Techniques and results of lobar lung transplantations†

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OBJECTIVES: We report our experience of lobar lung transplantations (LLTs) in patients with small thoracic volume.

METHODS: Since 1988, 50 LLTs were done for cystic fibrosis (n = 35), fibrosis (n = 7), bronchiectasis (n = 3), emphysema (n = 3) and lymphangiomyomatosis (n = 2). There were 44 females and 6 males (mean age 31 ± 13 years, mean size 155 ± 5.5 cm and mean predicted total lung capacity (TLC) 4463 ± 598 ml). Mean ratio between donor and recipient-predicted TLC was 1.65 ± 0.26. Six patients were transplanted on the high-emergency list and 2 of them were on veno-arterial ECMO as a bridge to transplantation. Forty middle/lower right lobe with left lower LLT, four bilateral lower LLT and six split left lung LLT were performed through a clamshell incision (n = 12) or a bilateral antero-lateral thoracotomy (n = 38), with epidural analgesia in 17 cases. Thirty-two patients were transplanted under circulatory support (CPB n = 16, veno-arterial ECMO n = 16). In 11 cases, the right venous Anastomosis was enlarged by a pericardial cuff. Ischaemic time was 4.4 ± 1.2 h for the first lobe and 6.1 ± 1.3 h for the second.

RESULTS: Median mechanical ventilation weaning time was 10.5 (1–136) days. Four patients were extubated in the operating room. Ten patients needed ECMO for primary graft dysfunction. In-hospital mortality was 28% related to sepsis (n = 2). Eight patients required endoscopic treatments for airway complications. Mean best FEV1 was 72 ± 16% of the theoretical value. The actuarial 3-year and 5-year survival rates were 60 and 46%, respectively.

CONCLUSIONS: LLTs are a reliable solution and can be performed with satisfactory functional results and survival rates.

Keywords: Donor-recipient size mismatch • Lobar lung transplantation • Thoracic epidural analgesia • EMCO

INTRODUCTION

For small adult recipients, the scarcity of suitable matching-sized donors increases the time on the waiting list. Furthermore, in the case of high-emergency listed patients, a major size discrepancy is a significant limitation to lung transplantation (LT). The use of lobar lung transplantation (LLT) affords an optimal strategy to overcome size mismatching between donor and recipient. Only a few centres have routinely developed these techniques [1, 2]. We report our experience of LLT in patients with small thoracic volume.

PATIENTS AND METHODS

Study group

We designed a retrospective study including every patient who underwent cadaveric LLT at Hôpital Foch from October 1988 to July 2012. During this period, among 495 LT, 50 LLT were performed. There were 44 females and 6 males, with a mean age of 31 ± 13 years, and a mean size of 155 ± 5.5 cm. Indications for LT were cystic fibrosis (CF, n = 36), pulmonary fibrosis (PF, n = 7), emphysema (n = 3), bronchiectasis (n = 2) and lymphangiomyomatosis (n = 3). Six patients were transplanted on the high-emergency list and 2 of them were on veno-venous ECMO as a bridge to transplantation. The median waiting time on the list was 72 (1–901) days. Recipient characteristics are detailed in Table 1.

Donor selection

Size matching of the donor lung was based on the predicted donor total lung capacity (TLC) estimated by the formula 7.99 × H – 7.08 in males and 6.6 × H – 5.79 in females, where H is height (m), and on the donor/recipient-predicted TLC ratio. Predicted forced expiratory volume in 1 s (FEV1) of the donor lung was also calculated as follows: 4.3 × H – 0.029 × age – 2.49 in males and 3.95 × H – 0.025 × age – 2.6 in females. Lastly, we estimated the predicted postoperative recipient TLC and FEV1 after size reduction according to the number of segments actually

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transplanted \((\text{Ppo TLC} = \text{predicted TLC}/19 \times N \text{ transplanted segments}, \text{Ppo FEV1} = \text{predicted FEV1} \times (1 - S \times 0.0526), S = \text{number of resected segments})\). In order to avoid excessive undersizing, we also applied an upsizing factor between 10 and 20% for patients with CF who usually have a chest wall distension, and a similar downsizing factor for restrictive patients with PF.

