

Chapter 5

Living Donor Lung Transplantation

Robbin G. Cohen, Mark L. Barr and Vaughn A. Starnes

Introduction

Living donor lobar lung transplantation (LDLLT) was originally developed in the early 1990s, in response to the growing number of patients who were dying while awaiting suitable cadaveric donors for lung transplantation [1]. The procedure involves bilateral lung transplantation using the right lower lobe from one living donor to replace the right lung of the recipient, and the left lower lobe from another living donor to replace the left lung (Fig. 5.1). Because both of the patient's lungs are replaced by lobes from healthy donors, our early experience was confined to children and young adults with cystic fibrosis who, by virtue of their small size, were predicted to receive adequate pulmonary reserve after receiving only two pulmonary lobes. In order to minimize ethical issues regarding the risks of subjecting two healthy donors to a lobectomy for each transplant, only parents or siblings were originally considered as potential donors. Once successful recipient and donor outcomes and safety were established, the use of living lobar lung transplantation

R. G. Cohen (✉)

Department of Cardiothoracic Surgery, Keck/USC University Hospital,
USC Healthcare Consultation Center II, Los Angeles, CA 90033, USA
e-mail: rcohen@usc.edu

M. L. Barr

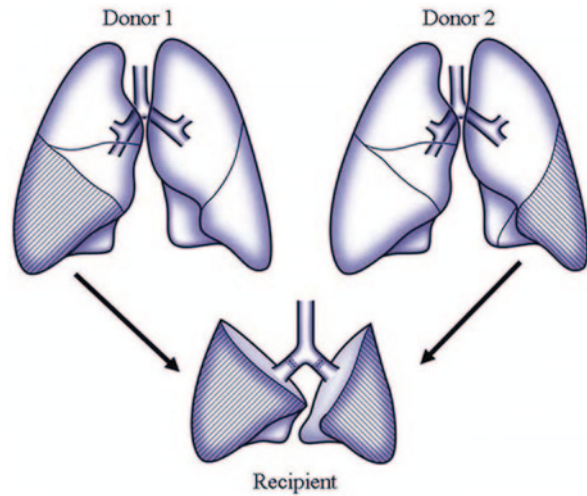
Department of Cardiothoracic Surgery, USC Transplantation Institute,
University of Southern California, Los Angeles, CA 90033, USA
e-mail: mbarr@surgery.usc.edu

V. A. Starnes

Department of Surgery, H. Russell Smith Foundation, Keck School of Medicine of the University
of Southern California, Keck Medical Center of USC, Los Angeles, CA 90033, USA

Department of Surgery, CardioVascular Thoracic Institute,
Keck School of Medicine of the University of Southern California,
Keck Medical Center of USC, Los Angeles, CA 90033, USA
e-mail: starnes@usc.edu

Fig. 5.1 Bilateral living donor lobar lung transplantation. Right and left lower lobes from two healthy donors are implanted in the recipient in place of whole right and left lungs, respectively. (Reprinted from [4], by permission of Oxford University Press)



expanded to include recipients with a wide range of pulmonary diseases, including other suppurative diseases of the lung, as well as pulmonary hypertension, pulmonary fibrosis, and pulmonary obstructive disease. Criteria for lung donation have expanded as well. Whereas the number of living donor lung transplants has decreased in the U.S. due to the success of the lung allocation scoring system implemented by the Organ Procurement and Transplantation Network in 2005, its use has expanded in countries like Japan, where waiting times for cadaveric lungs remain exceptionally long [2, 3].

Patient Selection

The recipient and donor selection process for LDLLT shares much in common with that of cadaveric lung transplantation. The goal is to transplant disease-free lungs that are as immunologically, anatomically, and physiologically compatible as possible in order to ensure the best possible recipient result. Because LDLLT requires that recipient pulmonary function be entirely dependent on two lobes instead of two whole lungs, a more extensive respiratory and anatomical evaluation of both donors and recipients is usually required. The fact that LDLLT utilizes live donors brings psychological and ethical issues into play. These must be carefully considered prior to subjecting healthy volunteers to the risks of major pulmonary surgery.

Recipient Selection

Recipient candidates for LDLLT should meet the criteria for cadaveric lung transplantation, and in the U.S. should be listed on the Organ Procurement and

Transplantation Network lung transplantation waiting list [5, 6]. Given that cadaveric whole lungs are preferable to lobes from living donors, most candidates for living donor lung transplantation should be expected to die or become too ill for transplantation while waiting to receive cadaveric lungs from the waiting list. Approximately 80% of our recipients of living donor lungs, both adult and pediatric, have been transplanted for end-stage pulmonary failure secondary to cystic fibrosis. Other diagnoses include pulmonary hypertension, idiopathic pulmonary fibrosis, bronchopulmonary dysplasia, and obliterative bronchiolitis [7]. Seventy-five percent of adults and 50% of children were hospitalized, and 18% of patients were ventilator dependent at the time of transplantation. In Japan, where cystic fibrosis is rare, interstitial pneumonia is the most common diagnosis, followed by bronchiolitis obliterans, pulmonary artery hypertension, bronchiectasis, and lymphangioleiomyomatosis [3].

