Lobar Transplantation

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Key Points

- Donor organ shortage remains a major problem in lung transplantation and many patients die on the waiting list.
- The estimated total lung capacity of the donor is recommended to be 75–125% of the recipient's predicted total lung capacity.
- An acceptable range of donor total lung capacity should be determined by radiological and physiological assessments.
- Size mismatch between donor lung and recipient thoracic cavity volume can have an important impact on outcomes.
- Problems of oversized graft include suboptimal chest wall mechanics, a tamponade effect and aatelectasis.
- Lobar lung transplantation is a technique applied in pediatric and adult patients in need of smaller-sized donor lungs.

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Cadaveric Lobar Lung Transplantation

Since the first successful single lung transplantation performed by Cooper et al. in 1983, lung transplantation (LTx) has gained an important place in the treatment of late-stage lung diseases. With the increase in the number of LTx over the years, survival rates have gradually improved. However, since the number of cadaver donor lungs has not increased at a sufficient level in parallel with the increase in the number of potential transplant candidates, there are problems in finding compatible donors. End-stage lung disease patients, and especially patients with small thoracic cavity such as in pulmonary fibrosis and cystic fibrosis, have to wait longer times for donor lungs of compatible sizes.

The use of cadaveric lobar lung transplantation is gradually increasing in an attempt to expand the pool of potential donors for patients who have worsened during the long waiting periods or who are in a critical condition. However, although lobectomy is a well-known standard and simple method, lobar lung transplantation is not routinely performed. In 1994, Bisson et al. reported the first cadaveric bilateral lobar lung transplantation in two recipients with cystic fibrosis. In these cases, they transplanted the left lower lobe and the right lower and middle lobes [1]. Subsequently, together with other

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centers, they reported their experiences on donor lung size reduction [2].

Anatomic Size Matching Between Donor and Recipient

Size compatibility is an important issue for lung transplantation that has an important impact on the clinical results. Size mismatch has been shown to be associated with longer lengths of stay on the intensive care unit, permanent atelectasis, expansion defects, hyperinflation, decreased exercise capacity and obliterative bronchiolitis syndrome [3].

The best size matching method is still a matter of debate. Commonly used strategies include chest X-ray comparison between donor and recipient; calculation of the ratio of patient heights; calculation of the predicted total lung capacity (pTLC) ratio; and estimation based on visual examination in the operating room [4] (Picture 1). Three-dimensional computed tomography (3D-CT) volumetry is a new and reliable method for the evaluation of lung volume. It has been shown that the total lung capacity (TLC) calculated using 3D-CT volumetry is well correlated with the lung volume measured by the use of spirometry, and that it can be used in the evaluation of respiratory function [5, 6].

It has been shown that if the donor pTLC is between 75 and 125% of the recipient pTLC, there will be no clinical or functional negative effects observed following heart-lung transplantation and bilateral lung transplantation [4–7]. Prediction of the donor TLC is important for optimum size matching and different methods have been recommended to this end.

For cadaveric LTx, it is possible to predict the donor TLC using a formula based on donor height and gender [8].

Donor pTLC (liters);

$$\text{For male donors, pTLC} = 7.99 \times \text{height in meters} - 7.08$$

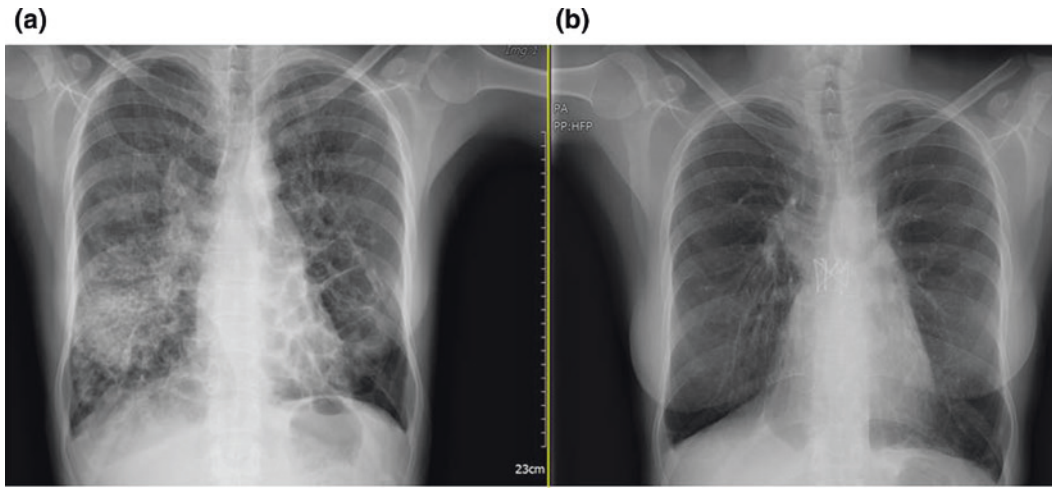
$$\text{For female donors, pTLC} = 6.6 \times \text{height in meters} - 5.79.$$

