Impaired Forced Expiratory Volume Across the Heart Failure Spectrum

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Patients with heart failure frequently develop concomitant pulmonary abnormalities, and vice versa. The reasons for this are multiple and may in many cases relate to the direct physiologic impact of one organ on the other. For instance, lung diffusion capacity for carbon monoxide and FVC are diminished in the setting of pulmonary interstitial edema secondary to elevated left-heart filling pressures.1,2 Similarly, right ventricular function is often diminished in restrictive lung disease secondary to increased right ventricular afterload.3 Conversely, a common exposure history may promote simultaneous disease in both organs even without direct physiologic interaction, as seen with heavy tobacco use and numerous connective tissue disorders. When secondary changes are observed in the heart or lung, these deficits may be permanent or they may be dynamic, fluctuating in association with the disease status in the primary organ. For example, in patients with COPD, impaired left ventricular filling may result from a reduction in preload caused by hyperinflation of the lungs, but ventricular filling is reversible with optimal COPD management.4 Nevertheless, even if the changes are dynamic and not necessarily reflective of intrinsic organ dysfunction, their existence may carry prognostic value for overall patient well-being or organ-specific outcomes.

In this context, in this issue of CHEST, Heidorn and colleagues5 have measured and analyzed the FEV1 in the setting of heart failure, looking to see whether diminished FEV1 is associated with heart failure outcomes. Most commonly, a reduced FEV1 is identified along with an overall obstructive airway pattern, defined by an FEV1/FVC ratio < 0.7. However, a reduced FEV1/FVC pattern is not absolute, and data indicate that isolated reductions in FEV1 can occur in heart failure independent of true airflow obstruction.6

In clinical settings, it may not be common practice to perform routine pulmonary function testing for all patients with heart failure. Thus, retrospective observational studies are inherently prone to bias from the selection of patients prone to underlying pulmonary disorders. To overcome this, these investigators are commended for the use of a large prospective cohort study of patients with heart failure, known as the MyoVasc Study.7

The MyoVasc study followed approximately 3,000 outpatient subjects, including 1,531 with symptomatic heart failure (American College of Cardiology/American Heart Association Stage C or D), 708 asymptomatic individuals with cardiac structural abnormalities (Stage B), and 757 individuals with no structural cardiac abnormalities or symptoms of heart failure (Stage 0/A). Subjects were enrolled between January 2013 and April 2018, and at baseline nearly all subjects underwent comprehensive baseline examination, including standardized pulmonary function testing and transthoracic echocardiography. Cohort entry was not dependent on any left ventricular ejection fraction criteria. Thus, the investigators were able to account for possible heterogeneity across different heart failure phenotypes, including heart failure with reduced ejection fraction (HFrEF), heart failure with preserved ejection fraction (HFpEF), and heart failure with borderline ejection fraction (HFpEF borderline).

Longitudinal outcomes were tracked via annual follow-up examinations and linkage to national vital status registries. For subjects with baseline heart failure (stages B, C, or D), the investigators defined a primary outcome of “heart failure worsening” in a survival analysis. This was a composite outcome defined according to baseline heart failure stage. The outcome was met among stage B subjects with heart failure with reduced ejection fraction (HFrEF). Subjects with heart failure with preserved ejection fraction (HFpEF) or heart failure with borderline ejection fraction (HFpEF borderline) did not experience the event. The investigators found a significant association between reduced FEV1 and worsening heart failure, with a hazard ratio (HR) of 1.58 (95% confidence interval [CI] 1.20-2.08) for subjects with heart failure with reduced ejection fraction (HFrEF) and a HR of 1.45 (95% CI 1.09-1.92) for subjects with heart failure with preserved ejection fraction (HFpEF). The investigators concluded that reduced FEV1 is associated with worsening heart failure, with similar findings across heart failure subtypes. This study highlights the importance of screening for pulmonary function abnormalities in patients with heart failure, as these abnormalities may have significant clinical implications.
subjects—baseline asymptomatic—if they developed onset of symptomatic heart failure or cardiac death. Among stage C/D subjects, the outcome was met if patients were hospitalized for heart failure or experienced cardiac death. Over a median follow-up of 2.6 years, a total of 235 individuals (10%) experienced the primary outcome.

Reduced FEV₁ was associated with myriad adverse baseline features and a higher likelihood of worsening heart failure. At baseline, lower FEV₁ was associated with more symptomatic heart failure and higher New York Heart Association functional status. Numerous echocardiographic measurements of cardiac function were also worse at baseline in patients with lower FEV₁, including lower left ventricular ejection fraction (a measure of systolic function), higher Doppler E/E’ ratio (a measure of diastolic dysfunction), and left ventricular hypertrophy. Finally, in longitudinal follow-up, lower FEV₁ was significantly associated with a greater chance of worsening heart failure—a 3.5-fold higher risk in the most extreme example comparing the lowest with the highest FEV₁ quartiles. Reduced FEV₁ seemed to be a general marker of comorbidity burden as well—associated with older age, higher N-terminal-pro hormone B-type natriuretic peptide (NT-proBNP), more cardiovascular risk factors, and more medical history of cardiovascular and renal pathologic conditions. Multivariable adjustment for baseline comorbidities mitigated only some of the magnitude of association between FEV₁ and outcomes, but much of the effect remained.

Two key observations from this study have additional clinical value. First, most patients with reduced FEV₁ lacked an obstructive airway pattern. Among the lowest quartile of FEV₁, as many as 41% exhibited obstruction, but this was the highest proportion of all the quartiles (all other quartiles had fewer than 10% of individuals with obstruction). Moreover, obstruction did not meaningfully modify the association between FEV₁ and the primary outcome in stratified analyses. Thus, reduced FEV₁ in heart failure has clinical utility beyond simply as a proxy measure for COPD. Second, FEV₁ had a more convincing and precise effect among individuals with HfPEF (hazard ratio 95% CI, 1.22-1.52) than with HFrEF (hazard ratio 95% CI, 0.96-1.52), although the level of precision was certainly impacted by sample size too: 566 individuals with HfPEF were studied, compared with only 295 with HFrEF. Beyond sample size, possibly more overlap exists between pulmonary disease and HfPEF because of HfPEF’s greater disease heterogeneity and more nebulous presentation.

Overall, this study advances the notion that FEV₁ is independently associated with adverse outcomes in heart failure. Presumably, this means that patients with heart failure could undergo pulmonary function testing as an additional method for risk stratification, although more work needs to be done to establish the utility of this testing. In particular, prognostic discrimination and calibration of FEV₁ should be measured and validated across multiple populations within and outside of the MyoVasc cohort. Beyond this, establishing whether the increased risk conferred by FEV₁ is fixed or modifiable in heart failure, using strategies that directly target improvements in FEV₁ in other settings, would be important.

References