Donor Selection

Though living donor kidney and liver transplantation had been performed for some time prior to the first living donor lung transplant, the potential risks associated with pulmonary lobectomy, as well as the need for two healthy donors for each recipient, raised potential ethical issues not previously seen in organ transplantation. In their discussion of the ethics of living donor lung transplantation, Wells and Barr pointed out that donation of a pulmonary lobe by a living volunteer was incompatible with the pillar of medical ethics as established by the Hippocratic maxim “primum non nocere” (first do no harm) [8]. The absence of physical benefit to the donors, coupled with the potential for pain, surgical complications, and long-term pulmonary compromise, required a more complex set of moral theories. These were provided by Beauchamp and Childress [9], who put these issues into the perspective of four basic principles of biomedical ethics:

1. Respect for autonomy: respecting and accepting the decision-making capacity of the autonomous individual.
2. Nonmaleficence (non nocere): minimizing the causation of harm.
3. Beneficence: providing a benefit and balancing this against risk and cost.
4. Justice: fairly distributing benefits, risks, and costs.

Using this framework, it becomes ethically possible to identify healthy donors with adequate pulmonary reserve, appropriate motivation, and an understanding and willingness to accept the risks of donation. Our criteria for donation are as follows:

- Age ≤ 55 years
- No significant past medical history
- No recent viral infections
- Normal echocardiogram
- Normal electrocardiogram
- Oxygen tension > 80 mmHg on room air
- Forced expiratory volume in 1 s and forced vital capacity $> 85\%$ predicted

- No significant pulmonary pathology on computed tomography (completely normal on donor side)
- No previous thoracic operation on donor side

Whereas we originally considered only parents as appropriate potential donors, we have expanded our criteria to include siblings, extended family members, and occasionally unrelated individuals who can demonstrate an appropriate nonfinancial relationship to the recipient. Potential donors are carefully interviewed and analyzed from a psychological and social standpoint to determine their relationship with the recipient, motivation for donation, ability to withstand the pain and recovery from the operation, and their understanding and ability to withstand a potentially poor recipient outcome. They are also interviewed independently in order to identify potential evidence of coercion or other emotional issues that might exclude them from participating.

After determination of ABO blood group compatibility with the potential recipient, potential donors undergo an anatomic and physiologic evaluation to determine their suitability for donation, and to choose one donor to donate the right lower lobe, and another for the left lower lobe. The evaluation includes a room air arterial blood gas, spirometry, echocardiography, ventilation-perfusion (VQ) scan, and computed tomography (CT) scan of the chest to exclude pulmonary pathology and to allow volumetric assessment of the lobes being considered [10]. Considerable attention must be paid to matching a given recipient with donor lobes that provide adequate function and fit. Undersized lobes run the risk of providing inadequate pulmonary reserve, as well as pleural space problems such as persistent air leaks, pleural effusions, and empyema. Oversized lungs run the risk of atelectasis with subsequent pneumonia, decreased diaphragmatic excursion with poor ventilation, or compression of the contralateral side. Some centers use three-dimensional CT to determine size compatibility of donor lobes and to predict post-transplant graft forced vital capacity [11, 12]. The chest CT scan can also be used to identify anatomic features that can be used to assist in choosing a donor for one side over another. These features might include variations in pulmonary arterial or venous anatomy, or the degree of completeness of the pulmonary fissures. Unilateral pathology, such as small granulomas or blebs, or a history of previous thoracic surgery on one side does not necessarily exclude individuals from donating a lower lobe from the contralateral side.

Operative Description

Bilateral living donor lung transplantation requires the simultaneous use of three operating rooms and operative teams. The recipient operation is performed using cardiopulmonary bypass. In order to minimize both cardiopulmonary bypass time in the recipient as well as ischemic time of the donor lobes, the timing of the three operations is coordinated so that the donor lobes become available when needed by the recipient team. Unlike cadaveric transplantation, the donor teams are responsible for the safety and well-being of the donors, who are both healthy and heroic,

as well as for providing grafts that are anatomically and functionally transplantable. Thus, the mindset of the living donor pulmonary surgeon must be one of balance between donor safety and recipient outcome.

Donor Lobectomies

The technical aspects of donor lobectomies are significantly different from lobectomies performed for cancer or other pathology. The donor surgeons must provide the recipient surgeon with grafts containing bronchial and vascular cuffs that are sufficient for surgical implantation using standard surgical anastomotic techniques. At the same time, an adequate margin must be left on each donor side in order to close the lobar bronchus, pulmonary artery, and pulmonary vein without compromising the remaining lungs. Variations in pulmonary vascular and bronchial anatomy, combined with varying degrees of completeness of the pulmonary fissures, can make these procedures challenging. Great care is taken to handle and manipulate the donor lobes as little as possible in order to avoid parenchymal injury that might translate into pulmonary damage or dysfunction in the recipient.