In order to calculate the total lung capacity of a lung after a certain number of segments has been resected (sr-TLC):

$$\text{sr-TLC} = \text{pTLC} \times (1 - \text{S} \times 0.0526),$$

$$\text{S} = \text{number of resected segments}$$

Published standard reference equations based on height and age can also be used for size matching of the lung between the donor and the recipient [9, 10].



Picture 1 **a** Preoperative chest X-ray. **b** 1 year postoperative X-ray

For adult male donors: TLC = 0.094 × height (cm) − 0.015 × age (years) − 9.167

For adult female donors: TLC = 0.079 × height (cm) − 0.008 × age (years) − 7.49

For donors of age ≤ 16 years old: TLC = 0.001002 × (height^2) − 0.22713 × height + 15.1397

However, volume predictions based only on age or height can be misleading. The thoracic volume of children is different compared to adults, and the thoracic cavity tends to be larger in male patients. Disease diagnosis of the recipient can also influence the thoracic volume. For instance, the thorax cavity is larger in patients with emphysema, while being smaller in patients with fibrotic conditions. In patients who develop pulmonary hypertension, lung volume can decrease due to cardiomegaly [4]. It is unclear whether the donor pTLC has any predictive value on the postoperative recipient lung function, especially in cases where the donor lung size has been reduced.

Surgical Technique

Due to the limited donor pool, volume reducing operations can be performed on larger donor lungs instead of turning down these organs. Of the available techniques, peripheral wedge resection is the most commonly performed, targeting the middle lobe or lingual segment. However, prolonged air leak is a significant risk with this approach. Loizzi et al. reviewed recipient who had standard lung and lobar transplantation, and concluded that the donor/recipient pTLC ratio should have an upper limit of 1.15–1.20, and that lobar transplantation should be performed in case it is >1.20 [11].

Anatomic resections such as segmentectomy, lobectomy and bilobectomy can be performed. Lobar and split-lung transplantation are the other options.

When an unexpected size mismatch is encountered during the transplant, there can be a dilemma of which technique to apply. Middle lobectomy decreases the donor lung capacity in the anteroposterior aspect, and is most appropriate for thin recipients that have a smaller anteroposterior diameter. Lower lobectomy is more appropriate for recipients with a high diaphragm, e.g. patients with pulmonary fibrosis. Upper lobectomy decreases the donor lung volume in the vertical aspect; however, with the residual lung parenchyma mainly below the hilum, this has the potential for creating an apical gap. Tackling a basal gap is generally easier compared to an apical gap, since the diaphragm can simply move upwards in the latter situation. Which lobe is to be excised should also take into account of the condition of the donor lung, such as severe contusion of the lower lobe, bullous disease or scarring of the upper lobe.

Size reduction lobectomy can be performed back-table or after implantation. Back-table lobectomy saves time, since it can be performed by another surgeon simultaneously with the preparation of the recipient. Furthermore, it avoids the situation of a large donor lung obscuring the view of the hilum within a small chest cavity. Finally, back table dissection allows for direct anastomosis between the donor lobar bronchus and recipient main bronchus. Therefore, the bronchial stump that is unavoidable in post-transplantation lobectomy does not occur in back-table lobectomy. However, with the lack of blood circulation in the pulmonary vessels, back-table lobectomy can sometimes be difficult. On the other hand, performing post-transplantation lobectomy can also be challenging due to having an oversized lung within a small chest cavity. Another disadvantage of post-implant lobectomy is that it can cause further injury to the transplanted lung through surgical manipulation of the recently reperfused lung.

