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Lobar transplantation, split lung transplantation and peripheral segmental resection – reliable procedures for downsizing donor lungs[☆]

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Abstract

Objectives: The increasing scarcity of donor lungs, especially for small and pediatric recipients has stimulated the development of new operative techniques, which allow larger lungs to be downsized for use in smaller recipients. This approach has only recently gained widespread use—especially for highly urgent recipients—however, it is still not considered a standard procedure. **Methods:** This report reviews the Vienna University experience with cadaveric split lung transplantation, lobar transplantation and by means of peripheral resection size reduced lung transplantation within the years 2001–2002. Peri-operative complications and outcome of those patients were retrospectively analysed and compared to the patients undergoing standard single or double lung transplantation during the observation period. **Results:** During the observation period 98 primary lung transplantations were performed, of which 27 (27.6%) were size reduced transplantations. Size reduction was achieved by lobar transplantation ($n = 9$), split lung transplantation ($n = 2$) or peripheral segmental resection ($n = 16$). There was no statistically significant difference between the size reduced and standard lung transplantation group with regard to the rate of bronchial healing problems ($n = 3/7$; $P = 0.85$) and the rate of post-operative bleeding ($n = 5/12$; $P = 0.85$). No other major thoracic surgical complications were observed. Three months survival rate was 85.2% in the size reduced group, compared to 92.9% in the standard group ($P = 0.13$). **Conclusions:** Size reduced lung transplantation, including split lung transplantation, lobar transplantation and peripheral segmental resection, is a reliable procedure providing equal results compared to standard lung transplantation.

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Keywords: Lung transplantation; Size reduced lung transplantation; Split lung; Lobar transplantation; Segmental resection

1. Background

Due to the increasing scarcity of donor lungs, especially for pediatric and small adult recipients, advanced operative strategies for the use of larger grafts for smaller recipients have been developed. Various methods of downsizing are applied for cadaveric donor lungs. While size reduction by peripheral segmental resection is a widely performed procedure, lobar transplantation and split lung transplantation are still not considered to be standard procedures and are performed only by a few centres on a regular basis.

2. Patients and methods

This report reviews the Vienna University experience with cadaveric split lung, lobar and by means of peripheral resection reduced size lung transplantation within the years 2001–2002.

During the observation period 98 patients underwent primary lung transplantation at our institution. In 27 patients (27.6%) size reduced lung transplantation was performed. Underlying diagnoses of these patients were cystic fibrosis ($n = 8$), primary pulmonary hypertension ($n = 5$), pulmonary fibrosis ($n = 5$), chronic obstructive pulmonary disease ($n = 5$), chronic thromboembolic pulmonary hypertension ($n = 2$), histiocytosis X ($n = 1$) and Swyer–James syndrome ($n = 1$). Thirteen patients were male, 14 female with a mean age of 32.26 ± 13.78 years (range 14–61 years) in the reduced size group compared to 39 male and 32 female patients with a mean age of 50.09 ± 13.94

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(range 16–71 years) in the standard group. Two patients in each group were on mechanical ventilation pre-operatively.

Size matching of the donor lung was based on the predicted total donor lung capacity and compared to the recipient's predicted and real total lung capacity as the primary method of size matching.

Harvesting of the cadaveric donor lungs was standardized. The lungs were removed en bloc after perfusion with a high molecular low potassium dextrane solution and 0.5 mg epoprostenol, separated at the back-table and stored separately in perfusion solution. Surgical approach for transplantation was either by anterolateral thoracotomy or bilateral transsternal thoracotomy.

Peripheral segmental wedge resections were performed with commercially available stapler devices, usually after implantation and full inflation of the lung, which allowed the necessary amount of lung resection to be estimated. No further coverage of the resection line was performed.

Back-table separation was used in split lung transplantation, where the left donor lung was bipartitioned as well as in lobar transplantation, which was performed using various combinations of lobes. Division of the parenchymal bridges was accomplished with commercial stapler devices. As much peribronchial tissue as possible was preserved to guarantee sufficient bronchial blood supply. The bronchial anastomosis was uniformly performed in an end to end fashion, usually with 5/0 PDS, and size discrepancies were adjusted over the whole circumference. The pulmonary vascular pedicles were kept short to avoid any kinking. The venous anastomosis was either performed with one pulmonary venous stump or with use of the whole atrial cuff.