The decision to perform a lobar reduction was finally based on a visual assessment of the chest wall cavity and of the inflated donor lung at the time of surgery.

In 31 cases, LLT was performed with a donor according to the classic lung-harvesting criteria: age <65 years, mechanical ventilation for <48 h, \(\text{PaO2/FiO2} > 300 \text{ mmHg}\), no bilateral infiltrate or focal alveolar opacities on chest X-rays and no infection at bronchoscopy. In 19 cases, extended criteria for donors were used and among them, normothermic \(\text{ex vivo}\) lung perfusion (EVLP) was performed in 3 recent cases (Table 2).

### Operative management

In 17 patients, thoracic epidural analgesia administration of ropivacaine and sufentanil was used; the catheter used for both peri- and postoperative analgesia was inserted while the patient was in the operating room prior to surgery. For the remaining patients, postoperative analgesia was provided by patient-controlled analgesia with intravenous morphine.

The surgical approach was initially a clamshell incision \((n = 12)\). In 2003, it was switched to bilateral anterolateral thoracotomies in the fourth intercostal space sparing the sternum \((n = 38)\). We performed 40 middle and lower lobe with left lower LLT (Fig. 1), 4 bilateral lower LLT and 6 left lung split transplantation (Fig. 2). Thirty-two patients required extracorporeal support with cardiopulmonary bypass in 16 cases and with peripheral veno-arterial extracorporeal membrane oxygenation (ECMO) in 16 cases. Eighteen patients were operated on with no extracorporeal support.

### Surgical techniques

#### Donor lung preparation

Since 1997, donor lung preservation has consisted of anterograde flush of Celsior, and both lungs were harvested en bloc. Graft dissection and lobar reduction were performed in our hospital on the back-table, usually during the first side pneumonectomy on the recipient. Upper lobectomies were performed with an extensive use of stapler devices.

### Table 1: Recipient characteristics

| Female/male | 44/6 |
| Age (years) | 31 ± 13 |
| Height (cm) | 155 ± 5.5 |
| Body mass index | 19 ± 3.87 |
| Predicted total lung capacity (ml) | 4463 ± 598 |
| Real total lung capacity (ml) | 4054 ± 1483 |
| FEV1 (ml) | 627 ± 241 |
| FEV1 (% of the theoretical value) | 23.6 ± 9.7 |
| Right lung perfusion scan (%) | 49.8 ± 14.5 |

**FEV1:** forced expiratory volume in the 1st second.

### Table 2: Donor characteristics

| Female/male | 5/45 |
| Age (years) | 39.4 ± 14 |
| Height (cm) | 180.6 ± 7.8 |
| Predicted total lung capacity (ml) | 7247 ± 741 |
| Donor/recipient predicted total lung capacity ratio | 1.65 ± 0.26 |
| Predicted FEV1 (ml) | 4089 ± 627 |
| Ppo total lung capacity (ml) | 4070 ± 440 |
| Ppo FEV1 (ml) | 2300 ± 370 |
| Pao2 mmHg/FiO2 (%) | 416 ± 93 |

**FEV1:** forced expiratory volume in the 1st second.

Figure 1: Lower/middle and left lower lobar transplantation.

Figure 2: Split left lung transplantation. (A) Separation of the lung. (B) Post-transplantation X-rays.

Peribronchial tissue was preserved to improve blood supply. On the right side, the bronchus was sectioned at the origin of the intermediate bronchus or immediately after the middle lobar bronchi if the middle lobe was not suitable. On the left side, the left bronchus was transected just at the level of the lobar division to perform the anastomosis far from the bronchus of the apical segment. The pulmonary artery (PA) was transected after the mediastinal branches. On the left side, the atrial cuff was divided, leaving a large cuff around the left inferior pulmonary vein. On the right side, the vein from the upper lobe was transected, but the whole atrial cuff was preserved. In 11 cases, a pericardial cuff was made to widen the atrial cuff and preserve the venous flow from the middle lobe (Fig. 3).

