Lobar Lung Transplantation: A Relevant Surgical Option in the Current Era of Lung Allocation Score

Norihisa Shigemura, MD, Jonathan D’Cunha, MD, Jay K. Bhamra, MD, Akira Shiose, MD, Ashraf Abou El Ela, MD, Amy Hackmann, MD, Diana Zaldonis, MPH, BSN, Yoshiya Toyoda, MD, Joseph M. Pilewski, MD, James D. Luketich, MD, and Christian A. Bermudez, MD

Department of Cardiothoracic Surgery and Division of Pulmonary, Allergy and Critical Care Medicine, Department of Medicine, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania

Background. With the implementation of the lung allocation score (LAS) system, an increased number of critically ill patients are considered for transplantation. However, LAS does not take size matching between donor and recipient lungs into consideration. Mortality on the waiting list is high (as high as 25%) for short-stature patients and for patients with restrictive lung disease. Here, we review our experience using cadaveric lobar lung transplantation as a surgical option in an attempt to decrease mortality while waiting.

Methods. We retrospectively reviewed patients with end-stage lung diseases and an LAS greater than 70 who underwent cadaveric lobar lung transplantation between 2010 and 2012 (n = 25) at our institution, a high-volume lung transplant center. Anatomic lobectomy was performed on all donor lungs before double lung transplantation.

Results. Median LAS was 85.6 (range, 72 to 94). Average waiting time after the patients’ LAS was updated to greater than 70 was 10 days (range, 1 to 41). There were 2 in-hospital deaths. The 90-day and 1-year survivals were 88% and 76%, respectively. Patient major morbidities included severe primary graft dysfunction requiring postoperative extracorporeal membrane oxygenation (7 patients), acute renal insufficiency (4 patients), and bleeding requiring reoperation (4 patients). No technical problems were identified, and repeated bronchoscopy demonstrated satisfactory healing of the bronchial stump after lobectomy. The average posttransplant peak for forced expiratory volume in 1 second was 85%.

Conclusions. Our initial experience supports the option of lobar lung transplantation for critically ill patients whose opportunities for transplant are limited by their stature. Long-term functional studies are warranted.


Organ allocation of donated lungs has been driven by the lung allocation score (LAS) since 2005, and with the implementation of the LAS, the demographics of the lung transplant recipients shifted with an increased number of critically ill patients being considered for lung transplantation [1, 2]. However, the LAS does not take size matching between donor and recipient lungs into consideration. This omission directly impacts mortality on the waiting list, which is high (as high as 25%) for patients who are shorter than average Americans and for patients with restrictive lung disease. Additionally, our recent data demonstrated that lung transplantation in patients with a high LAS is associated with significantly decreased survival and increased complications as compared with transplantation in patients with a low LAS, and this correlation is more pronounced in patients with restrictive lung diseases [3]. Waiting for the best size-matched donor, while the patient’s functional status declines and LAS increases, decreases the likelihood of survival after transplant. A definitive strategy is necessary to promote transplant and shorten the time on the waiting list for patients with restrictive lung diseases, particularly those shorter than 65 inches.

Recently, many shorter than average patients with restrictive lung disease have been referred to our practice. Of note, approximately 25% of them have been declined as transplant candidates at other lung transplant centers owing to the nature of their disease (eg, scleroderma), surgical complexity, or their stature. Most patients with restrictive lung diseases who were listed for lung transplantation at our center over the last 3 years were less than 65 inches tall (63%). Owing to their small chest cavity size and the nature of their disease, ideally sized donors were expected to be shorter than 60 inches; however, these potential donors comprised only 8% of all registered donors in our area (Fig 1). If the patients were forced to wait for size-matched donors, their window for transplant would be very limited and their health would continue to decline.

Since the first cadaveric lobar lung transplant (LLT) case was reported by Bisson and colleagues in 1994 [4],
the benefits of LLT for recipients with smaller than average chest cavities have been well described from resources, functional, and technical standpoints [5-8]. We have used a cadaveric LLT aggressively as a surgical option in an attempt to decrease the waiting mortality for patients with smaller than average stature and restrictive chest diseases, and LLT use has increased from 2% to 20% of all lung transplants over the last 3 years at our institution. This study is a review of that single-center experience at a high-volume lung transplant center.