After placement of an epidural catheter for postoperative analgesia, general anesthesia is induced and fiber-optic bronchoscopy performed to exclude bronchial pathology or identify variations in bronchial anatomy. After placement of a double-lumen endotracheal tube, donors are placed in the lateral decubitus position with the operative side up. An intravenous drip of prostaglandin E_1 is initiated and titrated to a systolic blood pressure of 90–100 mmHg in order to dilate the pulmonary vascular bed. A lateral thoracotomy incision is made and the pleural space entered through the fifth interspace. Though we usually start with a relatively small muscle-sparing incision, it is sometimes necessary to enlarge the incision in order to minimize handling of the lobe, as well as maximize safety when dissecting, transecting, and repairing the pulmonary artery and vein. After deflating the lung with the double-lumen endotracheal tube, the lung and pleural space are examined, and a time estimate forwarded to the recipient operating room. Using an atraumatic clamp on the lung for retraction, the inferior pulmonary ligament is incised up to the inferior pulmonary vein. The posterior mediastinal pleura is then incised from the inferior hilum to just below the takeoff of the upper lobe bronchus. After making sure that there are no branches draining either the middle or upper lobes into the inferior pulmonary vein, the inferior vein is circumferentially dissected. Care is taken not to manipulate or injure the phrenic nerve. The pericardium is then opened over the anterior aspect of the inferior pulmonary vein, and then incised circumferentially around the vein in order to maximize the amount of pulmonary venous cuff on the donor lobe. In fact, providing a donor graft with a small amount of left atrial cuff facilitates the venous anastomosis for the implanting surgeon. The pericardium will frequently be adherent to the inferior aspect of the inferior pulmonary vein, making dissection slightly more hazardous in that area. After this point, the dissections of the donor right and left lower lobes differ enough as to require that they be described separately.

Donor Right Lower Lobectomy

After dissecting the inferior pulmonary vein, the pulmonary artery is identified in the fissure between the middle and lower lobes. When the fissure between the middle and lower lobes is incomplete, the dissection is carried out on the middle lobe side of the fissure in order to minimize postoperative air leaks in the recipient. The pulmonary arterial trunk to the lower lobe is circumferentially dissected, identifying the middle lobe arteries as well as the artery to the superior segment of the lower lobe. The ideal anatomic configuration allows placement of a vascular clamp below the middle lobe arteries and above the superior segment artery, with sufficient margin to both close the donor artery as well as provide an adequate arterial cuff for implantation. Early in our experience, we removed and discarded the middle lobe in order to optimize the length of donor arterial cuff. This turned out to result not only in postoperative pleural space problems but also in a waste of donor pulmonary function. Since there are usually two arteries to the middle lobe, one of them can frequently be ligated and transected without significant consequences. We have also occasionally used either pericardial patch extension of the donor pulmonary artery or reimplantation of the middle lobe arteries with good results in order to preserve the middle lobe. It should be noted that the superior segment artery of the lower lobe provides pulmonary arterial flow to a significant portion of the donor lobe, and should be carefully identified and preserved when completing the fissure between the right lower and right upper lobes.

Once the lobar dissection has been completed and it has been determined that the recipient team is ready to receive the lobe, 10,000 units of heparin and 500 mg of methylprednisolone are administered intravenously, and the lung is reinflated and ventilated for 5–10 min to permit the drugs to circulate throughout the lung. During this time, a separate sterile table is set up to receive and perfuse the lobe with preservation solution prior to transporting it into the recipient operating room.

The right lung is then deflated once again so that explantation of the donor lobe can proceed. Once the pulmonary arterial and venous clamps are placed, initiating the graft ischemic time, the lobe is excised expeditiously but carefully and accurately. A difference of as little as a millimeter in vascular or bronchial cuffs can make a significant difference when implanting the donor lobe or closing the vascular and bronchial cuffs on the donor. In order to avoid vascular congestion, an angled vascular clamp is first placed across the donor pulmonary artery before clamping the pulmonary vein. A larger vascular clamp is then placed across the inferior pulmonary vein at the level of the left atrium. The inferior pulmonary vein is then transected, leaving a 2-mm cuff on the donor side that can be safely sutured once the lobe has been removed. Suction should be readily available to keep the blood coming from the partially transected pulmonary vein from obscuring the exposure, so that neither side of the transected vessel will be compromised. The pulmonary artery is then transected in the same fashion, exposing the underlying lobar bronchus.

After identifying the bronchus to the middle lobe, the bronchus to the lower lobe is carefully divided (Fig. 5.2). A no. 15 scalpel is used to open the bronchus just