Peri-operative outcome and complications of all patients who underwent split lung or reduced size lung transplantation were retrospectively analysed and compared to the patient cohort undergoing standard single or double lung transplantation during the observation period.

3. Results

Results are described as mean \pm SD unless otherwise indicated. During the observation period 27 (27.6%) out of 98 primary lung transplantations were size reduced. The patients receiving size reduced organs were significantly younger and underlying diagnoses were different to those patients receiving standard lung transplants. (Fig. 1). Two patients in the size reduced group and two patients in the standard group were on mechanical ventilation pre-operatively. Waiting list time was comparable with 98 ± 94 days in the standard group compared to 73 ± 71 days in the size reduced group ($P = 0.426$). Twenty-five patients in the size reduced group received bilateral transplants, two patients single lung transplants.

Donor/recipient (D/R) mean difference in height did not significantly differ (1.9 ± 8.0 cm standard group vs.

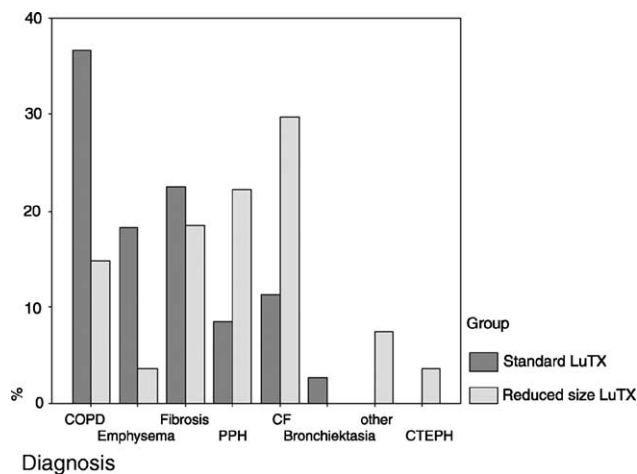


Fig. 1. Indications for lung transplantation.

3.0 ± 8.6 cm size reduced group, $P = 0.248$), however, D/R total lung capacity (TLC) difference (predicted donor TLC compared to real recipient TLC) was significantly larger in the size reduced group (0.2 ± 2.0 l standard group vs. 1.5 ± 1.6 l size reduced group, $P = 0.002$) as well as D/R body weight difference (9.3 ± 13.6 kg standard group vs. 17.3 ± 14.9 kg size reduced group, $P = 0.012$).

Since intraoperative extracorporeal membrane oxygenation (ECMO) support has replaced the use of cardiopulmonary bypass in our institution, 12 patients (44.4%) in the size reduced group were operated with ECMO support and one patient (3.7%) required cardiopulmonary bypass due to a concomitant cardiac defect. In the standard group ECMO was used in 23 patients intraoperatively (32.4%). Size reduction was achieved by lobar transplantation ($n = 9$), split lung transplantation ($n = 2$) or peripheral resection ($n = 16$). Operation time was longer in the size reduced group, however, this did not reach statistical significance compared to the standard group (2.5 ± 1.5 h standard group vs. 3.5 ± 0.5 h size reduced group, $P = 0.151$ for single lung transplantation and 4.3 ± 1.1 h standard group vs. 4.5 ± 1.3 h size reduced group, $P = 0.519$ for double lung transplantation). The additional time required for back-table preparation of the donor lung did not significantly prolong ischemic time (6.0 ± 1.1 h standard group vs. 6.3 ± 1.6 h size reduced group, $P = 0.427$).

There was a trend towards slightly prolonged intubation time in the size reduced group, this, however, was not statistically significant (11 ± 21 days standard group vs. 15 ± 25 days size reduced group, $P = 0.083$). Overall median time to extubation was 3 days. Intensive care unit time (15 ± 18 days standard group vs. 19 ± 25 days size reduced group, $P = 0.186$) and time until discharge from hospital (37 ± 31 days standard group vs. 43 ± 31 days size reduced group, $P = 0.169$) were comparable.