Patients and Methods

Patients

Human subject approval for this study was obtained from the University of Pittsburgh Medical Center before obtaining data (Institutional Review Board approval number PRO12110168). From July 2010 to July 2012, we performed primary lung transplantation in 225 patients with end-stage lung diseases at the University of Pittsburgh Medical Center, exclusive of heart-lung transplantation cases. Of those, 25 recipients (11%) underwent LLT using lungs from brain-dead donors. The primary indication for lung transplant was idiopathic pulmonary fibrosis in 9 patients, scleroderma (restricted) in 4, sarcoidosis in 4, cystic fibrosis in 2, and other in 6 patients. Indications for LLT included LAS greater than 70 and a small chest, as indicated by height less than 62 inches or chest roentgenogram measurement (from apex to diaphragm) less than 15 cm, or asymmetric chest (eg, after lobectomy, chest deformity). When indicated, the option of LLT was discussed and approved by our multidisciplinary committee for lung transplant and the final decision was made based on intraoperative findings of size-matching between the donors’ and recipients’ lungs. Of 25 patients, 7 patients were on extracorporeal membrane oxygenation (ECMO), 9 patients were on the ventilator, and 9 patients required high-flow oxygen with 15 L/min before LLT.

Donor Selection

Donors met the standard donor selection criteria [9]. In addition, lungs with completely fused, major fissures were excluded as suitable donor lungs for LLT. Our standard procurement protocol [9, 10] was utilized in this study, and a meticulous investigation for fissure completion in donor lungs was conducted.

Surgical Techniques

Once the decision was made to proceed with LLT, anatomic pulmonary lobectomy was performed using individual ligation/stapling techniques on the operating room back table before implantation. The decision of which lobe to remove was made based on the size discrepancy between the recipient and donor lungs. The decisions were made intraoperatively based empirical evaluation of donor and recipient size. Lower lobectomy on either side was preferred due to shorter procedure time and fewer procedure-related risks. If there were quality issues with other lobes (ie, contusion, consolidation), the affected lobe was removed instead. After the lobectomy was completed, the stapled bronchial stumps were reinforced using viable, pedicled donor pericardial tissues. Otherwise, all the hilar structures in the donor lungs, including bronchus, pulmonary artery and vein (atrial cuff), were prepared according to the protocol used for lung transplant using intact lungs. In the recipient, the implantation using a lobar lung was performed in the same fashion as for a typical lung transplant. The main bronchus, main pulmonary artery, and atrial cuff were anastomosed to the recipient’s main bronchus, main pulmonary artery, and atrial cuff, respectively.

Early Outcomes, Mortality, and Survival

We collected data on operative parameters and postoperative complications from our lung transplantation database, which documents all adverse outcomes using prospective data collection from patient clinical records. Renal dysfunction was defined as severe renal insufficiency requiring either temporary or permanent dialysis treatment. Primary graft dysfunction (PGD) was defined and graded using International Society for Heart and Lung Transplantation definitions [11]. It is our routine practice to perform pulmonary function tests 1, 3, 6, and 12 months after transplant, and yearly thereafter until 5 years after lung transplant. Additional testing was performed when clinically necessary.

Data Analysis

Statistical analysis was performed using the STATVIEW 5.0 software package (SAS Institute, Cary, NC).
Continuous variables are expressed as the median with the ranges. Comparisons between groups were done using Student’s t test, and categorical variables were analyzed by Fisher’s exact test. Survival was calculated and assessed with the Kaplan-Meier method and a log rank test.

Results

Patient Demographics
The median age of the recipients was 51 years (range, 14 to 71). Their median height was 64 inches (range, 56 to 69). All 25 recipients had a LAS above 70 (median 85; range, 72 to 94). The median time on the lung transplant waiting list was 10 days (range, 1 to 41). Among the patients who were on ECMO before transplant, the median duration of ECMO was 7 days (range, 1 to 28), and among patients who were on ventilator support, median duration of support was 10 days (range, 5 to 28). Median donor age was 31 years (range, 21 to 52) and median donor height was 69 inches (range, 66 to 74). The median donor-to-recipient height difference was 5 inches (range, −3 to +15 inches).

Operative Data
Of the 25 patients who underwent LLT, 12 patients received unilateral LLT and 13 patients received bilateral LLT. Warm ischemic time for lobectomy on the back table ranged from 15 to 33 minutes with a median of 21 minutes. Most patients (92%) required cardiopulmonary support during LLT (Table 1).