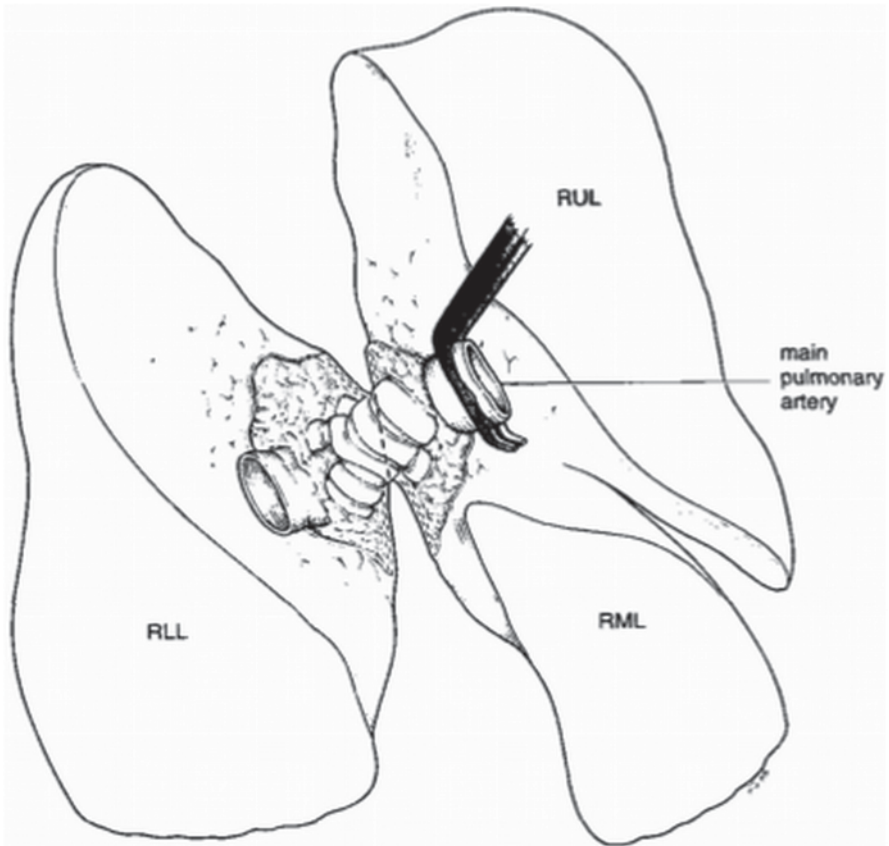


Fig. 5.2 Dissection for donor right lower lobectomy. After transecting the pulmonary artery, a diagonal incision is made across the bronchus to the right lower lobe, being careful not to compromise the right middle lobe bronchus. *RUL* right upper lobe, *RML* right middle lobe, *RLL* right lower lobe. (Reprinted from [13], Copyright 1994)

enough to visualize the inside of the airway, including the takeoff of the bronchus to the superior segment. The remainder of the bronchus is then incised. The angle of the bronchial incision is critical, providing enough bronchial cuff for implantation without compromising the bronchus to the middle lobe. The lobe is then quickly moved to the preservation table for perfusion and then transported to the recipient operating room.

The stump of the donor pulmonary vein is repaired with a double running over-sew stitch of 4-0 polypropylene. The pulmonary artery is repaired with a similar double suture using 6-0 polypropylene. Recently, instead of clamping the pulmonary artery and vein, we have had good results with occluding them with the TA-30 vascular stapler (Ethicon Inc.), and transecting those vessels on the graft side of the staple line. This eliminates the need for suture closure of the vascular stumps once the graft has been removed.

After excising the cartilaginous spur at the takeoff of the middle lobe bronchus, the donor bronchus is closed with interrupted 5-0 polypropylene sutures. Excising the cartilaginous spur allows the bronchus to be closed without any tension on the suture line. The pleural space is then irrigated with saline solution and the bronchial stump tested to 30 mmHg with positive pressure ventilation. Two chest tubes are closed and the chest closed in multiple layers.

Donor Left Lower Lobectomy

The initial steps of the donor left lower lobectomy, from positioning and incision through the dissection of the inferior pulmonary vein, are similar as for the right side. Whereas we have seen a more anatomical variation in pulmonary arterial anatomy on the right side, the left donor lobectomy can be challenging due to an incomplete fissure between the left upper and lower lobes, making the separation of the lobes and the identification of the pulmonary artery more difficult. Once the pulmonary artery is identified in the fissure, the superior segmental artery to the lower lobe and anteriorly positioned lingular artery to the upper lobe are identified. The lingular artery may be ligated and divided if it is relatively small and if its location would preclude creating an adequate pulmonary arterial cuff on the donor graft.

After completing the vascular dissection and completing the fissures with staplers, the lung is reinflated and heparin and methylprednisolone are administered. The lung is then deflated, and the pulmonary artery to the lower lobe and inferior pulmonary vein are then occluded with vascular clamps and divided in a fashion similar to the right side (Fig. 5.3). Once the pulmonary artery is divided, the bronchus is exposed and followed superiorly in order to identify the lingular bronchus. The incision on the bronchus begins at the base of the upper lobe bronchus and is carried in a tangential fashion to a spot just superior to the bronchus of the superior segment of the lower lobe. The donor left lower lobe graft is then immediately taken to the preservation table and then either briefly stored in an ice-filled cooler or taken to the recipient operating room for immediate implantation.

Donor Lobe Preservation

Because the donor lobes are harvested simultaneously with the recipient operation at the same institution, ischemic times are shorter for living related lung transplantation when compared with cadaveric lung transplants where the donor is harvested at a distant site. However, in situ flushing of the donor lobes with cold preservation solutions is not possible. This required a separate strategy for post-explantation preservation of the donor lobes. As previously mentioned, a continuous intravenous prostaglandin infusion is initiated at the beginning of the donor lobectomy operation. Once a donor lobe is excised, it is immediately taken to a separate sterile table where it is immersed in a cold crystalloid solution. Care is taken to protect the solution from entering the lobar bronchus. The pulmonary artery, vein, and bronchus are

