Quantitative Doppler-Echocardiographic Imaging and Clinical Outcomes With Left Ventricular Systolic Dysfunction

Independent Effect of Pulmonary Hypertension

Wayne L. Miller, MD, PhD; Douglas W. Mahoney, MSc; Maurice Enriquez-Sarano, MD

Background—Doppler-echocardiography provides quantitative imaging of systolic and diastolic left ventricular (LV) function, functional mitral regurgitation (FMR), and pulmonary hypertension (PH) in patients with LV systolic dysfunction. Whether PH is linked to survival independently of LV features and FMR in symptomatic and asymptomatic patients is unknown.

Methods and Results—Patients with LV ejection fraction ≤40% and quantitative Doppler-echocardiography assessment of FMR and PH were studied. Patients were frequency matched for those with Doppler-echocardiography estimated pulmonary systolic pressure ≥45 mm Hg (n=692) and those without PH (n=692; pulmonary systolic pressure, <45 mm Hg) for age, sex, LV ejection fraction, and quantified FMR severity and analyzed for long-term survival after diagnosis. During follow-up (median, 8.9 years), 885 deaths (63.5%) occurred, with PH being associated with higher 5-year mortality: 51±2% versus 37±2%, P<0.001. In multivariate analysis, PH demonstrated increased mortality risk independent of age, sex, severity of diastolic and systolic LV dysfunction, FMR, comorbidities, and symptom (hazard ratio, 1.34; 95% confidence limit, 1.17–1.53; P<0.001). Subgroup analysis, stratified by symptoms, degree of FMR, and severity of LV dysfunction, demonstrated that PH was associated with excess mortality in all subgroups.

Conclusions—In this large cohort of patients with LV systolic dysfunction, in whom FMR and LV characteristics were quantified and matched between those with and without PH, the presence of PH was an independent factor for excess mortality and not a surrogate for the severity of LV systolic dysfunction or FMR. In asymptomatic or symptomatic patients with or without FMR, PH is a critical marker for poor outcomes. (Circ Cardiovasc Imaging. 2014;7:330-336.)

Key Words: hypertension, pulmonary ▪ outcomes ▪ systolic dysfunction

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Cardiac imaging using Doppler-echocardiography (D-E) provides information on patients with left ventricular systolic dysfunction (LVSD) that goes beyond assessing LV ejection fraction (LVEF). Such imaging makes it possible to assess systolic and diastolic LV function and remodeling, the presence and severity of functional mitral regurgitation (FMR), and pulmonary hypertension (PH). All of these measures of LV remodeling can also be quantified during the same examination. However, the clinical significance and link to outcome of each individual measure are uncertain and difficult to extricate because of the frequent parallel development of multiple cardiac alterations. PH is of particular importance to analyze because it is a known complication of LVSD and can be measured and followed in serial examinations. However, the assessment of PH in the setting of LVSD is not a specified recommendation as either a primary or follow-up measurement by current American College of Cardiology Foundation/American Heart Association, Heart Failure Society of America, or European Society of Cardiology heart failure (HF) practice guidelines. Although it has been asserted that PH is associated with worsening outcomes, the available evidence has not been considered compelling because PH is the physiological consequence of multiple other hemodynamic alterations that include not only LVSD but also the severity of FMR and LV diastolic dysfunction (LVDD), both of which are important determinants of survival in LVSD. Furthermore, PH is often thought to be associated with severe HF symptoms, which are recognized as markers of outcome with LVSD. Therefore, in analyzing the value of D-E imaging, specifically in assessing the independent prognostic role of imaging-defined PH, it is uncertain whether it has incremental value to symptoms and other markers of LV remodeling. The consequences of establishing the independent prognostic role of imaging-defined PH are significant in terms of testing, guideline recommendations, and novel-targeted therapy. Reports focusing on the role of PH have been performed almost exclusively in patients with LVSD.
with overt congestive HF or after a hospitalization for an acute event, and where adjustments for LVSD and markers of LV remodeling were partially or often qualitatively acquired. Thus, the PH question remains unanswered, particularly with regard to the vast majority of LVSD outpatients without severe HF and accounting for quantified background descriptors of LV remodeling, such as FMR and LVDD. In addressing these complex issues, our clinical practice with large out-patient involvement and methodical quantitative approach to LVSD characterization, particularly FMR, provides the opportunity to assess the independent role of PH in patients with LVSD in a comprehensive design carefully. Therefore, the aim of this study was to compare survival after diagnosis of LVSD between patients with and without PH documented by D-E imaging with matching of these groups for major markers of outcome (age, sex, LVEF, severity of FMR) and to examine overall and in subsets of patients the hypothesis that PH is, in and of itself, an independent factor for all-cause mortality and not merely a colinear variable of LVSD.

