

Cite this article as: Van Raemdonck D, Ceulemans LJ, Vos R, Verleden GM. One size does not fit all patients in lung transplantation. *Eur J Cardiothorac Surg* 2021;60:1316–7.

One size does not fit all patients in lung transplantation

Dirk Van Raemdonck^{a,b,*}, Laurens J. Ceulemans^{a,b}, Robin Vos^{b,c} and Geert M. Verleden^{b,c}

^a Department of Thoracic Surgery, University Hospitals Leuven, Leuven, Belgium

^b Department of Chronic Diseases and Metabolism, Katholieke Universiteit Leuven, Leuven, Belgium

^c Department of Respiratory Diseases, University Hospitals Leuven, Leuven, Belgium

* Corresponding author. Department of Thoracic Surgery, University Hospital Gasthuisberg, Herestraat 49, B-3000 Leuven, Belgium. Tel: +32-16-34-68-23; fax: +32-16-34-68-24; e-mail: dirk.vanraemdonck@uzleuven.be (D. Van Raemdonck).

Keywords: Lung transplantation • Lobar transplantation • Graft reduction • Prioritized patients

'One size fits all' is a description for a product that would fit in all instances. However, many customers prefer to have custom-tailored clothing. Shoes are an example where sizes vary depending on the specific person [1]. 'Trimming' is a technique practised by gardeners to reduce a tree in size when it outgrows its space.

Donor (D) to recipient (R) size matching based on predicted total lung capacity is a parameter of special importance when choosing the right patient for lung transplantation (LTx). While grafting of an oversized liver in cirrhotic patients is feasible [2], compared to the abdomen the rigid chest cavity is less flexible to accommodate an oversized pulmonary graft. Cardiac tamponade, lung atelectasis and diaphragmatic dysfunction may result as a consequence [3].

Downsizing the pulmonary graft has been reported by many LTx groups as a successful method to transplant an oversized lung from a larger deceased donor into a smaller recipient. Two techniques have been described: lobectomy on the back table followed by lobar lung transplantation and peripheral non-anatomical shaving of the implanted lung with staplers or anatomical (middle) lobectomy after full-size LTx. This strategy is often practised in patients of small stature (e.g. female patients with restrictive lung disease, short cystic fibrosis patients or children) facing a long waiting time to find a size-matched donor.

Previous retrospective single-centre studies have reported good functional outcome and survival after graft volume reduction [3–5]. In the largest study up to date reported by the Vienna group [6], however, lobar LTx ($n = 138$) was associated with lower 1-year survival (65.1% vs 84.1%; $P < 0.001$) compared to standard LTx ($n = 539$). In a systematic review of 301 lobar LTx from deceased donors reported up to 2017, Eberlein *et al.* [7] found that the mean D/R predicted total lung capacity ratio before lobar resection was 1.25 ± 0.3 and the transplanted D/R predicted total lung capacity ratio after pre-transplant lobectomy was 0.76 ± 0.2 . One-year survival in the reduced-size lung group ranged from 50–100%, compared to 72–88% in the full-size lung group.

In this issue of the journal, authors from the Vall d'Hebrón University Hospital in Barcelona report their findings of a single-centre retrospective study between 01/2014 and 12/2018. Post-LTx outcome was compared between full-size versus reduced-

size lung recipients using propensity score-matched analysis ($n = 41$ patients each) [8]. Graft reduction surgery was performed by anatomic lobectomy pre-LTx in 69% of cases, generally simultaneous right lower lobectomy and left lower lobectomy. Non-anatomical wedge resection post-LTx was needed in 31% of patients, mostly in the right middle lobe and left lingular segment. The need for intraoperative cardiopulmonary bypass (54% vs 27%; $P = 0.017$) and for extracorporeal membrane oxygenation post-LTx for primary graft dysfunction was higher (15% vs 0%; $P = 0.025$) in the reduced-size group, while the median length of mechanical ventilation was longer (29 vs 15 days; $P = 0.008$). Pulmonary function at discharge, 3 and 6 months following LTx, was lower in the reduced-size group ($P < 0.05$). Survival at 1, 3 and 5 years post-LTx in recipients with a reduced-size graft was inferior (71%, 57% and 52% vs 87%, 75% and 64%, respectively; $P = 0.007$), while 1-year conditional survival was also worse ($P = 0.025$). Finally, graft reduction was identified as an independent risk factor for early mortality in univariable Cox regression analysis [HR (95% CI): 7.00 (1.59–30.80); $P = 0.010$ for pre-LTx lobectomy and 4.00 (1.34–11.96); $P = 0.013$ for stapling post-LTx]. The authors concluded that reduced-size LTx is associated with lower pulmonary function and overall survival, the exact reason for which is unclear. Nevertheless, the technique remains a viable option for prioritized candidates in urgent need who cannot wait any longer for a size-matched organ.

