


Concerns Raised by Lung Size-Mismatched Transplantation

To the Editor:

We read with great interest the article by Eberlein et al in CHEST (February 2012), which concluded that an oversized lung allograft (predicted total lung capacity [pTLC] ratio > 1.0) was associated with higher respiratory airflow capacity and a less frequent occurrence of bronchiolitis obliterans syndrome when compared with an undersized allograft (pTLC ratio ≤ 1.0). Undeniably, lung size mismatch is commonly encountered in pulmonary transplantation because donor allocation does not allow precise matching when a long list of patients is waiting for scarce donors. We are grateful to the authors for their important work. However, we would like to voice some significant concerns about the study design that need clarifications.

A heterogeneous population of 159 patients undergoing transplant from two different centers (Johns Hopkins Hospital from January 1996 to March 2010 and Inova Fairfax Hospital from January 1996 to December 2008) was included in this retrospective study. However, no data were available to show the comparability between the two centers and it is unknown if significant bias was introduced by different transplant protocols, which play a vital role in the prognosis of these patients. As a consequence, potential confounding factors not accounted for, including recipient and donor characteristics, should have been compared between the two centers before a combined analysis was conducted; otherwise, a separate analysis for each center would have been preferred.

The authors provide the pTLC ratio (donor pTLC/recipient pTLC) for their definition of size matching according to the regression equations. Although we indeed agree that the pTLC ratio is widely used to match donors with recipients, it is wrong to suggest that the pTLC ratio is a reliable marker of size matching, as stated by the authors, because no reference range of pTLC ratio was raised to address the ideal status of size matching. From our perspective, oversized allografts implanted into the smaller thorax cavity can lead to atelectasis and impaired airway clearance because of bronchial anatomy distortion.

Increasing evidence suggests that size-reduced lung transplants (graft volume reduction and lobar lung transplant) are beneficial to recipients receiving oversized allografts. Shigemura et al investigated lung volume reduction as an efficient tool for reducing short-term complications and improving pulmonary function in patients with size-mismatched allografts. A special approach for overcoming severe size disparities is lobar transplant, which is especially useful in pediatric lung transplants involving a small thorax cavity. Loizzi et al suggested the pTLC ratio as a marker of lobar transplant based on a receiver operating characteristic analysis: Patients with oversized allografts (pTLC ratio > 1.2) were considered for a lobar transplant, for which the higher the pTLC ratio, the higher the possibility that the patients were likely to benefit from it. Date et al also stated that size disparity in lobar transplants can be accepted when the total FVC of the two grafts is > 50% of the predicted FVC of the recipient, estimated by the following formula: Total FVC of the two grafts = measured FVC of the right donor × 5/19 + measured FVC of the left donor × 4/19 (the right lower lobe consists of five segments, the left lower lobe of four, and the whole lung of 19). Date et al suggested that in such a case, this is an alternative to conventional cadaveric lung transplant, resulting in a similar outcome. Additionally, comparable clinical outcomes were observed between patients who received size-matched allografts and size-reduced allografts. However, the authors did not describe in the article the situation of size-reduced lung transplantation for an oversized cohort, implying that lung trimming as a confounding factor may result in significant discrepancy. It would be helpful if this concern could be commented on, and further analysis of the study to address this important issue is required.

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**Response**

*To the Editor:*

We thank Dr Mao and colleagues for their comments on our article in *CHEST.* Investigations on lung transplantation are often single-center studies with limited external validity; thus, including data from two study sites strengthened our investigation. An analysis by study site showed comparable results for allograft function, and introducing study site as a variable into the Cox proportional hazard models for the occurrence of bronchiolitis obliterans syndrome (BOS) showed no significant interaction between study site and BOS ($P = .748$ for univariate and $P = .774$ for multivariate model).

Information on transplant protocols and recipient characteristics by study site for the same cohorts as in this investigation has been published. The concern was raised that oversizing the allograft could be associated with an increase in complications after bilateral lung transplant. The latter investigation was limited to the post-lung-allocation-score era, and the undersized cohort had a significantly higher lung allocation score, was more likely to be in the ICU prior to transplant, and had a higher need for cardiopulmonary bypass during transplant. Thus, differences in the acuity and complexity of undersized compared with oversized patients might account for some of the observed differences. Lung trimming because of an oversized allograft was required in only one patient in the study reporting on the effects of lung size mismatch early after lung transplantation.

Providing criteria for donor recipient size matching is beyond the scope of this investigation. However, we do believe that introducing study site as a variable into the Cox proportional hazard models for the occurrence of bronchiolitis obliterans syndrome (BOS) showed no significant interaction between study site and BOS ($P = .748$ for univariate and $P = .774$ for multivariate model).

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**Ciliary Beat Pattern Analysis Below 37°C May Increase Risk of Primary Ciliary Dyskinesia Misdiagnosis**

*To the Editor:*

We read with interest the article by Smith et al published in *CHEST* (July 2011). The authors analyzed ciliary function in 14 nasal turbinate brushing biopsy specimens that provided ciliated epithelium from healthy human volunteers. The authors stated that ciliary function was maintained at temperatures ranging between 37°C and 2°C, contrary to previous research suggesting that cilia stop beating at 4°C, and a sigmoid relationship between ciliary beat frequency (CBF) and temperature was observed. The authors suggested that a normal ciliary beat pattern (CBP) may be analyzed at temperatures as low as 2°C and that cooling of cilia may allow interrogation of CBF for diagnostic testing without the need for expensive, high-speed video microscopy. We are in agreement that additional CBF analysis is invaluable over CBF alone for the diagnosis of primary ciliary dyskinesia (PCD), particularly for those with normal CBF ranges. However, it is important to highlight that assessing CBF at temperatures below 37°C may increase the likelihood of misdiagnosis.

We were recently referred an 8-month-old girl with a strong clinical history of PCD (respiratory and nasal symptoms since birth, situs inversus, and serous otitis media). Using high-speed video microscopy we recorded abnormal and hyperfrequent ciliary function at 37°C on four separate occasions, despite normal ciliary ultrastructure consistent with atypical PCD. On two occasions the CBF and CBP were assessed at 37°C and room temperatures (measured at 21°C-24°C). CBF from at least six separate ciliated cell clusters measured at 37°C was hyperfrequent on both occasions (mean, 26.3 Hz [SD ± 3.4]; 34.4 Hz [SD ± 13.5]). However, when measured at room temperature, the CBF measurements were within normal range (11-18 Hz) (mean, 12.6 Hz [SD ± 0.8];