Methods

Patients undergoing comprehensive D-E evaluation as part of their outpatient clinical cardiovascular assessment at the Mayo Clinic, Rochester, during the period of August 1, 2001, to December 31, 2004, were retrospectively analyzed. Inclusion criteria were the following: age ≥18 years, presence of LV systolic dysfunction defined by an LVEF ≤40%, pulmonary systolic pressure (PSP) measurable by D-E using tricuspid regurgitation velocity, normal right ventricular systolic function as determined by measurement of tricuspid annular plane systolic excursion (normal range 17–20 mm) or tricuspid annular systolic tissue Doppler imaging (normal >12 cm/s), and quantitative assessment of severity of FMR. Exclusion criteria were atrial fibrillation; organic mitral, tricuspid, or aortic valvular disease other than mild, or status after mitral valve replacement/repair or any prosthetic valve; infiltrative, constrictive, or hypertrophic cardiomyopathy; myocardial infarction within 6 months of index D-E evaluation; chronic obstructive pulmonary disease other than mild; congenital heart disease; tachycardia-related dysrhythmias; primary pulmonary arterial hypertension or pulmonary thromboembolic disease; history of chest radiation; and collagen vascular diseases or status after cardiac or lung transplantation. Clinical data, including symptoms, were obtained by programmed electronic medical records abstraction. Where data were not electronically available or incomplete, patient records were manually reviewed and data abstracted. Patient survival/all-cause mortality status was confirmed through January 1, 2012 (censor date), using Mayo Clinic Rochester electronic medical records, Olmsted County, MN, medical record linkage system (Rochester Epidemiology Project), and the Social Security Mortality Index. The study was approved by the Mayo Foundation Institutional Research Review Board and met requirements for clinical research per Minnesota Statute 144.335/CRF 21 (Part 50).

Doppler-Echocardiography

A comprehensive 2-dimensional and D-E examination was performed on all patients. LV size and function (LVEF) were derived by standard methods according to American Society of Echocardiography recommendations. Continuous wave Doppler was used to assess maximal tricuspid regurgitation flow velocity to estimate the systolic pressure gradient between the right ventricle and the right atrium. Right ventricular systolic pressure was then calculated by adding estimated right atrial pressure. This derived pressure was considered to be identical to PSP after demonstrating the absence of any abnormality of the pulmonary or tricuspid valve. The threshold definition of PH was an estimated PSP ≥45 mmHg. Quantification of PSP by effective regurgitant orifice area, measures of LV diastolic function (mitral E/e' ratio, mitral valve deceleration time), cardiac index, and left atrial volume were undertaken as previously described.

Patient Matching Process

The initial data set consisted of 1174 patients with PSP ≥45 mmHg and 1929 patients with PSP <45 mmHg, all meeting inclusion/exclusion criteria. To control for the imbalances of the 2 groups with regard to the presence and severity of FMR and comorbidities and for the benefit of cost control, subjects with PSP ≥45 mmHg were matched to subjects with PSP <45 mmHg by creating sampling bins based on age (±3 years), sex, LVEF (±5%), FMR presence and severity, and year of index D-E examination. FMR was matched qualitatively (none-trivial, mild, moderate, or moderate-severe), and the quantitative strata of effective regurgitant orifice area and regurgitant volume measurements were similar in both subgroups as expected by the matching process. Within each sampling bin, an equal number of patients with and without PH were selected randomly, thus guaranteeing a frequency-matched cohort design. This procedure resulted in matching 1384 patients (692 in each group with and without PH) of the 3106 eligible patients.