Upper lobectomy of the donor lung is performed in order to transplant the middle and lower lobes on the right side. In this technique, the oblique fissure is dissected and the interlobar pulmonary artery is prepared. The upper lobe vein is then divided in such a way that does not distort the atrial cuff, which includes both the

superior and inferior veins. The upper part of the oblique fissure between the upper and lower lobes and the horizontal fissure between the upper and middle lobes can be separated with a stapler. Upper lobe branches of the pulmonary artery are dissected free, ligated and divided. The donor intermediary bronchus is transected only one ring above the apical segmental bronchus of the lower lobe, and attention is paid to preserving the peribronchial connective tissue. The main advantage of transplanting the lower and middle lobes is a reasonable size match between the diameter of the donor intermediary bronchus and the recipient main bronchus. The biggest disadvantage is the risk of distorting the inferior pulmonary vein. A large pericardial cuff or donor aorta graft can be used to widen the donor left atrial cuff to protect the venous flow from the middle lobe (Picture 2). The donor pulmonary artery should be kept long enough to allow anastomosis without any tension.

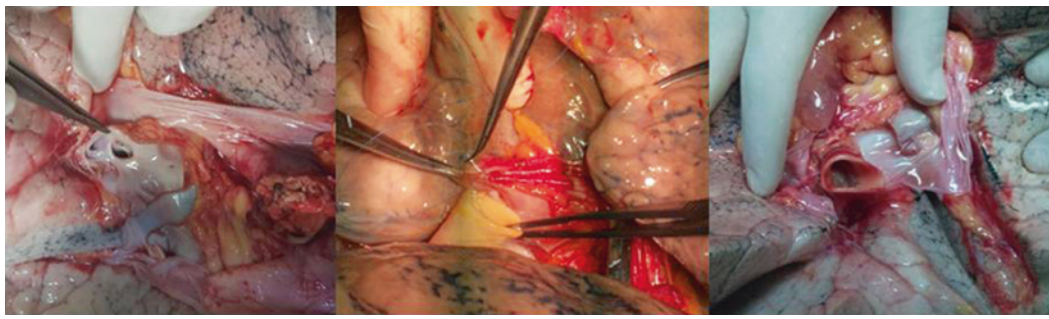
To implant the right upper lobe only, the oblique fissure is separated, and the interlobar pulmonary artery and middle lobe artery are dissected and divided while protecting the posterior ascending artery. The inferior and middle veins are dissected, ligated and divided taking care not to distort the left atrial cuff. The upper lobe bronchus is divided at its origin on the donor main bronchus.

To implant the upper and lower lobes only, the middle lobe is resected. The middle lobe vein and artery are dissected, ligated and divided. If the transverse fissure is incomplete, the upper and middle lobes can be separated using a stapler. The middle lobe bronchus is divided with the stapler; the main donor bronchus is divided one ring above the secondary carina.

To implant just one lobe from the left lung and excise the other lobe, the oblique fissure is opened and parenchymal attachments between the upper and lower lobes are divided with a stapler. The interlobar pulmonary artery is exposed. To implant the left lower lobe alone, the left upper lobe is excised by ligating and dividing arterial branches to the upper and lingual lobes. The superior pulmonary vein is disconnected from the left atrial cuff without distorting the latter. The left lower lobe bronchus is divided one ring proximal to the apical segment bronchus of the lower lobe.

To implant the left upper lobe only, the left lower lobe is excised by ligating and dividing arterial branches to the lower lobe. The inferior pulmonary vein is disconnected from the left atrial cuff without distorting the latter. The upper lobe bronchus is divided at the level in which it connects with the main bronchus.

Perioperative management and postoperative care in lobar LTx differ from that of standard LTx. Patients who are candidates for lobar LTx tend to be higher risk recipients. Following implantation of the first lobe and during the pneumectomy dissection of the second native lung, almost all the cardiac output goes to the implanted lobe. The limited vascular bed of the recently reperfused lobe together with the sudden surge in blood flow frequently result in increased pulmonary pressure, extravascular