Some findings are interesting to discuss. Firstly, looking at the total cohort of transplanted patients ($n = 366$ patients), predicted D/R TLC ratio in the standard group ($n = 321$) was 1.08 ± 0.24 vs 1.23 ± 0.31 ($P < 0.001$) in the study group prior to size reduction ($n = 45$). The latter group consisted of significantly more female patients ($P = 0.03$), more recipients of smaller stature ($P = 0.001$), and more patients with restrictive lung disease ($P = 0.02$). This confirms that finding a size-matched donor for patients with these characteristics is more difficult. Moreover, recipients of reduced-size pulmonary grafts had a higher ($P = 0.034$) lung allocation score suggesting that these patients could not wait much longer to find a size-matched donor, as higher lung allocation score generally is associated with a higher risk of waitlist mortality. Finally, recipients of reduced-size lungs had a more complex and invasive surgical procedure as reflected by the higher

proportion of bilateral lung transplants (87% vs 70%; $P=0.018$) and clam-shell incisions (89% vs 72%; $P=0.017$). Propensity score matching was therefore used to control for these co-variables.

Secondly, outcome in terms of pulmonary function and survival remained inferior in the reduced-size group, the exact reason remaining unclear. As recently became more evident, lower pulmonary function after LTx fits with the concept of baseline lung allograft dysfunction known as a risk factor for impaired survival [9].

Thirdly, the final decision whether or not to reduce the size of the donor lung is not always clear cut. As the authors discuss in their paper, a visual subjective assessment of the volume of the recipient's chest cavity versus the entire donor lung while inflated is needed prior to embarking on anatomical lobectomy on the back table (Supplemental Fig. 1A). In case a full-size pulmonary graft is implanted, the decision to reduce the graft by stapling is taken upon closure of the chest with lungs fully inflated (Supplemental Fig. 1B). Cardiopulmonary instability by external heart compression with need for higher inspiratory peak pressures during lung ventilation may guide the surgeon to reduce the volume of the implanted graft. In our personal opinion, this occurs more frequently when using a clam-shell incision compared to antero-lateral thoracotomy allowing better downwards replacement of the diaphragm.

Finally, the 'best' lobe for anatomical lobectomy pre-LTx can be discussed, yet should be cautiously decided. In case of upper lobectomy, the bronchial anastomosis is performed at the level of the lower lobe bronchus (or intermediate bronchus on the right side). In oversized donor lungs, the diameter of the donor's lower lobe bronchus usually fits well with the size of the recipient's main bronchus. In contrast to the preference by the Barcelona group, it is our opinion that lower lobectomy increases the risk for a broncho-pleural fistula, both at the level of the lower lobe bronchial stump and at the level of the bronchial anastomosis between a larger donor main bronchus and a smaller recipient main bronchus.

The Barcelona group is to be congratulated with their results and important contribution. The paper by Montoya *et al.* [8] adds to the evidence that reduction of the pulmonary graft is a valuable, but inferior option to transplant prioritized patients of smaller stature who cannot wait any longer for a size-matched organ with the risk of premature death during their waiting period.

One size does not fit all patients. Further multicentre studies are needed to compare long-term outcome between reduced-size versus full-size LTx in patients matched for lung allocation score and urgency status.

Funding

Dirk Van Raemdonck and Geert M. Verleden are supported by the Broere Charitable Foundation. Laurens J. Ceulemans is supported by a named chair at the KU Leuven funded by Medtronic and a postdoc research fellowship funded by the University Hospitals Leuven (KOOR). Robin Vos is a senior clinical research fellow of the Fund for Scientific Research Flanders (FWO).

REFERENCES

- [1] One size fits all. https://en.wikipedia.org/wiki/One_size_fits_all (23 April 2021, date last accessed).
- [2] Addeo P, Naegel B, De Mathelin P, Paul C, Faitot F, Schaaf C *et al.* Predicting the available space for liver transplantation in cirrhotic patients: a computed tomography-based volumetric study. *Hepatol Int* 2021;doi:10.1007/s12072-021-10187-6.
- [3] Santos F, Lama R, Alvarez A, Algar FJ, Quero F, Cerezo F *et al.* Pulmonary tailoring and lobar transplantation to overcome size disparities in lung transplantation. *Transplant Proc* 2005;37:1526–9.
- [4] Artemiou O, Wieselthaler G, Zuckermann A, Wisser W, Wekerle T, Senbaklavaci O *et al.* Downsizing of the donor lung: peripheral segmental resections and lobar transplantation. *Transplant Proc* 1997;29:2899–900.
- [5] Aigner C, Mazhar S, Jaksch P, Seebacher G, Taghavi S, Marta G *et al.* Lobar transplantation, split lung transplantation and peripheral segmental resection—reliable procedures for downsizing donor lungs. *Eur J Cardiothorac Surg* 2004;25:179–83.
- [6] Slama A, Ghanim B, Klikovits T, Scheed A, Hoda MA, Hoetzenecker K *et al.* Lobar lung transplantation—is it comparable with standard lung transplantation? *Transpl Int* 2014;27:909–16.
- [7] Eberlein M, Reed RM, Chahla M, Bolukbas S, Blevins A, Raemdonck DV *et al.* Lobar lung transplantation from deceased donors: a systematic review. *World J Transplant* 2017;7:70–80.
- [8] Montoya P, Bello I, Ascanio F, Romero L, Pérez J, Rosado J *et al.* Graft reduction surgery is associated with poorer outcome after lung transplantation; a single-center propensity-score matched analysis. *Eur J Cardiothorac Surg* 2021;60:1308–15.
- [9] Liu J, Jackson K, Weinkauff J, Kapasi A, Hirji A, Meyer S *et al.* Baseline lung allograft dysfunction is associated with impaired survival after double-lung transplantation. *J Heart Lung Transplant* 2018;37:895–902.