 mL. EBL was slightly higher in right-sided donors, but the difference was not statistically significant (241 ± 207 mL vs. 191 ± 130 mL, $p = 0.06$). Overall length of stay

Table 1: Demographics and preoperative characteristics of living lobar lung transplant donors

		Side of donation		
	Overall	Right	Left	p-value
Demographics	253	127	126	–
Male (%)	160 (63)	102 (64)	58 (36)	<0.0001
Female (%)	93 (37)	25 (27)	68 (73)	
Age (years)	36.5 ± 9.8	35.7 ± 9.9	37.2 ± 9.7	0.23
Height (inches)	68.5 ± 4.0	69.7 ± 3.4	67.2 ± 4.2	0.0001
Weight (lbs)	172 ± 31	179 ± 30	164 ± 33	0.0002
Preoperative characteristics				
Related to recipient (%)	176 (70)	87	89	0.78
Not related to recipient (%)	77 (30)	40	37	
Mean percentage FVC	108 ± 9.9	107 ± 8.7	108 ± 9.9	0.33
Mean percentage FEV_1	110 ± 10.2	110 ± 10.2	110 ± 10.2	0.92
Mean percentage $FEF_{25–75}$	96.2 ± 19.8	98.0 ± 22	96.2 ± 19.8	0.59
Mean Room air PaO_2	97.6 ± 8.7	93.4 ± 9.9	97.6 ± 8.7	0.03
Smoking history (%)	34 (13%)	20	14	–

Table 2: Perioperative characteristics of living lobar lung transplant donors

		Side of donation		
Complication	Overall	Right	Left	p-value
Estimated blood loss (ml)	216 ± 174	241 ± 207	191 ± 130	0.06
Length of stay (days)	9.4 ± 4.8	9.9 ± 5.3	9.0 ± 4.1	0.13
Time to 1st chest tube removal (days)	6.0 ± 3.2	6.4 ± 3.4	5.4 ± 3.0	0.05
Time to 2nd chest tube removal (days)	8.5 ± 4.0	9.1 ± 4.3	7.9 ± 3.6	0.06

was 9.4 ± 4.8 d, and did not differ between right- and left-sided donors. There was a trend toward earlier removal of both the first and second chest tubes in left-sided donors ($p = 0.05$ and 0.06) as compared with right-sided donors.

Perioperative complications in lobar donors

There has been no perioperative or long-term mortality in this cohort of 253 lobar donors. Two hundred and three (80.2%) of the 253 donors had no perioperative complications. Fifty (19.8%) of the 253 donors had one or more perioperative complications. The perioperative complications occurring in the lobar donors are listed in Table 3.

Intraoperative complications occurred in nine (3.6%) donors, and were primarily related to the right middle lobe. The right middle lobe was sacrificed in four donors due to variations in either arterial or venous anatomy, while three patients required re-implantation of the right middle lobe bronchus. In addition, one donor required one packed red blood cell unit secondary to blood loss after the clamp on the left atrium was inadvertently displaced. One patient with a history of Wolf–Parkinson–White syndrome developed a persistent supraventricular tachycardia which eventually responded to medical therapy; however, the patient subsequently required pacemaker placement.

Complications requiring re-operation occurred in eight (3.2%) donors. Three donors required re-operation for bleeding; however, none required a red blood cell transfusion. The source of bleeding in these patients was most commonly an intercostal artery. One patient underwent video-assisted thoracoscopy for evacuation of a loculated pleural effusion, while one required pericardiectomy for pericarditis unresponsive to medical management. The remaining three patients required re-operation for a sterile empyema, a retained sponge, and a bronchopulmonary fistula, respectively. The bronchopulmonary fistula was the result of a bronchial stump leak that did not involve re-implantation of the middle lobe.

Other perioperative complications occurred in 38 (15.0%) donors. The most common complication in this group, and overall, was the need for a thoracostomy tube for greater than 14 days postoperatively, either for persistent drainage or air leaks, or the placement of an additional thoracostomy tube. The most significant complication in this group occurred in two patients who developed pulmonary artery thrombosis. Both patients presented with severe respiratory distress; however, neither required intubation. Both patients had positive ventilation-perfusion scans, negative lower extremity duplex scans, and contrast magnetic resonance imaging and angiography studies consistent with thrombus at the pulmonary artery suture line. Both patients were successfully managed with systemic anticoagulation and suffered no long-term sequelae. Other complications included medically treated arrhythmias and pericarditis, as well as two minor epidural-related complications (hypotensive episodes resulting in syncope in two donors). One donor required

Table 3: Perioperative complications in living lobar lung transplant donors

Description of complication	Number of donors
Intraoperative complication	9
Sacrifice of right middle lobe	4
Re-implantation of right middle lobe bronchus	3
Blood loss requiring transfusion	1
Persistent supraventricular tachycardia	1
Complication requiring re-operation	8
Bleeding	3
Sterile empyema	1
Retained sponge	1
Loculated pleural effusion	1
Bronchopulmonary fistula	1
Pericardiectomy	1
Perioperative complication	38
Thoracostomy tube for ≥14 d	15
Required additional thoracostomy tube	7
Pulmonary artery thrombosis	2
Pericarditis – medically treated	4
Arrhythmias – medically treated	3
Minor epidural-related complications	2
Bronchoscopy for lobe collapse	1
Required readmission	4

bronchoscopy for right middle lobe collapse, but did not require re-operation. Four donors required readmission within 30 d of lobectomy, one for dehydration, one with shortness of breath, one with a pleural effusion managed conservatively, and one for presumed pneumonia without positive cultures.

