The use of surrogate end points in pulmonary arterial hypertension: Enhancing clinical decision making by improving time to clinical worsening observations

Pulmonary Arterial Hypertension (PAH) is defined as a mean pulmonary artery pressure (mPAP)>25 mmHg at rest and >30 mmHg during exercise. Available pharmacologic therapies target pre-capillary disease by reducing pulmonary artery (PA) pressures. The effects of relaxing the PA, mitigates right heart failure caused by prolonged elevation in PA pressures. Early recognition and intervention in clinical deterioration is paramount towards maintaining exercise capacity, quality of life (QOL) and survival in PAH, but current clinical end points are limited in their predictive ability to reduce the latency in time to clinical worsening (TTCW). Field tests such as the 6 minute walk test (6 mwt), cardiopulmonary exercise testing (CPET) and the incremental shuttle walk test (ISWT) are simple to perform, validated means to measure response to intervention and correlate with invasive right heart catheterization data, which is the gold standard measure of PAH. However, clinically significant changes in these field tests, after intervention, have not demonstrated improved morbidity, hospitalization or need for the initiation of rescue therapy. Newer surrogate markers of disease, such as the tricuspid annular plane systolic excursion (TAPSE) and cardiac MRI, allow noninvasive measurement right ventricular (RV) function and demonstrate prognostic ability in PAH. However, imaging studies lack the ability to predict time to worsening heart function, due to lack of correlation with exercise capacity information. Physical activity, assessed by steps taken per day, is a cost effective therapy improving QOL and correlates with exercise capacity measurements obtained during field testing. Unfortunately, measuring physical activity is limited due to concerns exercise training may increase the risk of adverse clinical events. Optimum management of PAH, centers on preservation of RV function by early treatment of PA elevation and early detection of changes to PA pressure, prior to patient report. This goal requires movement away from outdated clinical trial designs and combining surrogate end points that detect changes in physical activity, which may predate loss of RV function.

Biography
Keith J Robinson is an Associate Clinical Professor with Florida International University practicing with Pulmonary Physicians of South Florida, LLC. He has completed his Medical training from Indiana University, his Residency in Internal Medicine from The University of Florida, Jacksonville, FL, and his Fellowship in Pulmonary/Critical Care Medicine from the University of California, CA.

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