Peer Review File
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Reviewer A

Comment 1. The CT volumes for donor and recipient are comparable in case 1 and 2 (6% and 5% respectively) which are likely reasons leading to favourable outcomes (i.e. not requiring downsize and good recovery). However for case 3, the CT volume discrepancy is up to 49% and yet not requiring downsizing the graft during transplant operation. There will be doubt on its accuracy of CT volume to predict size matching.

Reply: Thank you for this comment. Case 3 highlights an important aspect regarding the value of CT volumetry, in that it provides not only accurate total lung volumes for comparison (as seen in cases 1 and 2), but also offers additional information regarding the laterality of lung volumes. In case 3, CT volumetry of the individual donor lung volumes (R 1,528mL and L 1,330mL) and recipient lung volumes (R 1,115mL and L 802mL) showed that the CT volume discrepancy was primarily localized on the left side, due to the higher burden of fibrotic lung disease in the left lung which was also shown on the patient's ventilation-perfusion scintigraphy. The CXR heights of the donor and recipient left lungs were similar (23cm vs 22cm) and the recipient also had larger clinical metrics such as BMI and height than the donor. Thus, the decision was made to accept the offer using this information collectively. CT volumetry was pivotal in this patient scenario to provide insight for determining whether this donor offer would be an acceptable match. In this particular recipient, we were prepared to perform a back table downsizing including a lobectomy of the left lung. However, intra-operative findings demonstrated that the graft was only mildly oversized for the left pleural space. Our experience has been that a delayed chest closure often mitigates the need for significant downsizing, as we observed in this case.

Changes in the text: We have revised our manuscript to incorporate these important details. Please see these changes on Page 9, Lines 6-16.

Comment 2. There is huge difference in the predicted TLC and CT volume for all the three cases (donor 1.49 times, 2.8 times and 2.75 times bigger than recipient.in case 1,2 and 3 respectively). There is doubt on the applicability/validity of the formula to the respective population.

Reply: Indeed, we observed large differences between calculated pTLC based on standard formulations and CTvol measurements in all cases, thus underscoring the unreliability of relying on pTLC values to estimate lung volumes. pTLC values are calculated using a generic formula that only incorporates patient age and height with slight adjustments for gender. Thus, pTLC fails to incorporate many other important

factors such as weight, thoracic cavity parameters, race, and etiology of pulmonary disease. We have expanded our discussion to highlight these considerations.
Changes in the text: Please see these changes on Page 10, Lines 7-13.

Comment 3. There are two Pulmonary hypertension (less common indication for lung transplant) cases and one interstitial lung disease case included in this report. The readers would be more interested in knowing if CT volumetry would help in more common diseases like COPD.

Reply: Thank you for this comment. We have revised our manuscript to include a 4th case in which CT volumetry was obtained to help evaluate lung size matching between a donor and a recipient with COPD. Similar to cases 1, 2, and 3, we found that CTvol measurements were quite different from pTLC values. Based on pTLC estimates, the donor lungs in this case were markedly oversized. However, CTvol revealed that donor lungs were actually smaller than the recipient's lungs. This emphasizes the value of image-guided lung volume measurements for patients with obstructive lung disease that may have notable thoracic cavity expansion.

Changes in the text: Please see this additional Case 4 in our manuscript on Page 9, Lines 19-23 and Page 10, Lines 1-3.

Reviewer B

Shepherd HM et al present a technique evaluating donor and recipient mismatch in lung transplantation, using CT volumetry. Notwithstanding the small number of patients included in this case series, I think that the use of imaging in matching donor and recipient in lung transplantation is of paramount importance and I agree with the authors that it is more reliable than the predicted TLC.

I have just one minor comment:
1. The authors should expand the discussion, for example by discussing the additional advantages of regularly performing CT scans, especially in donors. As such, it is possible to exclude donor malignancies, to better characterize the presence of infiltrates and atelectasis or poor ventilated areas, among others.

Reply: Thank you for your insightful comment. Indeed, in our experience, obtaining donor CT imaging has provided incredibly valuable information regarding donor factors including revealing occult structural lung disease, evaluating congenital anomalies, and better evaluation of pathologies such as atelectasis or consolidation. We have revised our manuscript to expand upon these points.

Changes in the text: Please see these changes to the Discussion on Page 10, Lines 18-21 and additional reference 16.

Reviewer C

The reviewer is honored to review an article about the use of CT volumetry for size matching before lung transplantation. The paper is well written and easy to understand. This paper has a meaning in that CT volumetry was used for the decision of lung transplantation. However, this paper is a case-series typed paper, whose evidence level is not so high. In Case 1, size matching based on pTLC was 132.6% (D/R), which means a bit oversized donor. However, we usually perform lung transplantation with such an oversized donor as this case. In Case 2, size matching based on pTLC was 153.6% (D/R), where some lung transplant center might decline in such donor and recipient combination. However, a donor and a recipient were so young, which means both lungs and thorax might be flexible. Atelectasis/consolidation might work as a natural reduction of size for a donor side. In Case 3, size matching based on pTLC was 90.4% (D/R), which means this combination was a size-matched case.

The reviewer wants to ask some questions, as follows:

1) The authors should mention that the respiratory phase was totally different between a donor and a recipient. While the recipient chest CT was taken in an intentionally deep- inspirated phase, the phase of the respiratory phase of the donor at the time of chest CT was dependent on the general condition of the donor. Sometimes, the donor was intubated, but the Ambu-bag was disconnected while chest CT was taken (deep expiratory phase with no voluntary respiration). This situation makes the CT volumetry value of the donor so small, which should be emphasized in the manuscript.

