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*Exploring the association of visceral intrathoracic fat with vascular stiffness in pulmonary hypertension*

### INTRODUCTION:

Pulmonary arterial stiffness plays a crucial role in right ventricular dysfunction in pulmonary hypertension (PH) and has been shown to be a strong predictor of mortality in various forms of PH. We propose to study the role of obesity in pulmonary vascular disease, particularly focusing on the impact of visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) on pulmonary arterial stiffness.

### BACKGROUND:

Adult obesity rates in the United States are increasing; a third of incident and prevalent patients with PH are obese. In the systemic vasculature, obesity is an important risk factor for vascular stiffness; specifically, abdominal VAT is linked to an increased risk of cardiovascular disease. While most adipokines secreted from adipose tissue are associated with atherogenesis, apoptosis, and inflammation, apelin, vaspin and C1q/tumor necrosis factor related protein (CTRP) are produced by VAT and have anti-inflammatory, anti-atherosclerotic, and anti-apoptotic effects. The effect of VAT on pulmonary hemodynamics, particularly thoracic VAT, whose lymphatics drain directly into the pulmonary circulation, has not been studied. The objective of this proposal is to study the role of obesity in pulmonary vascular disease, particularly focusing on the impact of thoracic VAT and SAT on pulmonary arterial stiffness in patients with PH. The proposal will utilize data from the Lung Transplant Body Composition (LTBC) Study, which is an NIH-funded, prospective, multicenter cohort study focused on primary graft dysfunction that has previously measured adipose tissue compartments using computed tomography (CT) of the chest in 540 individuals with advanced lung disease (ALD), assayed plasma cytokine and adipokine levels, and collected VAT biopsies (from explants) in patients undergoing lung transplantation (LTx).

### HYPOTHESIS AND OBJECTIVES:

We propose to examine the association of VAT/SAT with pulmonary vascular disease in patients with ALD from the LTBC study. Specifically, we hypothesize that lower thoracic VAT/SAT will be associated lower plasma levels of apelin, vaspin and CTRP and lower pulmonary arterial capacitance, higher pulmonary vascular resistance and lower cardiac output, independent of measures of age, sex, race/ethnicity, and severity of lung disease as indicated by lung function. Results from this analysis will provide critical preliminary data for future studies investigating the role of body fat composition modification through diet and exercise on pulmonary hemodynamics in patients with PH.

### SPECIFIC AIM 1:

To determine the associations of intrathoracic VAT and SAT volumes from quantitative chest CT with pulmonary hemodynamics in patients with ALD evaluated for LTx.

### SPECIFIC AIM 2:

To determine the associations of VAT and SAT volumes with plasma adipokine levels (apelin, CTRP and vaspin) in patients with ALD listed for LTx.

### SPECIFIC AIM 3:

To identify the gene expression signature of intrathoracic VAT in patients with PH.