In the size reduced group 3 patients experienced bronchial healing problems, compared to 7 patients in

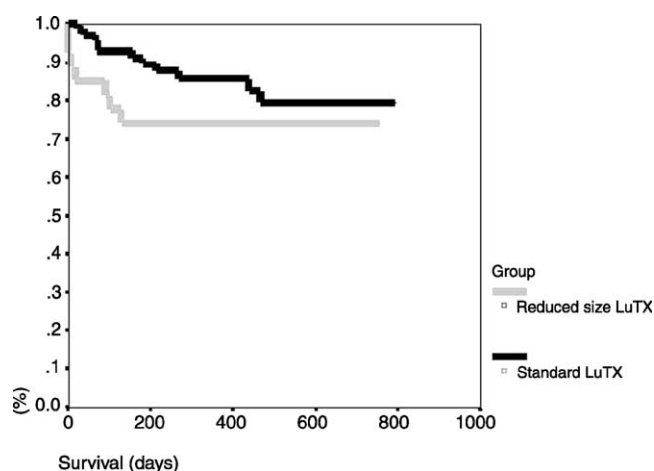


Fig. 2. Kaplan–Meier survival function.

the standard group ($P = 0.85$). This rate of bronchial healing problems was in both groups higher than reported in a previous study [1]. The rate of post-operative thoracic bleeding requiring operative revision did not show statistical significance either (five cases in the size reduced group vs. 12 cases in the standard group, $P = 0.85$). No prolonged air leaks, pneumothorax, vascular anastomotic problems, phrenic nerve paralysis or other major procedure related thoracic surgical complications were observed. The 3 months survival rates were comparable with 85.2% in the reduced group vs. 92.9% in the standard group ($P = 0.13$) (Fig. 2).

4. Discussion

Various methods are applied in order to increase the donor pool and use the available donor organs as efficacious as possible. Methods of downsizing cadaveric donor lungs are of special importance in urgent pediatric and small adult recipients, since they allow the use of larger grafts for these patients. Furthermore they are applicable if localized pathologies are found in one donor lobe or the organ is found to be unexpectedly large at harvesting.

It therefore can be expected that the patient collective receiving size reduced organs differs from standard lung transplant recipients in age, size and underlying diagnoses. Even if there are relatively few pediatric cases this also applies to our patients, which limits comparability. However, the fact that in both groups two patients were on mechanical ventilation pre-operatively and that in a center orientated allocation system even not ideally size matched organs were accepted for patients in order to reduce waiting time, indicates that the prognosis of those patients who received size reduced organs was certainly not better than the prognosis of those patients in the standard group.

Optimal size matching is especially important to avoid potential problems which can arise from an oversized donor

lung. Among these problems are perpetual atelectasis, distortion of bronchial anatomy with retention of secretions and increased risk for secondary infection. An undersized graft on the other hand can lead to hyperexpansion of the lung followed by increased breathing effort, persisting pneumothorax and in extreme cases even hemodynamic compromise with limited exercise tolerance or pulmonary hypertension. Parameters like body height and especially body weight turned out to be insufficient for estimating the actual intrathoracic volume and frequently led to gross mismatches between donor lungs and intrathoracic recipient volume. The TLC, determined by both height and sex, proved to be the most accurate value for thoracic size matching [2]. In our patient cohort the mean D/R TLC difference of the size reduced group was significantly larger than in the standard group. The D/R body size difference alone, however, did not significantly differ underlining the adequacy of this approach.

Depending on the magnitude of size difference various methods of downsizing donor lungs can be applied. Small differences in organ size can be overcome by simple stapler resection of peripheral lung segments or atypical resections. Preferentially on the right side the middle lobe is resected, whereas on the left side the lingula represents the primary target area. An initial series of patients where the donor lungs were downsized by this technique was described by our institution in 1996 [3]. This technique allows for a size reduction of approximately 10–15% and leads to a reduction of the graft size not only in its height, but also in its anterior–posterior diameter, since the upper lobe rotates towards the lower lobe. Usually the stapler resection line is completely airtight and only in occasional cases is oversewing with 4/0 PDS warranted.