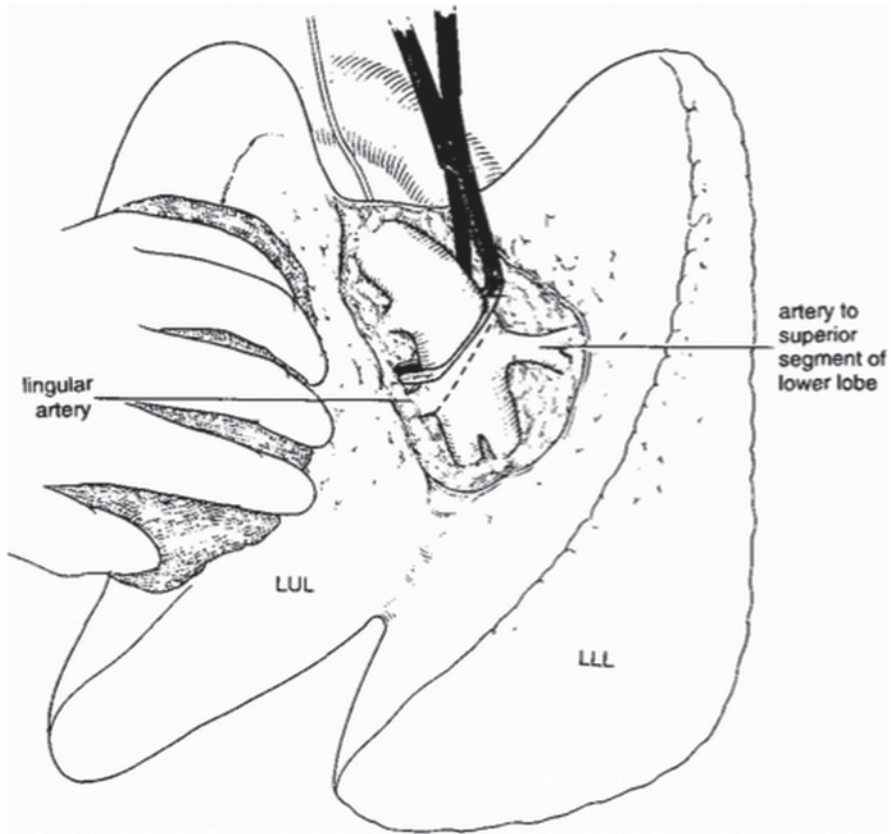


Fig. 5.3 Clamp placement for transection of pulmonary artery on donor left lower lobectomy. *LUL* left upper lobe, *LLL* left lower lobe. (Reprinted from [13], Copyright 1994)

handled with care. The lobar pulmonary artery trunk, which is short and branches early, is cannulated and gently perfused with cold Perfadex (low potassium, dextran, and glucose) solution. The bronchus is simultaneously cannulated and the lobe ventilated, using a manometer to inflate the lobe to a pressure of 20–25 mmHg. The lobe should quickly turn from pink to white and the pulmonary venous effluent from bloody to clear as the lobe is flushed. Selective cannulation of a branch pulmonary artery with a preservation solution or of a branch bronchus with a smaller cannula may be necessary to ensure that all segments of the lobe are both ventilated and perfused. We also routinely perfuse the lobe retrograde through the pulmonary venous stump with 200–300 cc of Perfadex to assure that all parts of the lobe are adequately preserved. Once approximately 1 L of Perfadex has been infused and the entire lobe is homogeneously white, it is approximately 75% inflated with the endobronchial cannula. A small vascular clamp is then gently placed across the bronchus as the cannula is quickly removed, and the partially inflated graft is placed in a sterile bag filled with cold storage solution. The lobe is then transported to the recipient operation room in an ice-filled cooler for implantation.

Recipient Operation

The recipient operation takes place in a third operating room with the patient in the supine position. The arms are carefully padded, extended, and abducted, and secured to a frame over the face. A bilateral submammary incision (clamshell) is made in the fourth interspace, and the sternum transected in a transverse fashion with an oscillating saw. The internal mammary arteries and veins are identified and carefully clipped or ligated. All recipient operations are performed on cardiopulmonary bypass without cooling. This facilitates and expedites the recipient pneumonectomies, optimizes surgical exposure, and allows for simultaneous reperfusion of both donor lobes. The pulmonary artery and veins are dissected and, if possible, transected at the level of the lobar branches in the hilum of the lungs. This allows the recipient surgeon the option of performing the vascular and bronchial anastomoses between the donor and lobar grafts, using donor structures that more closely approximate the size of the donor lobes. After the recipient pneumonectomies are completed, the pleural spaces are carefully inspected to achieve hemostasis, and then copiously irrigated with antibacterial and antifungal solutions.

It is usually not important which donor lobe is implanted first. The lobe is wrapped in iced, saline-soaked sponges and placed in the recipient pleural space with its hilum aligned with the hilum of the recipient. The bronchial anastomosis is performed using running 4-0 polypropylene sutures, aligning both donor and recipient cartilaginous and membranous bronchi as much as possible (Fig. 5.4). The lobar donor vein is then anastomosed to the superior pulmonary vein of the recipient using a 5-0 polypropylene suture. The suture on the pulmonary venous anastomosis is not tied so that the preservation perfusate can be allowed to escape when initially reperfusing the grafts. The pulmonary artery anastomosis is then performed, also with a 5-0 polypropylene suture. The first lobe to be implanted is then rewrapped in iced sponges and the contralateral implantation performed in a similar fashion.

