Response

To the Editor:

We thank Dr Mao and colleagues for their comments on our article in CHEST.1 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.2 The concern was raised that oversizing the allograft could be associated with an increase in early postoperative complications. We reported in a subsequent study that oversized allografts, as estimated by a predicted total lung capacity ratio > 1.0, were not associated with an increase in complications after bilateral lung transplant.3 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.3 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 on complications;4 however, we do not have comprehensive data on this for the entire cohort for this study, which we expressed in the discussion of study limitations.1

Providing criteria for donor recipient size matching is beyond the scope of this investigation. However, we do believe that a better understanding of the mechanisms linking parameters of expiratory airflow capacity early after lung transplantation to the risk of developing BOS holds the promise of uncovering modifiable factors influencing survival after lung transplantation.15

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References


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 al1 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,2,3 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 (PCD), particularly for those with normal CBF ranges. However, when measured at room temperature, the CBF measurements were within normal range (11-18 Hz) (mean, 12.6 Hz [SD ± 0.8]);
15.2 Hz (SD ± 4.5)). CBP at 37°C was consistently abnormal, with interrupted, dyskinetic, hyperfrequent ciliary beating, and cilia lacked the normal range of motion (Video 1). Cilia were directly compared on the same epithelial edge at 37°C and room temperature, and, as described previously, profoundly abnormal ciliary movement at 37°C (Video 1) reverted to a more normally coordinated beat pattern with a greater range of movement at room temperature (Video 2), suggesting a PCD variant with temperature-dependent CBP. We conclude that cooling of cilia to allow diagnostic interrogation of ciliary function, in the absence of temperature controlled high-speed video microscopy equipment, may be inappropriate for the diagnostic screening of nasal epithelium for PCD.

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**Other contributions:** Informed consent was provided by the parents of this case for use of clinical information and samples for academic research for “A study of the pathophysiology and clinical manifestations of PCD and other chronic respiratory disease of childhood” (LREC 06/Q1702/109).

**Additional information:** The videos can be found in the “Supplemental Materials” area of the online article.

**REFERENCES**


**Response**

To the Editor:

We originally described how analysis of ciliary beat pattern may be associated with the underlying ultrastructural defect in primary ciliary dyskinesia (PCD) and have since described the use of beat pattern analysis in diagnosing patients with PCD. Our article in CHEST referred to the maintenance, at low temperatures, of a normal ciliary beat pattern of cilia from subjects without PCD, which resulted in cilia slowing sufficiently to allow observation of their beat pattern. We are currently investigating whether such a low-cost alternative to slow-motion video analysis may be of use in the diagnostic testing of PCD.

We thank Dr Jackson and colleagues for their letter describing a potential problem relating to the possibility that a phenotype of PCD may exist, in which abnormalities in ciliary beat pattern may not be obvious at low temperatures. This is based on their description of one patient with a hyperfrequent ciliary beat frequency who had no associated ultrastructural abnormalities of the ciliary axoneme. Additional confirmatory evidence of PCD using cell culture or genetic testing would certainly be useful in this case.

We have recently had the opportunity to review with a member of the Southampton team the video files relating to the patient described and have also reviewed the files provided with the letter. The focus of the two videos is different at 37°C and at room temperature; however, each member of our nationally funded PCD diagnostic center independently felt the abnormal ciliary beat pattern could be seen at both the lower and higher temperatures. We do not agree, therefore, that this rare phenotype of PCD would be missed if the ciliary beat pattern was observed at a lower temperature.

It was also noted that the beat frequency at room temperature was within the normal range. However, this would have to be a normal range obtained from large numbers of patients at room temperature. It is unclear from the letter that this is the case. We do believe, however, that analysis of ciliary beat pattern in a cohort of patients with PCD using high-speed video analysis needs to be compared with results at low temperatures; this work is currently being undertaken.

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