Reply: Thank you for this point. The reviewer raises an important point regarding the margin of measurement error that arises with continuous ventilation in intubated donors and the need for protocols to implement standardization of CT scan acquisition. While scan acquisition for CT volumetry is ideally performed during inspiratory breath hold, this is not standardized practice at most donor organ procurement facilities including our own local recovery facility. The donors in this study were mechanically ventilated with continuous breathing during CT scan acquisition, as we have not yet instituted a protocol at our local facility. This may have contributed to underestimated donor CTvol measurements, and we have included this point in our revised manuscript. Additionally, protocol implementation to standardize ventilation settings and inspiratory hold during donor scan acquisition is needed to mitigate this measurement error. We have added these details and considerations to our discussion section. Please see these changes on Page 7, Lines 6-7, Page 10, Lines 11-13, Page 11, Lines 21-23, and Page 12, Lines 1-5.

2) The authors should provide the data of actual TLC data, which usually help a thoracic surgeon to decide about size-matching after donor allocation.

Reply: Of our 4 cases, 3 recipients had prior pulmonary function testing with TLC values. Recipient 2 had prior pulmonary function testing without a TLC value (only FVC and FEV1). We have listed the available recipient TLC values obtained by plethymography prior to transplant, which closely correlate with CT volumetry values.
Recipient 1: TLC 5.05 (CTvol 5.275, pTLC 5.529)
Recipient 2: no TLC prior to lung transplant
Recipient 3: TLC 2.22 (CTvol 1.917, pTLC 5.272)
Recipient 4: TLC 6.70 (CTvol 6.014, pTLC 5.100)

3) Postoperative CT volumetry data for recipients should be provided. Three months, six months, and 1 year after lung transplantation.

Reply: Postoperative CT volumetry data is not available for the recipients, as repeat CT imaging is not routinely performed following lung transplant at our institution per our post-transplant protocols. We have added this point to our revised manuscript. Please see these changes on Page 7, Lines 15-17.

4) There are many papers about preoperative volumetric size-matching in living-donor lobar lung transplantation. Please add some discussion about citing several papers, such as PMID27847159 (Date H, et al. JTCVS 2017).

Reply: Thank you for this comment. Indeed, prior studies investigating volumetric size matching in living-donor lobar lung transplantation have evaluated the use of CT volumetry (mainly used to evaluate oversized lung grafts) as well as pulmonary function testing (possible for living donors but not typically feasible for brain dead donors) as potential methods for donor-recipient size matching. Based on these studies, CT volumetry has been reported to be a useful adjunct for determining donor-recipient size matching of individual lung lobes and for unilateral lung transplantation. We have incorporated these points in our revised manuscript. Please see these changes on Page 6, Lines 11-13 and additional References 13 and 14.

Reviewer D

A novelty of this case series study is that 3D-CT volumetry can be useful for size matching between donor and recipient in lung transplantation. I have some comments as follows:

Comment: In the current clinical practice, what clinical parameters do the authors use for decision making on size matching between donor and recipient, pTLC or patient height? And what are the upper and lower limits? For example, in our region, when both the donor and recipient are ≥18 years old, the donor's predicted vital capacity (VC) should be 100±30% of the recipient's predicted VC. When the donor and/or recipient are <18 years old, the donor's height should be 100±12% of the recipient's height for bilateral transplantation.
Please give the information in the "Methods".

Reply: Our practice involves only adult lung transplantation and therefore we can only speak to patients >18 years old. At our institution, we predominately utilize height to guide size matching between donor and recipient. Our general threshold for donor and recipient height is +/-10-15%. We also utilize CXR lung heights, but do not have defined cutoff values for which we will reject a donor offer based on CXR lung heights alone. We do not routinely calculate pTLC to determine size matching between donor and recipient, given the inaccuracies of this formula in our personal experience. These details have been incorporated into the Methods section our revised manuscript. Please see these changes on Page 6, Line 23 and Page 7, Line 1.

Comment: I do not think the donors had some pulmonary restrictive lung diseases in the current study. However, all the donors showed significantly lower lung volume measured by CT volumetry than the pTLC. Please discuss about what made this discrepancy in the "Discussion".

Reply: Thank you for your comment. As mentioned by the reviewer, pTLC estimates are poorly correlative with measured lung volumes by CT volumetry and underscores the unreliability of using surrogate measures such as age and height to predict lung size. With regard to smaller donor lung volumes measured by CT volumetry, this may have been related to clinical factors such as atelectasis or consolidation that can diminish lung volumes, or other factors such as mechanical ventilation settings or measurement error related to continuous breathing during scan acquisition. The donors in this study were mechanically ventilated without inspiratory breath hold during CT scan acquisition, as we have not instituted a protocol at our local facility to standardize these variables. We have included these details and considerations in our revised manuscript. Please see these changes on Page 7, Lines 6-7, Page 10, Lines 11-13, Page 11, Lines 21-23, and Page 12, Lines 1-5.

Comment: Donor lung volume can be affected by mechanical ventilator settings and by atelectasis in lower lobe(s), which can hinder the accurate measurements of donor lung volume by CT volumetry? Please discuss about that in the "Discussion".

Reply: We agree that factors such as mechanical ventilator settings and atelectasis can impact CT volumetric lung volume measurements, and we have included these

important considerations in the discussion section of our revised manuscript. Please see Page 10, Lines 11-13, Lines 21-23, and Page 12, Lines 1-5.
Comment: The donor's calculated pTLC showed the same values "7,329 ml" in the Cases 1 and 2. Please confirm that the donor's pTLC was correct in the Case 2.

Reply: We appreciate this astute observation. Indeed, the donor in Case 1 and the donor in Case 2 both had pTLC values of 7,329 mL. This is because both donors were the same height (180cm) and both male, thus generated the same pTLC value (since the formula only incorporates individual height and gender). This point re-enforces the inaccuracy of the pTLC method of assessing lung volumes.