Statistical Analyses

Data are presented as mean±SD or median with 25th and 75th percentiles for continuous data and as number and percentage for categorical data. To assess univariate differences, baseline and hemodynamic variables were compared by Student t tests or the nonparametric Wilcoxon signed-rank test when normality assumptions were not achieved. Categorical variables were tested for significance using a likelihood ratio χ² test. Linear regression analyses were used to assess associations between hemodynamic variables. Logistic regression analysis was performed to identify variables associated with the presence of correlate PH. Results are presented as odds ratios with P values; the odds ratios for continuous variables are the odds of spanning the range of the data. Survival was estimated using the Kaplan–Meier method with log-rank analysis used to compare the end point of all-cause mortality among subgroups. Mortality was evaluated in univariate and multivariate analyses using Cox proportional hazards models adjusting for relevant baseline differences that would affect mortality. Risk factors were significantly different between the hemodynamic groups at baseline, and factors that were clinically important were evaluated for these models. Cox proportional hazards regression was used to assess the contribution to unadjusted hazards analysis for mortality based on hemodynamic parameters using different hemodynamic variables to define abnormality. Results are presented as forest plot with corresponding P values. The association of relative risk of death using hemodynamic parameters as continuous variables was investigated using penalized splines (p-splines) within the Cox model. The number of knots used for the smoothing spline was determined by the set defaults of the package and resulted in 12 equally spaced interior knots with increments of 10.74. With this approach, we were able to verify the proportional hazards assumption and robustly estimate the functional form of each variable with the risk of death. Figures are presented using a log scale (Y-axis) because this is the natural scale for testing the linearity of the hazard function. The Charlson index summing the patient’s individual comorbidities, including specific LVSD-related morbidity, was calculated to aid in the characterization of the cohort. Statistical testing was 2-tailed; P values <0.05 were accepted as statistically significant. Analyses were performed using JMP version 7 software and R version 2.14.

Results

Clinical and Hemodynamic Characteristics

A total of 1384 patients with and without PH met matching criteria according to age, sex, LVEF, and FMR (presence and distribution of severity of FMR). Patient demographic and clinical characteristics are shown for the matched cohorts in Table 1. The median PSP in the cohort with PH was 54 mmHg (25th to 75th percentile of 48–62 mmHg) and 32 mmHg (28–37 mmHg) in patients without PH. The 2 cohorts were well matched with the exception of a higher prevalence...
Table 1. Clinical and Demographic Characteristics of Matched Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>PSP&lt;45 mm Hg (n=692)</th>
<th>PSP≥45 mm Hg (n=692)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>70±13.6</td>
<td>70±13.8</td>
<td>0.65</td>
</tr>
<tr>
<td>Male, sex, %</td>
<td>62</td>
<td>61</td>
<td>0.98</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.4±6.1</td>
<td>28.3±9.8</td>
<td>0.05</td>
</tr>
<tr>
<td>Cause of heart failure</td>
<td></td>
<td></td>
<td>0.36</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>394 (57%)</td>
<td>381 (55%)</td>
<td></td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>298 (43%)</td>
<td>311 (45%)</td>
<td></td>
</tr>
<tr>
<td>Laboratory tests</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium, mEq/L</td>
<td>139±3.4</td>
<td>139±4.0</td>
<td>0.31</td>
</tr>
<tr>
<td>Potassium, mEq/L</td>
<td>4.3±0.52</td>
<td>4.3±0.51</td>
<td>0.54</td>
</tr>
<tr>
<td>Creatinine, mg/dL</td>
<td>1.2±0.37</td>
<td>1.3±0.64</td>
<td>0.001</td>
</tr>
<tr>
<td>BUN, mg/dL</td>
<td>25±15</td>
<td>27±15</td>
<td>0.01</td>
</tr>
<tr>
<td>Hemoglobin, g/dL</td>
<td>12.8±1.8</td>
<td>12.5±2.2</td>
<td>0.005</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>3.1±3.04</td>
<td>3.2±3.10</td>
<td>0.51</td>
</tr>
</tbody>
</table>

Comorbidities, %

- Hypertension: 40 vs 35, P=0.089
- Diabetes mellitus: 22 vs 28, P=0.01
- Myocardial infarction history: 33 vs 32, P=0.7
- Peripheral vascular disease history: 14 vs 15, P=0.64
- Cerebrovascular accident history: 17 vs 19, P=0.44
- Chronic obstructive pulmonary disease (none greater than mild): 20 vs 24, P=0.15
- Connective tissue disease: 3 vs 4, P=0.88

Medications, %

- Converting enzyme inhibitor: 60 vs 61, P=0.73
- Angiotensin receptor blocker: 10 vs 11, P=0.42
- β-blocker: 58 vs 59, P=0.42
- Calcium channel blocker: 6 vs 6, P=0.86
- Digoxin: 32 vs 31, P=0.86
- Nitrites: 13 vs 16, P=0.18
- Loop diuretics: 45 vs 59, P<0.001
- Thiazide diuretic: 8 vs 11, P=0.14
- Statins: 43 vs 40, P=0.32
- Aspirin: 53 vs 53, P=0.98
- Warfarin: 23 vs 22, P=0.76
- Diabetic drugs: 18 vs 26, P=0.035

Symptoms/signs, %

- Dyspnea/dyspnea on exertion: 56 vs 69, P<0.001
- Lower extremity edema: 20 vs 30, P<0.001
- Chest pain/discomfort: 32 vs 29, P=0.27
- Presyncope/syncope: 35 vs 33, P=0.74
- Palpitations: 30 vs 31, P=0.59
- Fatigue/weakness: 25 vs 36, P<0.001