After completing the bilateral implants, attention is focused on gently reperfusing the grafts. Continuous nitric oxide is initiated at 20 ppm via the anesthesia circuit, as are intermittent doses of aerosolized bronchodilators. The pulmonary venous clamps are removed, followed by the pulmonary arterial clamps. As the lobes begin to reperfuse, the remaining perfusate is allowed to escape from the pulmonary venous anastomoses before tying the sutures. The lungs are then gently inflated by hand bagging, and cardiopulmonary bypass weaned to half flow for approximately 10 min. This regulates the amount of systemic and pulmonary blood flow as the donor grafts are gently reperfused. The recipient is then weaned from cardiopulmonary bypass, and the pulmonary venous flow evaluated with transesophageal echocardiography to assure patency of the venous anastomoses. Bronchoscopy is then performed to remove secretions and to evaluate the patency of the bronchial anastomoses. The recipient is decannulated and the chest closed.

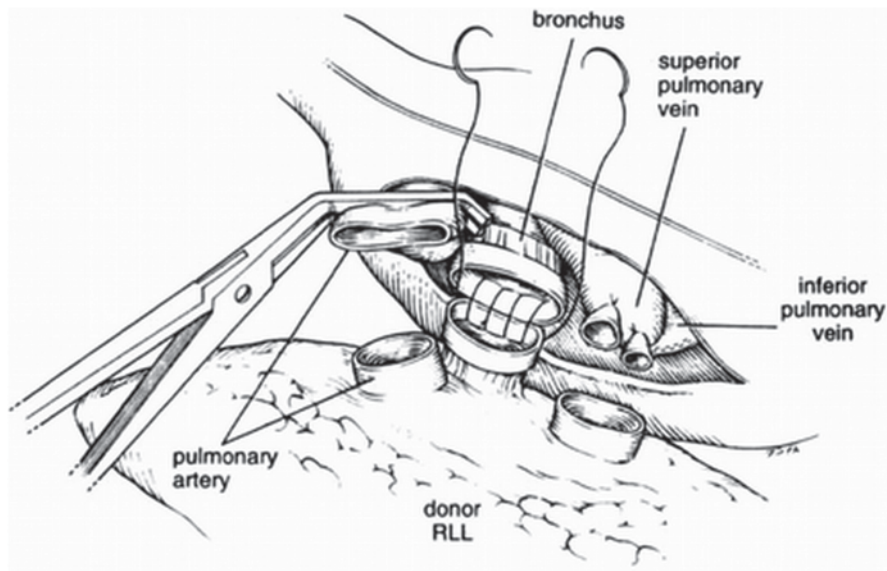


Fig. 5.4 The recipient bronchial anastomosis. (Reprinted with permission from [1])

Postoperative Management

Donor Management

For the most part, donor management is focused on pain control, management of the pleural space on the operative side, prevention of postoperative complications including pulmonary emboli and wound infections, and emotional support. Continuous epidural infusions under the supervision of the anesthesia pain service are the mainstay of pain control. The epidural can be supplemented with nonsteroidal anti-inflammatory agents or oral narcotics as necessary. Epidural catheters are usually removed when a donor's pain is well controlled and the chest tubes have been removed.

Pleural tubes are initially maintained on a suction apparatus but are placed on water seal and then removed when there is no air leak and daily drainage falls below 200 cc/day. Early in our experience, prolonged air leaks (>7 days) and pleural space problems presented a challenge, especially when both the right middle and lower lobes were removed due to anatomical issues. Prolonged air leaks have become uncommon as we learned to identify potential donors with complete fissures on chest CT, and as we gained more experience with the donor operation.

Emotional support for donors is an important and potentially complicated aspect of living donor lung transplantation. Though significant attention is focused on the preoperative evaluation and education of donors, there is no sufficient way to describe the physical and potential emotional pain that can ensue. This is particularly

true when the recipient has a complicated postoperative course, or when a donor's lobe functions poorly, gets infected, or develops rejection in the recipient. When this occurs, a donor's sense of altruism can easily be replaced by guilt. The most dreaded scenario is when a recipient dies in the peri- or postoperative period, leaving the donors to potentially feel as if they have endured significant pain and inconvenience in vain. It is extremely important that a living donor lung transplant program be staffed with social workers, psychologists, and psychiatrists who are prepared for the unique emotional aspects of living donor transplantation. Furthermore, the entire transplant team should be trained to be particularly sensitive to the potential for these issues.

Recipient Management

The pulmonary physiology and early postoperative management of living donor lung transplant recipients is significantly different than for recipients who receive bilateral whole lung cadaveric grafts. Because the pulmonary volumes and vascular beds of the combined transplanted lobes are significantly less than cadaveric lungs, care must be taken to carefully control both ventilation and perfusion of the transplanted lobes. Recipients remain sedated and on the ventilator for at least 48 h, with positive end-expiratory pressures maintained at no more than 5–10 cm H₂O. Because of the potential size mismatch between the donor lungs and recipient pleural space, we have found that conventional chest tube suction at 20 cm H₂O can impair deflation of the transplanted lobes during expiration. This can result in air trapping, increased airway pressures, and increased pulmonary vascular resistance. These phenomena can be prevented by applying what is known at our institution as the “chest tube dance” for the first 24 postoperative hours. Low-level suction (10 cm H₂O) is applied sequentially to each tube, rotating at 1-h intervals. When suction is not being applied to a chest tube, it is placed to water seal. After 24 h, all tubes are placed to suction that is gradually increased to 20 cm H₂O over the subsequent 48 h. Because the transplanted lobes may not completely fill the pleural spaces, chest tube output and the need for prolonged drainage are not uncommon. It is not unusual for chest tube drain to be maintained for 2–3 weeks.