Postoperative Outcomes
Postoperative outcomes are shown in Table 2. There were 2 in-hospital deaths that occurred at the beginning of our experience. One patient was on ECMO for 4 weeks before LLT and came off ECMO after LLT with good pulmonary function, but recovery was complicated with hepatic failure and the patient died of sepsis and multiorgan failure. The other patient was the oldest patient in this cohort (71 years old). After transplant, the patient had PGD followed by severe ischemic colitis, resulting in sepsis and death after multiple abdominal surgeries. Severe PGD requiring ECMO was experienced by 7 patients (28%); 5 of them were on ECMO support before LLT and their ECMO was continued after LLT was completed using the existing cannulas; however, all of these patients were weaned off ECMO within 5 days after LLT. The other 2 patients included the oldest patient in the series, detailed above, and a patient who had late-onset, acute lung edema after extubation, was reintubated, and was subsequently placed on ECMO. The lung edema resolved after aggressive diuresis, and she was discharged to home. Other major complications included acute renal insufficiency requiring hemodialysis (4 patients [16%]) and postoperative bleeding requiring reoperation (4 patients [16%]). During the observation period, no patient in this cohort had airway dehiscence, including bronchial stump dehiscence.

Allograft quality during routine follow-up (follow-up ranged from 6 months to 2 years) was evaluated using the posttransplant peak forced expiratory volume of air in 1 second and peak forced vital capacity. Median peak forced expiratory volume of air in 1 second was 85.2% and peak forced vital capacity was 73.2%. In the patients who underwent LLT, the 90-day survival rate was 88% and the 1-year survival rate was 76%.

Comment
Cadaveric lobar lung transplantation is neither a new technique nor a new concept, but we have translated the experience to our high-volume practice because of the potential for high mortality rate on the waiting list. Long-term functional and survival outcomes after LLT have

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Table 1. Operative Data

<table>
<thead>
<tr>
<th>Operative Variable</th>
<th>Number of Patients (Unless Specified Otherwise)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cold ischemic time (median)</td>
<td>398 min (range, 311–530)</td>
</tr>
<tr>
<td>Warm ischemic time (median) (min)</td>
<td></td>
</tr>
<tr>
<td>At back table (for lobectomy)</td>
<td>21 min (range, 15–33)</td>
</tr>
<tr>
<td>At front (for implantation)</td>
<td>63 min (range, 54–72)</td>
</tr>
<tr>
<td>Type of lobectomy</td>
<td></td>
</tr>
<tr>
<td>Single lobe</td>
<td>11</td>
</tr>
<tr>
<td>Multiple lobes</td>
<td>14</td>
</tr>
<tr>
<td>Lower lobectomy</td>
<td>33 (RLL 21, LLL 12)</td>
</tr>
<tr>
<td>Middle lobectomy</td>
<td>2</td>
</tr>
<tr>
<td>Upper lobectomy</td>
<td>2 (both were RUL )</td>
</tr>
<tr>
<td>Cardiopulmonary support during LLT</td>
<td></td>
</tr>
<tr>
<td>Cardiopulmonary bypass</td>
<td>18</td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenation</td>
<td>5</td>
</tr>
<tr>
<td>No support</td>
<td>2</td>
</tr>
<tr>
<td>Duration of support (min)</td>
<td>235 min (range, 131–521)</td>
</tr>
</tbody>
</table>

LLL = left lower lobe; RLL = right lower lobe; RUL = right upper lobe.

Table 2. Short-Term Outcomes and Lung Allograft Quality

<table>
<thead>
<tr>
<th>Postoperative Parameter</th>
<th>N (%) (Unless Specified Otherwise)</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital death</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Ninety-day mortality</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>One-year survival</td>
<td>76%</td>
</tr>
<tr>
<td>Short-term complications</td>
<td></td>
</tr>
<tr>
<td>Severe PGD requiring ECMO</td>
<td>7 (32%)</td>
</tr>
<tr>
<td>Acute renal insufficiency on dialysis</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>Bleeding requiring reoperation</td>
<td>4 (16%)</td>
</tr>
<tr>
<td>Bronchial stump dehiscence</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Allograft quality outcomes</td>
<td></td>
</tr>
<tr>
<td>Peak forced expiratory volume in 1 s</td>
<td>85.2%</td>
</tr>
<tr>
<td>Peak forced vital capacity</td>
<td>73.2%</td>
</tr>
</tbody>
</table>

ECMO = extracorporeal membrane oxygenation; PGD = primary graft dysfunction.
been reported from multiple institutions [4–8]; however, questions remained regarding the application of LLT in critically ill patients. Given the benefits and risks of cadaveric LLT, this surgical option should show its highest value when it is carried out as the last resort option for lung transplant in patients who might not survive otherwise. This study, to the best of our knowledge, is the first report of cadaveric LLT in critically ill patients with restrictive lung disease, and the largest single-center experience to date. In addition, this is the first report of cadaveric LLT from the United States.