For a left split lung procedure, the upper and lower lobe bronchi were separated at the level of the segmental bronchi. The
PA was divided between the apical branch of the lower lobe and the lingula artery while the proximal side was closed by a stapler. The pulmonary veins were dissected on their mediastinal side and separated from each other, keeping a small cuff of atrial tissue.

Recipient operation. In case of unbalanced lung perfusion, the less-perfused lung was removed first. Otherwise, the right pneumonectomy was first performed. Vascular pedicles were carefully left long to facilitate the anastomosis: PA was dissected proximally and also distally after its first branches to ensure a greater length, particularly in the case of a split LLT. In addition, the pericardium around the pulmonary veins was widely opened, giving longer venous stumps, which were stapled. The bronchus was transected on both sides at the level of the main bronchus, except for a split LLT, where the bronchus was cut on the right side at the origin of the intermediate bronchus. The first lobe was placed into the chest cavity in a way that anticipated its future position after inflation. The bronchial anastomosis was performed in an end-to-end fashion, usually with a running suture of 4/0 polydioxanone (PDS; Ethicon, Inc., Sommerville, NJ, USA) in the cartilage section. The membranous part of the bronchi and interrupted suture of Vicryl (Ethicon, Inc., Sommerville, NJ, USA) in the cartilage section. The venous stumps were opened, and the venous anastomosis was performed in most cases with the use of the whole atrial cuff to guarantee a wide lumen. Finally, the arterial tension-free anastomosis was performed, followed by a gradual controlled reperfusion while de-clamping. Mean ischaemic time was 4.4 ± 1.2 h for the first lobe and 6.1 ± 1.3 h for the second.

Statistical analysis

Normally, continuous variables were reported as mean and standard deviation. Variables with non-normal distribution were reported as median and range. Survival was depicted with Kaplan–Meier estimate and compared with the log-rank test. A probability value of $P < 0.05$ was considered significant. For correlation analysis, Pearson’s correlation test was used. Data analyses were performed with the software XLSTAT.

RESULTS

Early follow-up

Four patients were extubated in the operative room. However, the median duration of mechanical ventilation was 10.5 (0–136) days, and half of the patients needed tracheotomy. Primary graft dysfunction (PGD) defined as PaO₂/FiO₂ < 300 mmHg at H6 occurred in 27 patients and 10 of them needed a prolonged veno-arterial ECMO for a median time of 7 days (4–39 days). Severe hypoxaemia (PaO₂/FiO₂ < 100 mmHg) was the main criteria for prolonging or inserting a postoperative ECMO. Ten patients had to be reoperated on for haemothorax ($n = 4$), venous anastomotic twist ($n = 2$), PA stenosis ($n = 1$), PA rupture ($n = 1$), bronchial dehiscence ($n = 1$) and groin bleeding ($n = 1$) (Table 3). In-hospital overall mortality of the whole series reached 28%, caused by sepsis ($n = 6$), PGD ($n = 3$), haemorrhage ($n = 2$), broncho-vascular fistula ($n = 1$) and multiorgan failure ($n = 2$).

Long-term results

Airway complications requiring repeated endoscopic treatments occurred in 8 patients. In 3 cases, bilateral endoscopic stenting was needed and in 2 others, a right-sided prosthesis was necessary. Three middle lobe stenoses were observed and a middle lobectomy was performed in 1 case.

The long-term lung function was assessed by the best FEV1 measured after transplantation (1975 ± 467 ml, 72 ± 16% of the theoretical value), the maximum postoperative real TLC (4360 ± 645 ml) and the right lung perfusion (56.8 ± 14%). The long-term evolution of the FEV1 is documented in Fig. 4a. Fig. 4b shows the correlation between Ppo FEV1 and the best FEV1 registered after LLT. Bronchiolitis obliterans syndrome (BOS) occurred in 9 patients: among 3 patients classified as BOS stage 3, 2 were retransplanted and 1 is on the waiting list. Six other patients were classified as BOS stage 0-p.