The pulmonary vascular bed of the transplanted lobes is limited when compared with cadaveric lungs. In order to prevent pulmonary edema secondary to overperfusion, recipients are managed in a relatively hypovolemic state, with systemic blood pressures in the range of 90 mmHg. An intravenous nitroglycerin infusion as well as continuous aerosolized nitric oxide are administered for the first 48–72 h of the postoperative period.

Immunosuppression, antibiotic therapy and prophylaxis, and follow-up in our transplant clinic with imaging and pulmonary function testing are similar as for standard cadaveric lung transplant recipients. Bronchoscopy is performed only when clinically indicated by symptoms, changes on imaging, or a decrease in spirometry. Because of the danger of significant parenchymal bleeding, we are reluctant to do transbronchial biopsies unless absolutely necessary.

Clinical Results

Since introducing bilateral living donor lung transplantation in 1992, we have accumulated the largest experience with this procedure in the U.S. at the University of Southern California and Children's Hospital Los Angeles, followed by Washington University in St. Louis. The primary indication for transplantation in the great majority of the patients in the U.S. has been cystic fibrosis, with the remaining recipients having a variety of other diagnoses, including primary pulmonary hypertension and pulmonary fibrosis. At the time of transplantation, many of the patients were critically ill, with most being hospital bound and a significant number being ventilator dependent. Overall, recipient survival in the US cohort has matched that of the International Society for Heart and Lung Transplantation (ISHLT) registry data. Deaths occurring within 30 days of transplantation have been largely due to infection or primary graft failure. Deaths occurring between 30 days and 1 year after transplantation have usually been due to infectious etiologies. Deaths greater than 1 year after transplantation have been predominantly due to infection or bronchiolitis obliterans syndrome. As opposed to cadaveric double lung transplantation in which rejection almost always presents in a bilateral fashion, rejection episodes in the lobar recipients have been predominantly unilateral. There has been no clear pattern with regard to which lobe will be rejected based on the preoperative human leukocyte antigen (HLA) donor-recipient match. Those patients on ventilators preoperatively had significantly worse outcomes [7].

A study of postoperative pulmonary function testing has demonstrated a steady improvement in pulmonary function in those recipients surviving greater than 3 months during the first 12 months post-transplant, which is comparable to cadaveric lung transplant recipients. Maximum workloads at peak exercise, maximum heart rates, peak VO_2 , and the ability to maintain oxygen saturation were also similar between living lobar and cadaveric lung transplant recipients. Hemodynamic assessment at 1-year follow-up in a subset of patients demonstrated normal pulmonary arterial pressure and pulmonary vascular resistance, confirming the ability of two lobes to accept a normal cardiac output [14].

With the adoption of the lung allocation score (LAS) system in the U.S. that was instituted in the spring of 2005, the number of lung transplants utilizing living donors steadily decreased over the ensuing 8 years to the point that this operation is now performed only once or twice per year at our institution. However, during the past 10 years, outside of the U.S., this procedure has played a significant role in countries in which there are low rates of deceased donation due to cultural, religious, or legislative barriers to organ availability. Increasing numbers of centers are performing the procedure, with Japan having the greatest annual volumes and smaller activity in Brazil, Canada, China, and parts of Europe. The most recent reports from Japan in a cohort of 100 transplants have yielded an excellent 5-year recipient survival of 81%, which equals or exceeds any other published survival rates in the field of lung transplantation, regardless of the donor source [15].

With regard to the donors, short-term outcomes were studied by the Lung Working Group of the Vancouver Forum which compiled and published a retrospective

review of 550 live lung donors, which constituted 98% of the global experience at that time. In that study, there was no reported perioperative mortality of a lung donor. There were life-threatening complications in 0.5% including intraoperative ventricular fibrillation arrest and postoperative pulmonary artery thrombosis. The mean length of the initial hospitalization following the lung lobectomy was 8.5 days. Approximately 4% experienced an intraoperative complication that included ventricular fibrillation arrest, the necessity for right middle lobe sacrifice, the necessity for right middle lobe reimplantation, the necessity of nonautologous packed red blood cell transfusion, and permanent phrenic nerve injury. Approximately 5% experienced complications requiring surgical or bronchoscopic intervention. These complications included bleeding, bronchopleural fistula, pleural effusion, empyema, bronchial stricture, pericarditis requiring pericardiectomy, arrhythmias requiring ablation, and chylothorax. As much as 2.6% of the live lung donors were readmitted to the hospital because of pneumothorax, arrhythmia, empyema, pericarditis, dyspnea, pleural effusion, bronchial stricture, bronchopleural fistula, pneumonia, hemoptysis, or dehydration. The long-term (defined as greater than 1 year) donor complaints, which were not qualified or quantitated in that study, included chronic incisional pain, dyspnea, pericarditis, and nonproductive cough [16].