Picture 2 Donor lung atrium injury and reconstruction with aortic graft

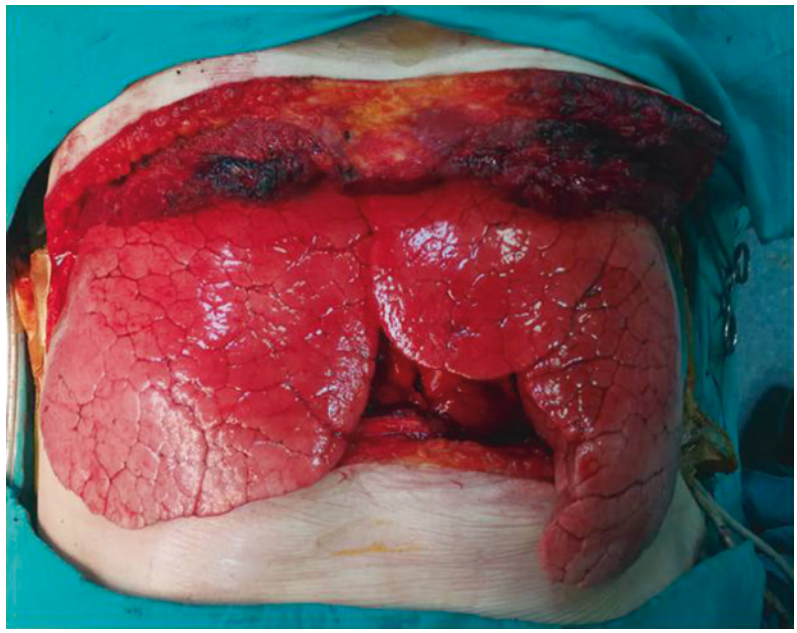
fluid leakage and lung edema. Cardiopulmonary bypass (CPB) limits the pulmonary blood flow during this time and could prevent overloading of the pulmonary vascular bed [12]. In recent times, the use of peripheral or central venoarterial ECMO, which requires less heparin, has been favored over the use of CPB [13, 14].

Split implantation of the left donor lung has also been described. The donor left lower lobe was implanted in the recipient's left thorax cavity and the left upper lobe was implanted into the right. The right donor lung can then be transplanted into another patient thereby making the best use of the available donor lungs [15, 16].

Oversized and Undersized Graft

In LTx, inappropriate size match could negatively impact post-transplant outcomes and survival. It has been shown that an excessively large graft could result in atelectasis, distorted diaphragm movement, high pulmonary vascular resistance and impaired gas exchange through shunting. Greater attention should be paid to size matching, especially for emphysematous patients in which the chest wall and diaphragm movement are distorted and hyperventilation is predominant. If there is uncertainty regarding the resection size required, or the recipient becomes unstable on attempts at chest closure, the chest wall can be left open, with only skin closure [17]. The amount of size reduction can be subsequently decided once the lung reperfusion edema has settled and the transplanted lung has adapted to the recipient chest cavity. This will help prevent the post-transplantation respiratory problems associated with the resection of too much lung tissue (Picture 3).

The most common complication observed immediately after LTx is primary graft dysfunction (PGD). This manifests within the first 72 hours after LTx through widespread pulmonary infiltrates and hypoxia. Implanting an undersized donor lung into a large chest cavity and mechanical ventilation with high tidal volume caused by size mismatch early is an important risk factor [18]. Small grafts can also lead to increased risk of postoperative bleeding and higher pulmonary vascular resistance, persistent pleural spaces, pleural effusion and infection.



Picture 3 Delayed chest closure after lung transplantation

It has been demonstrated that oversizing lungs can increase survival in the presence of pulmonary hypertension. Eberlein et al. found that the median survival of LTX recipients with donor/recipient pTLC ratio of 1.24 ± 0.1 is 831 days longer when compared to patients with D:R pTLC ratio of 0.93 ± 0.1 [19].

