Clinical Trials

Heart Failure and Respiratory Hospitalizations Are Reduced in Patients With Heart Failure and Chronic Obstructive Pulmonary Disease With the Use of an Implantable Pulmonary Artery Pressure Monitoring Device

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a frequent comorbidity in patients with heart failure (HF). Elevated pulmonary arterial (PA) pressure can be seen in both conditions and has been shown to predict morbidity and mortality.

Methods and Results: A total of 550 subjects with New York Heart Association functional class III HF were randomly assigned to the treatment (n = 270) and control (n = 280) groups in the CHAMPION Trial. Physicians had access to the PA pressure measurements in the treatment group only, in which HF therapy was used to lower the elevated pressures. HF and respiratory hospitalizations were compared in both groups. A total of 187 subjects met criteria for classification into the COPD subgroup. In the entire cohort, the treatment group had a 37% reduction in HF hospitalization rates ($P < .0001$) and a 49% reduction in respiratory hospitalization rates ($P = .0061$). In the COPD subgroup, the treatment group had a 41% reduction in HF hospitalization rates ($P = .0009$) and a 62% reduction in respiratory hospitalization rates ($P = .0023$). The rate of respiratory hospitalizations in subjects without COPD was not statistically different ($P = .76$).

Conclusions: HF management incorporating hemodynamic information from an implantable PA pressure monitor significantly reduces HF and respiratory hospitalizations in HF subjects with comorbid COPD compared with standard care. (*J Cardiac Fail 2015;21:240–249*)

Key Words: Heart failure, chronic obstructive pulmonary disease, implantable pulmonary artery pressure monitor, hospitalization.

Chronic obstructive pulmonary disease (COPD) and heart failure (HF) are global epidemics and are leading causes of morbidity and mortality.[1–3] Both of these conditions are major public health problems and present a significant burden on the health care system.[4–10] COPD is a frequent comorbidity in patients with HF, but there are few reports that describe the clinical characteristics and outcomes in this population.[11–13] Elevated pulmonary arterial (PA) pressure can be seen in both conditions, particularly during exacerbation as the disease progresses, and has been shown to be a predictor of morbidity and mortality.[14–17] Despite current treatment regimens, hospital admission rates for both COPD and HF continue to

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increase. Improvements in outpatient management of patients with COPD and HF are needed to address the burden of increased exacerbations requiring hospitalizations. Earlier studies in subjects with HF have shown that increases in intracardiac and PA pressures occur before onset of clinical symptoms[18,19] and that early intervention in response to the elevated pressures decreases hospitalization rates.[20,21]

To our knowledge, no data exist that analyze the impact of an implantable hemodynamic monitoring device on COPD management and respiratory exacerbations requiring hospitalization. We studied a cohort of subjects enrolled in the Cardiomems Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Subjects (CHAMPION) trial who met criteria for classification into the COPD subgroup. The CHAMPION trial previously demonstrated that medical management incorporating hemodynamic information from an implantable PA pressure sensor was superior to standard care practices and significantly reduced HF hospitalization rates. In addition, this strategy led to significant decreases in PA pressures, fewer patients hospitalized for HF, more days alive outside of the hospital, improved quality of life, and a trend toward improved mortality in the treatment than in the control group.[22]

Studies have shown that pulmonary vascular disease is an important risk factor for respiratory exacerbations and mortality in patients with COPD.[23–25] In addition, studies have shown that elevated pulmonary hemodynamic variables are important predictors of hospitalization and mortality in HF patients with secondary pulmonary hypertension.[26–28] Although the benefit of PA pressure monitoring and its direct impact on the underlying pathophysiology and disease progression in acute decompensated HF requiring hospitalization is well understood, the potential role of PA pressure monitoring and its impact on the underlying pathophysiology and disease progression for respiratory exacerbations requiring hospitalization in patients with COPD has not been studied in detail and is therefore less established. We acknowledge that the majority of acute exacerbations for COPD requiring hospitalization are directly caused by bacterial and viral infections as well as the other etiologies[29] and the ability for PA pressure monitoring and the optimization of outpatient HF medical management to alter these causes is less clear. We also acknowledge that titrations for diuretic therapy are not the mainstay for direct treatment of COPD exacerbations. However, we think that PA pressure monitoring in patients with HF may affect the precursor risk factors that may contribute to acute exacerbations of COPD requiring hospitalization and therefore PA pressure monitoring may be useful for indirect prevention of these events.

Specifically, studies have shown that increased PA pressures and pulmonary vascular stress contribute to worsening hypoxemia and increase the risk for further acute exacerbations of COPD requiring hospitalization.[23,24,30] In addition, it is well known that HF patients in general are at increased risk for pulmonary infections owing in part to the presence of excess volume and pulmonary congestion, which in turn may add hypoxia to the increased metabolic demands and is associated with worse outcomes.[2,31] Because outpatient HF medical management optimization through PA pressure monitoring is beneficial in preventing episodes of pulmonary congestion and excess volume, we think that this approach may indirectly reduce acute respiratory exacerbations requiring hospitalization as a result of lowering patient risk for pulmonary infections and/or worsening hypoxemia episodes that are directly affected by increased PA pressures, pulmonary vascular stress, and volume overload. Consequently, we hypothesized that a management strategy incorporating PA pressure monitoring may improve both clinical conditions, particularly in HF patients with comorbid COPD who are at increased risk for both HF and respiratory exacerbations.

To evaluate this concept, we compared HF and respiratory hospitalization rates in the entire CHAMPION cohort with the rates observed within the COPD and non-COPD subgroups. All patients in the CHAMPION trial were at high risk for HF hospitalizations, which was the primary focus of the trial. We hypothesized that a medical management strategy incorporating hemodynamic information from an implantable PA pressure sensor would likely result in a consistent treatment effect in reducing HF hospitalization rates in the COPD and non-COPD subgroups because both groups are at risk for HF. The COPD subgroup, however, was also at increased risk for respiratory exacerbations compared with the non-COPD subgroup. We therefore hypothesized that this strategy may also reduce the risk of respiratory exacerbations requiring hospitalization in COPD subjects in the treatment group. In contrast, this treatment effect would likely be diminished in non-COPD subjects because they are already at low risk for respiratory exacerbations.

Materials and Methods

Subjects

The trial enrolled subjects who were male or female ≥18 years of age, diagnosed with New York Heart Association (NYHA) functional class III heart failure for ≥3 months, regardless of left ventricular ejection fraction or cause, and had ≥1 heart failure hospitalization ≤12 months of the baseline visit. Subjects were excluded if they had an active infection, had a history of recurrent (>1) pulmonary embolism or deep vein thrombosis, were unable to tolerate right heart catheterization, experienced a major cardiovascular event (eg, myocardial infarction, stroke) ≤2 months of the baseline visit, had a cardiac resynchronization device (CRT) implanted ≤3 months before enrollment, or had stage IV or V chronic kidney disease (glomerular filtration rate [GFR] <25 mL min^{-1} 1.73 m^{-2}). The other inclusion and exclusion criteria have been described previously.[20] The Institutional Review Board of each participating center approved the study protocol, and every subject provided written informed consent.

COPD Classification Process

The criteria for COPD classification included a comprehensive review of each patient's clinical source documents and electronic