In response to the lack of high-quality follow-up information, the National Institute of Allergy and Infectious Diseases (NIAID) is funding an ongoing study of the majority of those individuals who were living lung donors in the U.S. from 1993 to 2006. Preliminary results were recently reported for the retrospective cohort study that assessed short-term morbidity and mortality utilizing the Social Security Death Master File and Scientific Registry of Transplant Recipients databases in 369 lobar donors. A total of 15.7% had in-hospital postoperative complications and 6.5% had a related rehospitalization within 30 days after the donation hospitalization day of discharge. There were no mortalities with a minimal follow-up of 4 years and a maximum of 17 years [17]. The prospective cross-sectional study is currently underway to assess the long-term lung function and psychosocial outcomes [18].

Conclusion

Bilateral living donor lung transplantation has evolved into an alternative to cadaveric lung transplantation for selected patients with end-stage pulmonary diseases, and has been potentially lifesaving for hundreds who might have died while waiting for transplantation with cadaveric donor lungs. The process of evaluating both potential donors and recipients requires a multidisciplinary team with the capacity to address ethical and psychosocial issues, in addition to the medical and surgical issues commonly associated with lung transplantation. Though recipients receive significantly less pulmonary reserve than with cadaveric whole lung transplantation, current results have proven to be adequate for most recipients. The living donor lobectomy has proven to be safe and well tolerated by most donors, though the truly long-term sequelae of being a living lung donor are currently being examined.

References

1. Starnes VA, Barr ML, Cohen RG. Lobar transplantation: indications, technique, and outcome. *J Thorac Cardiovasc Surg.* 1994;108:403.
2. Egan TM, Murray S, Bustami RT, Shearon TH, McCullough KP, Edwards LB, et al. Development of the new lung allocation system in the United States. *Am J Transplant.* 2006;6:1212.
3. Date H. Update on living-donor lobar lung transplantation. *Curr Opin Organ Transplant.* 2011;16:453–7.
4. Date H, Aoe M, Sano Y, Goto K, Kawada M, Shimizu N. Bilateral living-donor lobar lung transplantation. *Multimedia manual of cardio-thoracic surgery.* 2005 Jan 1;2005(0809).
5. Orens JB, Estenne M, Arcasoy S, Conte JV, Corris P, Egan JJ, et al. International guidelines for the selection of lung transplant candidates: 2006 update—a consensus report from the Pulmonary Scientific Council of the International Society for Heart and Lung Transplantation. *J Heart Lung Transplant.* 2006;25:745.
6. Barr ML, Starnes VA. Living Lobar Lung Transplantation. In: Sugarbaker DJ, Bueno R, Krasna MJ, Mentzer SJ, Zellos L, editors. *Adult Chest Surgery.* 2nd ed. New York: McGraw Hill; 2013.
7. Starnes VA, Bowdish ME, Woo MS, Barbers RG, Schenkel FA, Horn MV, et al. A decade of living lobar lung transplantation: recipient outcomes. *J Thorac Cardiovasc Surg.* 2004;127:114.
8. Wells WJ, Barr ML. The ethics of living donor lung transplantation. *Thorac Surg Clin.* 2005;15:519.
9. Beauchamp TL, Childress JF. *Principles of biomedical ethics.* 5th ed. New York: Oxford University Press; 2001.
10. Cohen RG, Barr ML, Starnes VA. . In: Shumway SJ, Shumway NE, editors. *Lobar Pulmonary Transplantation. Thoracic Transplantation.* Cambridge, MA: Blackwell Science; 1995.
11. Kojimma K, Kato K, Oto T, Mitsuhashi T, Shinya T, Sei T, Okumura Y, et al. Preoperative graft volume assessment with 3D-CT volumetry in living-donor lobar lung transplantations. *Acta Med Okayama.* 2011;65(4):265–8.
12. Camargo JJP, Irion KL, Marchiori E, Hochhegger B, Hochhegger B, Porto NS, Moraes BG, et al. Computed tomography measurement of lung volume in preoperative assessment for living donor lung transplantation: Volume calculation using 3D surface rendering in the determination of size compatibility. *Pediatr Transplantation.* 2009;13:429–39.
13. Cohen RG, Barr ML, Schenkel FA, DeMeester TR, Wells WJ, Starnes VA. Living-related donor lobectomy for bilateral lobar transplantation in patients with cystic fibrosis. *Ann Thorac Surg.* 57:1423–8.
14. Bowdish ME, Pessotto R, Barbers RG, Schenkel FA, Starnes VA, Barr ML. Long-term pulmonary function after living-donor lobar lung transplantation in adults. *Ann Thorac Surg.* 2005;79:418–25.
15. Egawa H, Tanabe K, Fukushima N, Date H, Sugitani A, Haga H. Current status of organ transplantation in Japan. *Am J Transplant.* 2012;12:523.
16. Barr ML, Belghiti J, Villamil FG, Pomfret EA, Sutherland DS, Gruessner RW, et al. A report of the Vancouver Forum on the care of the live organ donor: lung, liver, pancreas, and intestine data and medical guidelines. *Transplantation.* 2006;81:1373–85.
17. Yusef RD, Hong B, Murray SK, et al. Morbidity and mortality of 369 Live Lung Donors. *Am J Transplant.* 2011;11 Suppl 2:49.
18. Barr ML. 5UO1AI069545-05. http://projectreporter.nih.gov/project_info_description.cfm?aid=7899950&icde=11981871&ddparam=&ddvalue=&ddsub=&cr=1&csb=default&cs=ASC.