Conclusion

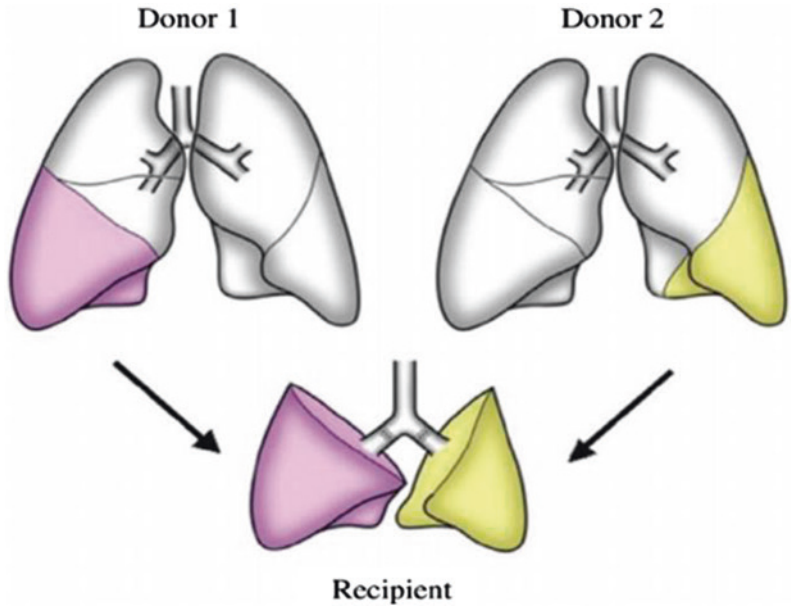
Results reported by various groups show that lobar lung transplantation can be performed with an acceptable level of risk in patients that have an urgent need for small donor organ, so as to decrease the mortalities observed while these patients are waiting.

Living Donor Lobar Lung Transplantation

Key Points

- Lobar lung transplantation from a live donor can be life-saving for recipients with end-stage lung disease who cannot be expected to survive until a cadaveric organ becomes available due to deterioration of lung function and clinical conditions.
- Lobar lung transplantation is an alternative to cadaver lung transplantation.
- The right and left lower lobes from two separate larger donors are implanted in the recipient instead of the whole right and left lung.
- The most important feature that distinguishes donor lobectomy from standard lobectomy is the preservation of adequate arteries, veins and bronchial stumps, which allows the anastomoses to be performed at the implantation stage.
- The ideal timing for offering living donor lobar lung transplantation is controversial.
- Because of the surgical risks that the live donors are exposed to through donating one of their lobes, cadaver lung transplantation is preferred. However, live lobar lung transplantation should continue to be considered in appropriately selected cases.

Lobar lung transplantation from live donor was first described by Starnes et al. [20] for pediatric patients with an urgent indication for LTx.



Picture 4 The right lower lobe from the first donor is on the right side of the recipient, the left lower lobe from the second donor is implanted on the left side [24]

In this procedure, the right lower lobe is taken from one of the two adult live donors whilst the left lower lobe is taken from the other donor, and both are then implant into the recipient (Picture 4). Since this procedure requires two healthy donors to undergo lobectomy and exposing them to major surgical risks, living donor lobar lung transplantation (LDLLT) potentially puts three people at risk while only offering the chance to improve the quality of life for one [22]. This has at times raised ethical concerns. The transition to the lung allocation scoring system in the United States has brought with it a decrease in the waiting list mortality [21]. This has in turn led to a decrease in the use of LDLLT. Although its use is decreasing worldwide, centers in Japan have continued to perform this procedure and further developing it due to the rarity of cadaveric organ donors in that country [23].

Patient Selection

Similar criteria apply for the selection of candidates for cadaver and live donor LTx. The generally-accepted approach is to consider offering LDLLT to patients who are gradually deteriorating on the waiting list and who are not expected to survive the long waiting times, but who are, at the same time, predicted to have the necessary reserve to recover from this major surgery. While in the United States and Europe, LDLLT tends to be performed more on cystic fibrosis patients, in Japan, it is performed for a wide range of diagnoses including pulmonary hypertension, idiopathic pulmonary fibrosis, bronchiolitis obliterans, bronchiectasis and lymphangioleiomyomatosis.

Criteria to be live lobar donor; [24]

Age: Between 20 and 60 years,
Absence of a history of previous surgical interventions on the donor lung side,
Absence of an active or intensive smoking history,
Absence of a history of active lung disease on the donor lung side,
Absence of a defined risk of familial lung disease,
Absence of cachexia (body mass index (BMI) < 18 kg/m^2) or obesity (BMI > 30 kg/m^2),
ABO blood type compatibility with the recipient,
Compatibility of the donor lung lobe size with the recipient's hemithorax,
Having normal pulmonary function and normal values for arterial blood gasses,
Absence of conditions that increase the general anesthesia, surgical or postoperative risks,
Absence of psychological and ethical issues or concerns regarding the donor's motivation,
Absence of pregnancy,
Absence of active malignancy,
Absence of a significant active infection (HIV, hepatitis, acute CMV).