The median survival of this series was 53 months and the 3- and 5-year survival rates were 60 and 46%, respectively. Survival analysis showed no significant difference between the LLT group and the cohort of all other LT. Twenty-six patients are still alive and 10 died either from neoplasia ($n = 4$), haemoptysis ($n = 2$), aspergillosis ($n = 1$) or other ($n = 3$) (Fig. 5).

DISCUSSION

Donor lung downsizing by peripheral stapler resection or by a middle lobectomy is a current practice when there is a small size...
developed the use of lower and middle LLT [6], which has several advantages: it affords a greater lung volume with adequate downsizing factor according to the recipient size. In order to avoid such excessive undersizing, we applied an up- or downsizing factor according to the recipient’s pathology.

A variety of LLT have been reported, including lobar reduction after a standard bilateral LT [1, 2, 4]. Our surgical strategy was to perform a bilateral LLT after upper lobectomy, which has already been undertaken on the back-table. On the right side, we have developed the use of lower and middle LLT [6], which has several advantages: it affords a greater lung volume with adequate anatomical position in the chest cavity and a larger anastomosis on the intermediate bronchus. A major drawback is the risk of impairment of the venous drainage, which we observed in 2 cases requiring reoperation; we thus developed an extensive use of a pericardial cuff to enlarge the donor’s atrial anastomosis and preserve the venous flow from the middle lobe. The surgical technique of pulmonary bipartitioning was first reported by Couetil [7, 8]. In 6 cases, we used this split left lung procedure when only a large left lung was available on the donor. This LLT remains difficult, and some technical points must be outlined. A careful positioning of the left upper lobe after inflation has to be anticipated. The proximal native PA must be kept long enough to allow an anastomosis without any tension. As for all other LLT, we performed the venous anastomosis with the whole donor atrial cuff. Interestingly, in 2 of our cases, bronchial diameters allowed us to perform the right bronchial anastomosis on the recipient’s main bronchus.

Thoracic epidural analgesia has been proved to be adaptive for general thoracic surgery. Compared with intravenous analgesia, perioperative epidural analgesia is associated with a better control of postoperative pain, lung function, atelectasia and pulmonary infections [9]. We have developed an extensive use of thoracic epidural analgesia since 2001, and for LLT it has been routinely used since 2009. It is usually associated with continuous intravenous administration of the short half-life analgesic remifentanyl and the hypnotic propofol, allowing short recovery and, in some cases, extubation in the operating room [10].

Earlier in our experience, extracorporeal support with CPB was used in the case of severe pulmonary hypertension, perioperative circulatory instability or severe hypoxemia. Since then, it has been routinely used to avoid initial overflow on the first implanted lobe, which might result in a significant reperfusion oedema [11]. As advocated by the group of Vienna [12] we have developed, during the recent period, an extensive use of peripheral veno-arterial ECMO requiring less heparin and allowing thoracic epidural analgesia.

Ten patients sustained a severe PGD and needed a postoperative ECMO support. The 90-day mortality for LLT is higher than for our cohort of other LT, but this retrospective study concerned a long period during which the management of lung transplant patients has evolved in our institution. Several explanations can be underlined. Firstly, LLT concerned mainly CF patients, which is a difficult group of patients and 6 of them were on a high-emergency list. Secondly, severe infectious complications are more likely to occur in this group of patients related to their...
bronical colonisation with multiresistant germs. Hence, one patient’s death was related to *B. cepacia*, which is still a debated obstacle for LT. Thirdly, as a result of the use of extended donor criteria since 2003, the number of LT and LLT has increased, but we also deployed a higher mortality in patients who received such donor lungs (10 of 14 cases). Furthermore, controversial results have been reported with the use of these extended criteria donors [10]. However, the recent use of EVLP might afford a new perspective to optimize such donor lungs [13]. Finally, the comparison of our experience of LTT before and after 2003 demonstrated a drop of in-hospital mortality from 45 to 23% (P = 0.11).