The technical aspects of LLT have been well addressed in the literature [7, 8]. With experienced hands, it is not technically demanding to perform lobectomy of any lobe in donor lungs at the operating room back table, although lobectomy on donor lungs is different from the pulmonary lobectomies that thoracic surgeons are accustomed to performing for lung cancer, because there may be no distented vascular structures. According to published reports, bronchial stump complications are the biggest technical concern after a lobar transplant and occur in as many as 13% of recipients [5–8]. Therefore, it should be emphasized that while this lobectomy is not technically difficult, it deserves special technical attention because all the postlobectomy structures, especially the bronchial stumps, can be inevitably compromised in their quality by immunosuppression with steroids, interrupted bronchial blood supply, and suboptimal oxygenation due to potential PGD. Furthermore, special technical considerations are important not only from a surgical standpoint including the use of optimal reinforcement techniques for covering the stumps but also from a postsurgical management standpoint, including fluid balance, steroid dosage, and bronchoscopic surveillance. For these reasons, LLT may be best performed by experienced surgeons at institutions with well-established postoperative protocols.

We had 2 in-hospital deaths in our series. Severe PGD requiring ECMO was the most common complication. Postoperative ECMO was required in 7 patients: 1 who died in-hospital after transplant, 5 who were on ECMO before transplant, and 1 who required postoperative ECMO owing to late onset of acute lung edema, which may have been related to the small lung allografts implanted. In our recently published series of critically ill patients who were on ECMO as a bridge to lung transplantation [12], 30-day survival was 81% and 1-year survival was 74%. In addition, recent data from the United Network for Organ Sharing demonstrated that recipients with an LAS above 75 had significantly worse actuarial survival when compared with recipients with a low LAS, and these findings were more noticeable in those with pulmonary fibrosis. Patients with pulmonary fibrosis and an LAS greater than 75 had 1-year survival as low as 58%. [2] In the current series of critically ill patients who underwent LLT, 30-day survival was 92% and 1-year survival was 76%. Although further long-term observation is warranted, given the critically ill condition of the patients in the current series and narrow window for transplant, these results are very encouraging.

Published studies have suggested that LLT does not increase the morbidity or mortality of lung transplantation [6, 8]. Based on the results shown in this study, we agree that LLT appears to be safe with acceptable procedure-related risks. However, given the risk of potential bronchial stump complications and the additional warm ischemic time required to perform the lobectomy, we do not currently consider LLT equivalent in quality to lung transplant using intact lungs. Because of these potential disadvantages and our experience in this series of 1 patient having late-onset, acute lung edema after extubation—potentially as a result of perfusing a small lobar lung with normal cardiac outputs—we currently recommend remaining selective when deciding whether to perform LLT, especially for stable patients.

The primary limitations of this study are its retrospective nature and the small sample size. However, the criticism of the sample size can be tempered by the fact that this report is to the best of our knowledge the first reported series of cadaveric lobar lung transplantation for critically ill patients, and it may pave the way for the use of LLT in patients who are not benefiting from the current LAS system.

In conclusion, our initial experience supports the potential for moving forward with LLT as an option for critically ill patients, particularly patients with a small chest cavity whose opportunities for transplant are diminished. With confidence that we are heading in the right direction, we advocate further investigation into the potential viability of LLT for these patients and other patients who may benefit from lung transplantation before clinical decompensation.

We thank Shannon L. Wyszomierski, PhD, for her excellent editing assistance.

References


DISCUSSION

DR ROBERT DUANE DAVIS (Durham, NC): Can you share some of your protocols? Is your posttransplant management the same for a lobar as compared to a full cadaveric lung? There are a lot of data particularly in living donor lobe kidney that makes sense, compared to a living donor kidney, you want to manage it differently, such as performing them always on pump, allowing permissive hypoperfusion to try to minimize primary graft dysfunction (PGD), and so forth.

DR SHIGEMURA: Yes. That is a great question. And in fact, we really value the postoperative management specifically for those lobar lung transplantations. We actually have recently protocolized all of the management for lobar lung transplant cases, which includes the fluid balance, bronchoscopic surveillance, prolonged usage of nitric oxide, timing of extubation, and so forth. For instance, if somebody who is not familiar with the surgical anatomy does the branch and if they just ignore the stumps, there would be catastrophic complications. So those protocolized management should be valued.