Predictors for perioperative complications in lobar donors

Fisher's exact tests were performed to identify patient variables that might predict the occurrence of perioperative complications. As shown in Table 4, the odds ratios were not significant for gender, age, relationship of donor to recipient, presence or absence of smoking history, estimated blood loss less then or greater than 300 mL, or donation during the first 5 years of the experience. Donation of the right lower lobe was associated with an increased risk of perioperative complication (odds ratio 2.02, $p = 0.04$).

Discussion

Living lobar lung transplantation was introduced by our group in 1993 in response to the cadaveric lung donor shortage. This technique involves the transplantation of the right and left lower lobes from a pair of adult donors to adult or pediatric recipients. In general, the recipients of living lobar lung transplants have included an extremely ill cohort of patients, predominantly with cystic fibrosis. The procedure has allowed an increase in the number of lung transplants, and of even greater importance, the ability to perform lung transplantation in an urgent time frame.

We recently reported our recipient outcomes during our first decade of experience with living lobar lung transplantation (11). One hundred and twenty-eight transplants were performed in 123 patients during this time period. Actuarial survival with this procedure is 70%, 54%, and 45% at 1, 3, and 5 years, respectively, which is similar to the actuarial survival reported for double-lung cadaveric transplantation from the International Society for Heart and Lung Transplantation Registry (74%, 59%, and 49.5% at 1, 3, and 5 years, respectively). We were also able to show that patients intubated preoperatively and those undergoing re-transplantation had higher postoperative mortalities, suggesting caution in these populations. Although cadaveric transplantation remains preferable, these results have shown that living lobar lung transplantation has been life-saving in a select group of severely ill patients who would have either died or become unsuitable recipients before a cadaveric organ became available.

Table 4: Risk of perioperative complication by patient variable

Characteristic subgroup	Variable	Total no. in group	No. of donors with complication	Odds ratio (95% confidence interval)	p value
Gender	Male	160	31	0.94 (0.49–1.77)	0.87
	Female	93	19		
Age of donor (years)	≤ 40	142	28	0.99 (0.53–1.85)	1.00
	> 40	111	22		
Related to recipient	Yes	176	36	1.16 (0.58–2.30)	0.73
	No	77	14		
Smoking history	Yes	34	7	1.06 (0.43–2.60)	1.00
	No	219	43		
EBL > 300 mL	Yes	106	21	1.01 (0.54–1.88)	1.00
	No	147	29		
Donor in first 5 years of experience (1993–97)	Yes	123	24	0.97 (0.52–1.80)	1.00
	No	130	26		
Right lobe donated	Yes	127	32	2.02 (1.07–3.83)	0.04
	No	126	18		

EBL: estimated blood loss.

The number of living donors utilized for transplants continues to increase – 12% per year since 1996 – primarily among kidney and liver transplantation (2). However, the issue of donor safety cannot be ignored, as the use of living donors for organ transplantation creates the unique situation whereby the treatment approach affects not only the recipient with end-stage disease, but also the live organ donor. This is especially important with living lobar lung transplantation given the unique nature of this technique in that not one, but two donors are put at risk for each recipient.

Early complications among 16 395 living organ donors reported to the UNOS/OPTN database between October, 25, 1999 and June 30, 2002 were recently analyzed (6). The most common early complications among the 15 162 kidney donors were the need for transfusion (1.5%), infection (0.7%), pulmonary embolism (0.1%) and re-operation (0.5%), while the most common complications among the 1134 liver donors were the need for transfusion (11.9%), infection (4.4%), pulmonary embolism (0.6%), and re-operation (2.3%). Importantly, two of the kidney donors and one of the liver donors died prior to discharge, while two additional liver donors were placed on the liver transplant waiting list. This analysis underscores the need for more complete short- and long-term living-donor follow-up in the national transplant databases (2,15).