Eight of our patients had significant bronchial complications requiring iterative endoscopic treatments that may be challenging due to the bronchial diameter. However, no severe airway complication was observed in the recent period. The rate of airway complications is not different from the incidence observed in our overall cohort of LT, as reported by other authors [2].

Optimized lung size matching is of major importance to achieve the best functional result. The group of Vienna has already shown that postoperative recipient TLC in size-reduced LT can be predicted by the donor’s predicted TLC [5]. Others have demonstrated that the recipient’s best FEV1 could be predicted from the donor’s calculated and corrected FEV1 with respect to its size reduction [3]. In our series, we also observed this latter correlation.

To date, our study reports the longest significant follow-up after LTT. In our experience, the long-term survival rate of the LTT group is not significantly different from the cohort of all other LT. In conclusion, LTT are a reliable surgical option and can be performed with satisfactory functional results and long-term survival rates. Improvements in perioperative management such as the use of epidural thoracic analgesia and ECMO, as well as technical modifications, have contributed to a better outcome.

**Conflict of interest:** none declared.

**REFERENCES**


**APPENDIX. CONFERENCE DISCUSSION**

**Dr G. Marulli (Padua, Italy):** This is a very large experience on bilateral lobar lung transplantation with good long-term results. It is undoubtedly a very difficult subset of patients for several reasons: it is a technically demanding operation, issues relating to patient selection, and difficult intraoperative and postoperative management.

I have a couple of questions. You reported the use of clamshell access in 12 patients; but the use of cardiopulmonary bypass, such as ECMO, in 16 patients. Can you explain which type of cannulation you used in patients undergoing cardiopulmonary bypass and having bilateral anterolateral thoracotomy? Moreover, do you not consider the best approach to be the clamshell approach in order to obtain a better exposure in small patients?

**Dr Mitilian:** We use bilateral anterolateral thoracotomy, as we use for other lung transplantations. For these patients now, as we use peripheral ECMO, we don’t actually need the clamshell incision to perform cardiopulmonary bypass; actually, we don’t use it anymore and it is not advantageous. I think for cardiopulmonary bypass, you can cannulate the patient from the right without any big problem, I think, but usually we don’t do it.

**Dr Marulli:** You had a pretty high in-hospital mortality and morbidity rate, such as a high percentage of various degrees of primary graft dysfunction and bleeding problems. Did you look at any other risk factors for the marginal donors, such as the use of cardiopulmonary bypass or ECMO, the use of split-lung transplantation, that may increase the mortality rate or the use of emergency indications?

**Dr Mitilian:** Well, we had actually 19 lobar transplantations from extended criteria donors, and among them, there were 10 patients who died. So maybe there is a link. I didn’t really check on whether extended criteria donors had ECMO, but, as you can see, there are many patients who needed ECMO, so I don’t know if it is significant.

**Dr Marulli:** In the majority of patients, you used lower lobes, I think for anatomical reasons.

**Dr Mitilian:** Yes.

**Dr Marulli:** But usually the lower lobes are more atelectatic, more congested, which therefore may increase the risk of complications. Have you considered the use of upper lobes, in particular from the left side, in order to overcome this problem?

**Dr Mitilian:** In our centre, actually we never did lobar transplantation with upper lobes. We used either middle and lower lobes or both lower lobes because we didn’t want to leave an ischaemic bronchial stump mainly. Also, we prefer to perform bronchial anastomosis on the intermediate bronchus.

**Dr C. Aigner (Vienna, Austria):** You mentioned that your management with regard to intraoperative extracorporeal support has evolved over time. There is a rate of 40% of patients where you did not use intraoperative support and at the same time you have a relatively high incidence of PGD. Were these the patients who did not receive intraoperative support, or was there an equal distribution?

**Dr Mitilian:** It is difficult to answer, because at the beginning of our experience we used cardiopulmonary bypass as an emergency means, and now, actually, we really use ECMO routinely, and always for the second lung implantation. So I don’t know if I can say if it is linked to PGD or not.

**Dr Aigner:** Regarding the size matching, you mentioned that you are using the predicted TLC of the recipient for size matching. However, there sometimes
is a huge discrepancy between the predicted and the real TLC measured in the lung function. Did you take this into account as well?