DR ANKIT BHARAT (St. Louis, MO): Thank you for sharing your data with us. One of the dilemmas that comes up intraoperatively is whether to do a lobectomy back table or to implant the lung and do wedge resections. Patients who are being offered lungs from a donor with greater stature discordance are typically sicker, have higher lung allocation scores, and are likely to have much higher postoperative complications. So it might sometimes seem counterintuitive sometimes to take a functional lobe even before implantation. Can you tell us how you decide between back table lobectomy versus wedge resection after implantation?

DR SHIGEMURA: Thank you for the questions. In terms of postimplant lobectomy, I really think it technically difficult. That needs another deflation, which can result in a high risk of PGD too. Yes, we need to have another warm ischemic time at back table for preimplant lobectomy, but once it’s accustomed, it takes only 15 minutes, at most 20 minutes. So at this moment we think it is much better to do lobectomy before transplant instead of doing after implantation.

DR BHARAT: I’m sorry. I meant not postimplant lobectomy but wedge resection. So you don’t really—it’s a short deflation time. See, there are a few problems here. You certainly need another surgeon to do a back table lobectomy, so you need two surgeons, and sometimes that’s not available at a lot of institutions. And then certainly you’re increasing the warm ischemia time opposed to doing a wedge. You can actually take the entire middle lobe, entire lingula, and actually a lot of the lower lobe out doing a big wedge resection after implant.

So that’s why I was trying to understand your practice at University of Pittsburgh Medical Center, how you make that decision, not postimplant lobectomy but big wedge resections in these patients. What is sort of some of the guidelines that you guys follow there?

DR SHIGEMURA: Fortunately, I have been involved in all of those lobar lung transplant cases so I can answer that question of decision-making process correctly. Based on the donor/recipient height discrepancy as well as both donor and recipient chest X-ray films, we have some anticipation before the surgery if we likely need to do a lobar or not. Then after my evaluating the size discrepancy between donor lung and recipient chest cavity in the operating room, I make a final decision to proceed or not. Yes, of course another surgeon is needed to minimize the cold ischemic time, but once it’s organized, it’s not that complicated.

DR BERMUDEZ: Great presentation. I wanted to make a few comments regarding the lobar transplant and why we came up with the strategy. And we have Dr Toyoda here who participated in the first case.

We have done a lot of nonanatomical resections. In the old days, we didn’t use roentgenograms. We didn’t have them. We just took the size and brought the lungs, and we trained lungs back and forth. They actually were published, the data, recently, a few years ago. But we ended up leaving the chest open. We couldn’t do the resection immediately. Brought the patient back a few days later, had multiple resections, and we followed those patients. And theoretically, even though they survived, they ended up with lower functional capacity.

So when we had patients on extracorporeal membrane oxygenation (ECMO) recently with very small chest cavities, we really wanted to do them soon, and that’s how we started our experience. And we did a few cases with actually very good outcomes. We didn’t need to leave the chest open. We also have changed the strategy. As you see, there were some done on ECMO support, which we believe is much better than pump. So we tried to do them all on support. We did 2 cases, very exceptional, off pump. But we have learned it is much better to do an anatomical resection in a planned fashion, close the chest, and take that patient back to the intensive care unit.

Functionally they’ve done very well. We have had only one stump dehiscence. That was after this paper was submitted, but 2% bronchial dehiscence, and that is a very low rate. But we believe, we are not sure yet, we could apply this to patients who are less sick. But it’s a great alternative, we believe, for this patient population. Thank you.

DR YOSHIYA TOYODA (Philadelphia, PA): In 2009 I actually started this, but at that time, in answer to you, just we use right brain, just based on the visual inspection, chest cavity, his lung size. We decided to go ahead and ask Shigemura to do lobectomy on the back table.

So we need to figure out when we should do lobectomy versus wedge resection.

DR SHIGEMURA: Thank you, Yoshiya. It depends. It’s difficult to predict, I mean, when we should do a lobe. The most important thing is how sick the recipient is and also how long they can wait. In the sense that the size discrepancy to me doesn’t matter, because as you did see, we use the lungs with 16-inch
discrepancy. So we can do anything using those big lungs for the small patients, but more important is indication of the recipients.

DR DAVIS: We’ve done a bunch of these, but I’ll tell you the one I hate is when you do a lobe and it’s still too big. Do you have any of the cases here that you actually had to do wedge resections on the lobe transplant?

DR SHIGEMURA: Yes. Actually, of 25 cases, we had 2 cases where we added a wedge resection in the middle lobes. After we did the lobal lobectomy, we found still the allograft oversized. So at that case, we actually left the chest open because of the coagulopathic status and the patient’s critical condition. And then for the second take-back, we did wedge resection as graft volume reduction. That worked well.

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