After identifying two potentially compatible donors, it is necessary to define the method for comparing the lower lobes of both donors with the optimal size for the recipient. For preoperative evaluation, the Kyoto group choses donor lungs of compatible volume and normal vascular structure by using high definition computed tomography and three-dimensional CT (3D-CT) [25].

During live donor lobectomy, adequate lengths of artery, vein and bronchial stumps should be left so as to allow anastomoses to be performed during implantation. Following fissure dissection, the lower lobe arteries are isolated, and for the right side, the middle lobe artery is also isolated. The pericardium surrounding the inferior pulmonary vein is opened circumferentially. Prostaglandin E1, 10,000 units of heparin and 500 mg methylprednisolone are administered intravenously, after which the lower lobe artery, the inferior pulmonary vein and lower lobe bronchus are divided. On the patient end, the vascular stumps are closed with a 5-0 Prolene continuous suture, while the bronchial stump is closed with a 3-0 Prolene suture supported with pericardial fat tissue. The donated lobe is taken to the back table and

perfused anterogradely and retrogradely with one liter of cold Perfadex solution. During this process, the lobe is gently ventilated with room air [26, 27].

Until the end of 2017, there have been 388 cadaveric LTx performed in Japan compared to 208 LDLLT. For cadaveric LTx, the 5- and 10-year survival rates were 71.7% and 55.7%, respectively. The long-term results of LDLLT were somewhat superior with 5- and 10-year survival rates of 73.4% and 64.1% respectively [28]. Chronic lung allograft dysfunction, and especially restrictive allograft syndrome, is seen later in LDLLT compared to cadaveric LTx, and it is also observed to have a lower impact on overall survival after LDLLT [29].

Conclusion

Although the lung allocation scoring has decreased waiting times and waiting list mortality rates, LDLLT is still considered to be appropriate for young patients who become critical during the waiting period, and for cases in which an organ donor is urgently needed. Although cadaver LTx is preferred due to donor risks, it has been determined that in centers with a good experience of LDLLT, its long-term results are better than that after cadaveric LTx.

Self-study

1. Which statement is true?
   (a) In split lung transplantation, the left lower lobe of the donor is implanted into the left thoracic cavity and the left upper lobe is implanted in the right thoracic cavity.
   (b) Lobar transplantation is more commonly performed than peripheral wedge resection to reduce the volume of an oversized donor lung.
   (c) The estimated total lung capacity of the donor is recommended to be between 60 and 140% of the recipient's pTLC.
   (d) Undersized graft results in atelectasis, distorted diaphragm movement, high pulmonary vascular resistance and poor gas exchange.
2. Which statement/statements is/are true?
   (a) In living donor lobectomy, adequate arteries, veins and bronchial stumps should be maintained to facilitate the anastomoses at implantation.
   (b) Live donor lobar lung transplantation is not an alternative to cadaver lung transplantation.
   (c) Decrease in the lung transplant waiting list mortality has also led to a decrease in the use of living donor lobar lung transplantation.
   (d) a and c.
   (e) b and c.

Answers

1. Which statement is true?
   (a) CORRECT. In split lung transplantation, the left lower lobe of the donor is implanted into the left thoracic cavity and the left upper lobe is implanted in the right thoracic cavity. The estimated total lung capacity of the donor is recommended to be between 75 and 125% of the recipient's pTLC.
   (b) INCORRECT. Peripheral wedge resection is the most common method for volume reduction. Small grafts cause lung hyperextension, persistent pleural spaces, pleural effusion, infection, hyperinflation, increased risk of postoperative bleeding, risk of acute lung damage due to high tidal volume in mechanical ventilation and higher pulmonary vascular resistance.
   (c) INCORRECT. The estimated total lung capacity of the donor is recommended to be between 60 and 140% of the recipient's pTLC.
   (d) INCORRECT. Undersized graft results in hyperinflation, increased risk of primary graft dysfunction and postoperative bleeding, higher pulmonary vascular resistance, persistent pleural spaces, pleural effusion and infection.

2. Which statement/statements is/are true?
   (a) CORRECT
   (b) INCORRECT. Live donor lobar lung transplantation is an alternative to cadaver lung transplantation for cases that become critical during the waiting period, and for cases in which an organ donor is urgently needed.
   (c) CORRECT.

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