Response

To the Editor:

We appreciate the comments by Dr O'Connell and colleagues on our article published in *CHEST*¹ describing the cumulative incidence and pretransplant risk factors for post-lung transplant renal dysfunction in adult patients with cystic fibrosis (CF).

We agree that serum creatinine concentration alone should not be relied upon solely to assess renal function in CF because of its poor sensitivity. Although the use of glomerular filtration rate (GFR) estimating equations, such as the Cockcroft-Gault formula and the abbreviated Modified Diet in Renal Disease (aMDRD) equation, represent improvements compared with serum creatinine alone, as they factor in patient age, weight, and sex, these equations still tend to overestimate renal function in CF compared with gold standard measurement techniques.² Patients with CF tend to be malnourished compared with the general population, with less muscle mass per body weight. Low muscle mass leads to reduced creatinine production, which results in overestimation of GFR.³ The estimated 2-year cumulative incidence of post-lung transplant renal dysfunction of 35% derived in our study is conservative, since we used the Cockcroft-Gault formula and have likely overestimated renal function. Future studies are required to identify more sensitive markers of renal function with less reliance on serum creatinine.

We also agree that patients with CF have several unique risk factors for the development of renal dysfunction posttransplant, which may increase their risk relative to patients with idiopathic pulmonary fibrosis or COPD. However, we are not aware of any studies that have specifically compared the risk of renal dysfunction in these recipient populations. Our study did not focus on post-lung transplant risk factors, but we appreciate Dr O'Connell and colleagues pointing out that oxalate nephropathy and pigmented tubulopathy are well-recognized histopathologic findings following renal biopsy in the early posttransplant period and are likely related to perioperative stressors such as dehydration, hypoxia, and antibiotics.⁴ Our analysis excluded patients diagnosed with renal dysfunction in the first month post-lung transplant to reduce the chance of including acute cases. Our study found that CF-related diabetes requiring insulin is an important pretransplant risk factor and likely plays an important role in renal function loss in the late posttransplant period. This is in keeping with a published renal biopsy series, which demonstrated that histopathologic findings responsible for late episodes of renal function loss were primarily vascular (ie, diabetic glomerulosclerosis).⁴

A large registry-based study has demonstrated that post-lung transplant renal dysfunction is associated with worse post-lung transplant survival.⁵ Therefore, further studies are needed targeting modifiable risk factors in the CF population.

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Therapeutics, Aptalis, Pharmaxis Ltd, and INSMED Inc investigators meetings, but none of these activities relate to the topic of this manuscript. Dr Goss has received travel money and research grant money from INSMED Inc to attend investigator meetings and integrate a symptom questionnaire into a clinical trial. He has also received honoraria from Hoffman-La Roche, Inc and Johns Hopkins University for CME courses and course material. He has also received honoraria donated to CF research to attend an advisory meeting with KaloBios Pharmaceuticals, Inc. Drs Quon and Mayer-Hamblett have reported that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

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Diastolic Dysfunction With Nondilated Left Atrium

To the Editor:

We read with great interest the article on cardiac diastolic dysfunction in patients with pulmonary arterial hypertension by Tonelli et al¹ published in *CHEST* (June 2012). We appreciate their original and interesting contribution, especially when there is limited knowledge on the topic. Echocardiography is the most commonly used method for studying diastolic dysfunction. However, we should keep in mind that current echocardiographic diastolic classification may not be suited to respiratory patients because in these patients the volume of the left atrium is decreased, as Tonelli et al¹ and other authors² have reported. In most patients with diastolic dysfunction, the dysfunction occurs when the left atrium is dilated, reflecting the cumulative effects of filling pressures over time. This dilatation is a key point in the diagnosis of diastolic dysfunction, even in mild (or grade I type) cases. In specific patients with a nondilated left atrium, caution should be exercised when diastolic classification is applied.

On the other hand, echocardiographic diastolic classification is complex, and sometimes the parameters obtained may be discordant; thus, classification into diastolic stages can be difficult. When diastolic dysfunction is graded by experienced observers according to current guidelines,³ interobserver variability and accuracy depend on how each investigator resolves conflicting observations that make the classification into one specific type of diastolic dysfunction difficult. It would be interesting to learn if the authors experienced discrepancies with regard to the diastolic