Dr Mitilian: We did take it into account, but the main criterion was the predicted donor TLC, as previously described by your team and other teams actually.

Dr G. Dellgren (Gothenburg, Sweden): I’m a little bit curious about the six bipartitioned lungs. How did it go for those 6 patients?

Dr Mitilian: You mean specific follow-up?

Dr Dellgren: Long-term, yes.

Dr Mitilian: Actually, of the six, there were two early deaths and four patients are still alive.

Dr Dellgren: So from a technical point of view, the grafts are functioning well in those four long-term?

Dr Mitilian: Yes. I think the main point for this technique is the difficulty in performing it in the right way, the right anatomical position, but if it works, I mean if you have good pulmonary volume, it may work quite well.

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**EDITORIAL COMMENT**

**Lobar lung transplantation: more than bits and pieces**

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Lobar lung transplantation has evolved as an important method to reduce donor organ shortage for paediatric and small adult recipients who would otherwise not receive a suitable donor organ in due time. Furthermore, it allows the use of unexpectedly large donor organs as well as the utilization of lungs with a localized pathology in one lobe. This report from the Foch group [1] represents one of the largest series of lobar lung transplantation with a detailed long-term follow-up and an analysis of the evolution of the technical steps required to perform this procedure. Six patients in this report have been transplanted with the split lung technique, which represents the most efficient method of organ utilization. Only a few centres worldwide have accumulated a large experience with lobar lung transplantation from brain dead donors [2–5]. However, compared with the overall number of lung transplantations performed annually, lobar transplantation still accounts only for a small percentage.

Technically, lobar lung transplantation is more challenging than standard lung transplantation, and recipients are typically younger and smaller than standard lung recipients and represent, in the current report, mainly patients with cystic fibrosis (CF) and pulmonary fibrosis. The important technical aspects of lobar lung transplantation are clearly outlined in the paper. The perioperative management in lung transplantation has significantly evolved over the long observation period reported in the study.

A relatively high number of transplants in the early phase of the observation period were performed without the use of either cardiopulmonary bypass or extracorporeal membrane oxygenation. Since there was no significant difference in the development of primary graft dysfunction (PGD) in the various groups, there is no clear answer whether a reduction of the relatively high PGD incidence could have been achieved by adopting a routine use earlier. An important fact that has to be kept in mind is that the vascular bed of a single lobe is usually not sufficient to take up the entire cardiac output without developing reperfusion oedema; therefore, in our centre, lobar transplantation is nowadays routinely performed with the help of extracorporeal support.

The authors report—except for the cases of split lung transplantation—exclusively on the use of lower lobes as their standardized technique for performing lobar transplantation. However, the use of upper lobes might have some distinct advantages in specific situations. The basis of the lower lobe can be very broad and, particularly on the left side in patients with a hypertrophic heart, the upper lobe frequently fits the anatomical situation of the chest cavity much better.

Size matching is of crucial importance in lobar transplantation. The actual chest configuration of the donor and recipient has to be taken into account, as well as the real recipient total lung capacity (TLC), which can vary substantially from the predicted TLC. A correction factor of 10–20% compared with the predicted recipient TLC for upsizing CF patients and downsizing patients with pulmonary fibrosis is utilized by the authors. This will certainly serve as a gross estimation; however, the use of a real recipient TLC obtained by body plethysmography is certainly desirable to be able to make the most accurate judgement possible [6]. Original-sized chest X-rays in a posterior–anterior and lateral view have also proven to be helpful in estimating the size match at the donor hospital. The final choice of which lobes are used is usually taken directly at the transplant procedure as mentioned by the authors.

The bronchial anastomosis in lobar transplantation is more delicate to suture since usually a size mismatch has to be corrected. The rate of bronchial complications varies among reports on lobar lung transplantation. The anastomotic technique used by the Foch group is a widespread method that, however, is still associated with a substantial rate of anastomotic problems. Satisfying results can, in our experience, also be achieved with a single running suture technique [7].