To achieve a higher degree of size reduction, transplantation of single lobes can be applied. Our initial experience with this technique was published in 1996 [4]. Separation of the donor lung lobes is performed on the back-table immediately before implantation. Different combinations of lobar transplantation are applicable. For a bilateral lung transplantation in patients with asymmetric chest cavities, where one side is particularly small, a transplantation of a whole lung together with only a lobe on the opposite side is feasible. For a higher degree of size reduction bilateral transplantation of single lobes can be performed. Basically, all lobes are suitable for transplantation. On the right side a combination of the lower lobe together with the middle lobe or the upper lobe with the middle lobe can be used as well. The choice of a particular lobe is dependent on its anatomical size in relation to the configuration of the recipients' thoracic cavity. In addition, use of single lobes is warranted if one other lobe presents with a localized pathology. Especially for patients with pulmonary hypertension and enlarged cardiac diameters, where the lower part of the left hemithorax is especially small, the use of a left upper lobe is preferred.

Table 1
Pre-, peri-, and post-operative parameters

	Standard Tx	P-value	Size reduced Tx	Lobar/split lung only	Peripheral resections only
Waiting time (days)	98 ± 94 (1–343)	0.426	73 ± 71 (1–267)	68 ± 63 (7–183)	76 ± 77 (1–267)
D/R size difference (cm)	1.9 ± 8.0 (–13–20)	0.248	3.0 ± 6.8 (–12–18)	4.7 ± 7.1 (–9–18)	3.3 ± 7.3 (–12–13)
D/R weight difference (kg)	9.3 ± 13.6 (–19–51)	0.012	17.3 ± 14.9 (–10–47)	22.6 ± 10.0 (8–37)	14.3 ± 15.8 (–10–47)
D/R TLC difference (l)	0.2 ± 2.0 (–4.0–4.3)	0.002	1.5 ± 1.6 (–1.7–4.4)	1.7 ± 1.4 (–0.4–4.4)	1.3 ± 1.7 (–1.7 ± 4.2)
OP time (hours) SL	2.5 ± 1.5	0.151	3.5 ± 0.5	–	3.5 ± 0.5
OP time (hours) DL	4.3 ± 1.1	0.519	4.5 ± 1.3	4.6 ± 1.1	4.4 ± 1.5
Ischemic time (hours)	6.0 ± 1.1 (3.3–8.5)	0.427	6.3 ± 1.6 (3.8–11)	6.6 ± 2.0 (4.0–11.0)	6.2 ± 1.4 (3.8–8.5)
Post-operative bleeding	n = 12	0.850	n = 5	n = 3	n = 2
Extubation (days postop)	11 ± 21 (0–140)	0.083	15 ± 25 (1–128)	23 ± 38 (1–128)	10 ± 9 (1–33)
ICU time (days)	15 ± 18 (1–85)	0.186	19 ± 25 (1–128)	27 ± 37 (1–128)	13 ± 9 (2–34)
Hospital time (days)	37 ± 31 (10–173)	0.169	43 ± 31 (1–128)	50 ± 39 (1–128)	39 ± 24 (7–100)
Bronchial complications	n = 7	0.850	n = 3	n = 1	n = 2
3 Months survival (%)	92.9	0.130	85.2	81.8	87.5

Handling of the lobes is standardized. Parenchymal bridges are divided with commercial stapler devices and peribronchial tissue is preserved as much as possible to guarantee sufficient bronchial blood supply. The bronchial anastomosis is performed in an end to end fashion, usually with 5/0 PDS and size discrepancies are adjusted over the whole circumference. For the vascular anastomosis short stumps are important to avoid any kinking and the venous anastomosis can either be performed with one pulmonary venous stump or with use of the whole atrial cuff to guarantee a wide lumen. Implantation of the lobes should be performed in general with some sort of cardiopulmonary support to avoid initial overflow of the first implanted lobe, which might result in significant reperfusion edema.