The only report in the literature of donor complications after donor lobecotmy is from the Washington University group in 2000, in which they analyzed perioperative complications for 62 donors undergoing donor lobectomy for living lobar lung transplantation at their institution (12). In this series, 38 out of 62 donors (61.3%) had perioperative complications, with 12 major complications occurring in 10 patients. Major complications included pleural effusions necessitating drainage (n = 4), bronchial stump fistulas (n = 3), bilobectomy (n = 1), hemorrhage necessitating red cell transfusion (n = 1), phrenic nerve injury (n = 1), atrial fibrillation necessitating electophysiologic ablation (n = 1), and bronchial stricture necessitating dilatation (n = 1). 'Minor' complications accounted for the remainder. There was only one re-operation in this series and no mortality. The authors of this series equated the risk of donor lobectomy to that of a pulmonary sleeve resection as opposed to a standard lobectomy. Given the small nature of these studies and the importance of understanding the outcomes and risks associated with lobar donation in terms of donor safety, we examined the perioperative outcomes and complications after 253 donor lobectomies during our first decade of living lobar lung transplantation.

Appropriate donor selection remains of paramount importance to both donor and recipient outcomes, as inappropriate donor selection will surely lead to both poor donor and recipient outcomes. The demographics of the current series reflect our selection bias of selecting relatively young and healthy donors with supra-normal pulmonary function tests, utilizing the taller donor as the right-sided donors. This selection process can be both time-consuming and difficult. In a review of 28 of our lobar recipients, a total of 220 candidates were screened as potential donors (16). Of these, 164 (75%) were not accepted due to either decreased expiratory flows (34%), height (20%), did not want to donate (11%), ABO blood type incompatibilities (11%), social reasons (11%), obesity (8%), or age (5%). Only two of the recipients required only two donor screenings, while the other 26 recipients required a mean of 8.3 donor evaluations to identify suitable donors.

There has been no perioperative or long-term donor mortality after donor lobectomy in our series, or to our knowledge, at other centers. However, one or more perioperative complications occurred in 50 (19.8%) of the donors. This complication rate is lower than that reported by the Washington University group, but is similar to perioperative complications rates reported for lung resections which vary from 7% to 49% (17–21).

The most common complication in this series was the need for an additional thoracostomy tube or the need for a thoracostomy tube for more than 14 d postoperatively, which occurred in 8.7% of patients. Only one of these patients (0.4%) developed a bronchopulmonary fistula requiring operative intervention. This is again similar to that reported for lung resections as the most common complications after lung resection are bronchopulmonary fistulas (incidence 3.1–15%) and prolonged (greater than 7 days) air leaks (4–26%) (18,21–25).

Although clearly a different operation than standard lung resections, these complications are not surprising after donor lobectomy and are likely the result of two factors: (i) the need to perform the majority of the dissection in the fissure on the donor's remaining side which potentially causes air leaks and (ii) the possibility that the remaining lung with normal compliance and elasticity may not fill the space as rapidly as the diseased, overly compliant lung seen in many cancer patients, thereby resulting in prolonged pleural fluid drainage.

The only variable we were able to identify which might predict the occurrence of perioperative complications was donation of the right lobe; however, this difference was primarily related to the anatomical relationship of the right middle and lower lobe, as seven of the nine intraoperative complications can be explained by anatomic differences (three re-implantations of the right middle lobe bronchus and four bilobectomies).

An important question which remains unanswered by the present study is the long-term outcomes and functional effects of lobar donation. This has proven very difficult to follow closely, due to the fact that many donors live far away from the medical center and are reluctant to return for routine follow-up evaluation. The death of the

recipient further exacerbates this situation as we are then reluctant to insist on further routine exams for a grieving donor. Although this may not reflect the postoperative pulmonary function of the entire group of donors, initial 1 and 2 year postoperative pulmonary function testing in our intermediate experience, demonstrated an average decrease of 17% in forced vital capacity, 15% in forced expiratory volume in 1 s, and 16% in total lung capacity from preoperative values (8). Loss of lung function should be considered an expected aspect of this procedure, and is explained, as such, to the potential donor during the process of obtaining informed consent.

In summary, there has been no perioperative or long-term mortality after lobectomy for living lobar lung transplantation, and the perioperative risks associated with donor lobectomy are similar to those seen with standard lung resections. These risks might increase if the procedure is offered on an occasional basis and not within a well-established program. Further long-term outcome data is ideally needed, similar to live donor renal and liver transplantation. Given these results, we still favor performing living lobar lung transplantation only for the patient with a clinically deteriorating condition. We feel that prospective donors should be informed of the morbidity associated with donor lobectomy and the potential for mortality, as well of potential recipient outcomes with regard to life expectancy and quality of life after transplantation. A constant concern regarding the risk to the living donors must be maintained with any live donor organ transplantation program, and comprehensive short- and long-term follow-up should be strongly encouraged to maintain the viability of these potentially life-saving programs.

Acknowledgments

M.E.B. was the recipient of the 2002 American Society of Transplant Surgeons Thoracic Surgery Fellowship. M.L.B was funded in part by grants from the Heart and Lung Surgery Foundation of Los Angeles and the University of Southern California University Hospital. Additional funding was provided by the Hastings Foundation.

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