JACC: CARDIOVASCULAR IMAGING
VOL. 7, NO. 11, 2014

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
http://dx.doi.org/10.1016/j.jcmg.2014.08.004

EDITORIAL COMMENT

RV Dysfunction After Lung Transplantation

A New Prognostic Marker or Mainly a Correlate of Lung Allograft Function?*

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In recent years, more attention has been given to right ventricular (RV) function in cardiovascular and pulmonary disease (1,2). Ghio et al. (3) were the first to clearly demonstrate that the presence of RV systolic dysfunction and pulmonary hypertension (PH) increases the likelihood of a poor outcome in patients with heart failure with reduced ejection fraction. More recently, among 406 patients with PH, Fine et al. (4) showed that RV global longitudinal strain (GLS) is a strong and independent prognostic marker of event-free survival along with functional class and N-terminal B-type natriuretic peptide levels. The study of Kusunose et al. (5), in this issue of *iJACC*, builds on these previous studies but with an original focus on post-lung transplantation outcome. Consistent with the findings of Ghio et al. (3) and Fine et al. (4), the authors highlight the potential prognostic importance of post-lung transplantation RVGLS and PH.

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In recent years, there has been a great interest in using myocardial strain as a metric of ventricular function. This stems from the observation that RV longitudinal strain may represent an earlier marker of ventricular dysfunction compared with ejection fraction or annular displacement. In addition, RV strain measures could be more reproducible than right ventricular fractional area change (RVFAC). Conceptually, strain refers to an object's fractional or percent of change from its original unstressed dimension (i.e., a change in length corrected for the original length or [L1 − L0]/L0, where L0 is the original length and L1 the length after deformation). Strain can be calculated in several dimensions; longitudinal, circumferential, or radial and a more negative value of strain corresponds to better ventricular function. Using 2-dimensional echocardiography, RV strain is usually only measured in the longitudinal dimension as the right ventricle is not often completely visualized in the short-axis planes. RV longitudinal stain is higher than LV strain and "normal" values are reported to be lower than −25% (RV free wall excluding the septal component) (4). Current studies are ongoing to determine the most accurate, reproducible, and time-efficient method to measure RVGLS. At the present time, different methods of RV strain have been described including manual tracing, tissue Doppler imaging, speckle tracking, and, as recently described, a 3-dimensional method (6–8). Compared with tissue Doppler, speckle imaging has the advantage of being less influenced by the insonation angle or ventricular wall motion, as is currently the most frequently used method.

In their study, Kusunose et al. (5) describe the extent of RV and left ventricular remodeling after lung transplantation for advanced lung disease (9). Among functional indexes, the improvements were more notable for RVFAC and RVGLS. In contrast, tricuspid annular plane systolic excursion (TAPSE) did not show significant change after lung transplantation, a finding highlighting the less sensitive nature of TAPSE for global changes in ventricular function. Among factors potentially influencing the remodeling process, the authors observed that patients with pulmonary fibrosis and higher baseline pulmonary pressure had a greater degree of remodeling and functional improvement. The more significant change in patients with pulmonary fibrosis

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

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may be in part secondary to the fact that they had higher baseline pulmonary vascular resistance and lower baseline RVGLS.

As highlighted by several studies, the right ventricle has a remarkable ability to reverse remodel and improve its function after a decrease in RV afterload (1,2,10). Frist et al. (9) were one of the first groups to demonstrate that, in patients with pulmonary arterial hypertension undergoing lung transplantation, the right heart reverse remodels almost to normal by 1 year post-transplantation. The study of Frist et al. (9) also points to the importance of standardizing the time of RV assessment because the remodeling process may take up to 1 year. This may be less important in advanced lung disease as in the study of Kusunose et al. (5) because the extent of RV dysfunction at baseline is less severe, and remodeling may occur earlier. Pathophysiologically, the greater capacity of the right ventricle to reverse remodel compared with the pressure-overloaded left ventricle may be in part explained by the smaller extent of fibrosis observed (11–14).

The other major finding of the study was the fact that patients with both RV dysfunction and PH after lung transplantation had significantly worst outcomes. As the authors acknowledge, however, the retrospective nature of the study, the potential of selection biases, the variable timing of the echocardiographic evaluation, and the absence of a validation cohort make the interpretation of the outcome analysis more challenging. For example, only patients who had a follow-up echocardiogram were included in the study; these patients may have signs of heart failure or lung allograft dysfunction at time of evaluation. Also, the variable timing of post-transplantation echocardiographic evaluation may introduce a time bias because the remodeling process may not be at the same stage in each patient. The authors did, however, attempt to adjust for this by adding follow-up time in the survival analysis. Finally and more importantly, we wonder whether RV function and PH are "truly" independent prognostic markers of event-free survival after lung transplantation or mainly markers of worse lung allograft function. In fact, the missing covariate in the multivariable model is the presence of bronchiolitis obliterans syndrome or pulmonary function test results (15). Bronchiolitis obliterans already represents a very strong prognostic marker in lung transplantation but usually occurs later in the post-transplantation course (15). Notwithstanding these limitations, the study does point to very important observations with regard to RV function and outcome after lung transplantation. In fact, as the authors highlight, pre-transplantation RV function does not appear to be associated with post-transplantation outcome. Also consistent with the study Fine et al. (4), the findings suggest that RVGLS could carry more prognostic information than RVFAC or TAPSE. Interestingly, the findings of the study are strongly reminiscent of the Kaplan-Meier survival curve of the study of Ghio et al. (3).

This study not only brings novel insights to RV function after lung transplantation but also guides future studies on the topic. Whether RV function brings incremental prognostic information to the presence of bronchiolitis obliterans and whether an intervention can improve outcomes in these higher risk individuals will require further study.

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KEY WORDS echocardiography, hypertension, lung transplantation, myocardial deformation imaging, pulmonary survival, right ventricular function