Currently the most efficient use of donor lungs represents the technique of pulmonary bipartitioning, that was first described by Couetil et al. [5]. With this technique, a left lung can be splitted into upper and lower lobe and is used for bilateral transplantation in a recipient with approximately 50% of TLC of the donor. The right lung remains for use as a single lung graft in another patient [6]. Only recently Couetil has reported a similar technique for splitting of the right lung [7].

A completely different approach of size reduced lung transplantation is the living related or unrelated lobar donation, first only used in cystic fibrosis patients, however, now used in recipients with other diagnoses as well [8]. If the use of other size reduction techniques gains a more widespread use, allowing a more efficient use of available cadaveric donor organs—especially for pediatric recipients—the need for living donation might be considerably reduced.

A question that remains currently not yet fully answered is whether lung growth occurs when adult lobes are transplanted in pediatric recipients. A recent report suggests that alveolar dilation rather than alveolarization, is the primary mechanism of increased lung volume in children following lung transplantation [9].

In our patient cohort no significant differences in procedure related peri-operative complications and survival could be observed. Operative time and ischemic time were comparable to standard lung transplantation as well as the initial post-operative course including time until extubation, ICU time and hospital stay (Table 1). The long term survival has yet to be evaluated. The incidence of bronchial anastomotic healing problems was higher than previously reported by our group. The reasons for this accumulation are unclear. In the size reduced group, three patients experienced bronchial anastomotic stenosis. However, only in one patient was a split lung transplantation resulting in enlarged D/R bronchial diameter difference performed; the other two patients underwent peripheral segmental wedge resections. This demonstrates that split lung or lobar transplantation requiring adaption of bronchial size discrepancies do not increase the incidence of bronchial anastomotic complications.

In conclusion this analysis of routine use of size reduction methods for lung transplantation gives evidence that split lung transplantation, lobar transplantation and by means of peripheral segmental resection size reduced lung transplantation are reliable procedures providing equal results compared to standard lung transplantation.

References

- [1] Aigner C, Jaksch P, Seebacher G, Neuhauser P, Wissner W, Klepetko W. Single running suture—the new standard technique for bronchial anastomoses in lung transplantation. *Eur J Cardiothorac Surg* 2003; 23(4):488–93.
- [2] Ouwens JP, van der Mark TW, van der Bij W, Geertsma A, de Boer WJ, Koeter GH. Size matching in lung transplantation using predicted total lung capacity. *Eur Respir J* 2002;20(6):1419–22.
- [3] Wissner W, Klepetko W, Wekerle T, Laufer G, Stift A, Hiesmayr M, Schlick W. Tailoring of the lung to overcome size disparities in lung transplantation. *J Heart Lung Transplant* 1996;15(3):239–42.
- [4] Artemiou O, Wieselthaler G, Zuckermann A, Wissner W, Wekerle T, Senbaklavaci O, Birsan T, Dekan G, Kritzing M, Klepetko W.

- Downsizing of the donor lung: peripheral segmental resections and lobar transplantation. *Transplant Proc* 1997;29(7):2899–900.
- [5] Couetil JP, Tolan MJ, Loulmet DF, Guinvarch A, Chevalier PG, Achkar A, Birnbaum P, Carpentier AF. Pulmonary bipartitioning and lobar transplantation: a new approach to donor organ shortage. *J Thorac Cardiovasc Surg* 1997;113(3):529–37.
- [6] Artemiou O, Birsan T, Taghavi S, Eichler I, Wisser W, Wolner E, Klepetko W. Bilateral lobar transplantation with the split lung technique. *J Thorac Cardiovasc Surg* 1999;118(2):369–70.
- [7] Couetil JP, Argyriadis PG, Amrein C, Chevalier P, Guillemain R, Achkar A, Carpentier A. Right split lung technique with bilateral lobar transplantation: an alternative approach to organ shortage. Abstract presented at the joint EACTS/ESTS Annual Meeting Sept. 2001, Lisbon.
- [8] 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* 1994;57(6):1423–7.
- [9] Sritippayawan S, Keens TG, Horn MV, MacLaughlin EF, Barr ML, Starnes VA, Woo MS. Does lung growth occur when mature lobes are transplanted into children? *Pediatr Transplant* 2002;6(6):500–4.