Survival After Diagnosis

The median follow-up time for the combined cohorts was 8.9 years (limits, 1 month to 11.7 years), and during the study 885 patients died (64%). Of these, 478 had PH and 407 were without PH. Figure 1 shows the Kaplan–Meier survival estimates for the matched cohorts with PSP≥45 mm Hg, demonstrating a significantly poorer outcome than PSP<45 mm Hg. Although PSP is most commonly analyzed as a dichotomous variable clinically, we also evaluated this parameter as a continuous variable. Figure 2 (cubic spline analysis) shows the relationship where progressively higher PSP is associated with a progressively higher risk for all-cause mortality. The threshold at which the relative mortality risk crosses unity (60 mm Hg with a linear increase in risk) was demonstrated.

Cox proportional hazards regression analysis was used to evaluate the association between PSP and all-cause mortality, and with adjustment for baseline characteristics of age, sex, FMR, LVEF, Charlson index, symptoms, and LVDD (Table 3). These variables were selected for their

of diabetes mellitus in patients with PH and associated greater diabetic medication use. Other medication usage was well distributed between groups. The patients with PH were more often symptomatic. The comorbidity burden was moderately high in both cohorts, with an average Charlson index of 3 without significant differences between groups. Table 2 shows the D-E features of the matched cohorts. Systolic blood pressure and heart rate were statistically higher in patients with PH, but the differences were not clinically significant. Doppler-derived hemodynamic parameters of LV diastolic function (E/e′ ratio and mitral valve deceleration time) were more often abnormal in patients with PH, but such a link is expected in view of the association between LVDD and PH we and others have previously reported.13,15,16,30,31 Left atrial volume, also a marker of diastolic dysfunction,32 was higher in patients with PH.
common clinical association with LVSD and to adjust for baseline cohort differences in these variables. Using multivariate analysis, PH remained an independent and strong contributor to mortality even when adjusted for the multiple confounding clinical variables of risk. Furthermore, when adjustment included variables assessing LVDD, the independent risk associated with PH was unaffected whether E/e′ (hazard ratio [HR], 1.24; 95% confidence limit [CL], 1.02–1.53; P=0.048), mitral valve deceleration time (HR, 1.31; 95% CL, 1.12–1.54; P<0.001), or left atrial volume (HR, 1.30, 95% CL, 1.10–1.53; P=0.002) was used as the adjusting factor to the full model (Table 3), demonstrating the robustness of the link of PH to mortality in this cohort with LVSD. Also, when PSP was evaluated as a continuous variable of risk in the Cox model with adjusted HR for 10 mm Hg increases in pulmonary artery systolic pressure, PSP remained an independent marker of mortality by multivariate analysis (Table 3). This included the addition to the model of markers of LVDD (mitral valve deceleration time [HR, 1.12; 95% CL, 1.06–1.18; P<0.001] and LA volume [HR, 1.09; 95% CL, 1.03–1.15; P=0.005]). However, when E/e′ ratio was added to the model, PSP did not remain an independent marker (HR, 1.06; 95% CL, 0.98–1.14; P=0.12).

Table 3. Univariate and Adjusted Cox Proportional Hazards Model of All-Cause Mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazards Ratio (95% CL)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH: univariate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSP≥45 mm Hg</td>
<td>1.41 (1.23–1.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PSP continuous variable</td>
<td>1.13 (1.08–1.18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PH adjusted for age and sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSP≥45 mm Hg</td>
<td>1.41 (1.23–1.61)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PSP, continuous variable</td>
<td>1.14 (1.09–1.20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PH adjusted for age, sex plus FMR and LVEF</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSP≥45 mm Hg</td>
<td>1.40 (1.23–1.60)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PSP, continuous variable</td>
<td>1.15 (1.09–1.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PH adjusted for age, sex, FMR, LVEF plus clinical variables*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSP≥45 mm Hg</td>
<td>1.34 (1.17–1.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PSP, continuous variable</td>
<td>1.13 (1.07–1.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PH adjusted for age, sex, FMR, LVEF, clinical variables plus parameters of LVDD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSP≥45 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVDT</td>
<td>1.31 (1.12–1.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/e′</td>
<td>1.24 (1.02–1.53)</td>
<td>0.048</td>
</tr>
<tr>
<td>LA vol</td>
<td>1.30 (1.10–1.53)</td>
<td>0.002</td>
</tr>
<tr>
<td>PSP, continuous variable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVDT</td>
<td>1.12 (1.06–1.18)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/e′</td>
<td>1.06 (0.98–1.14)</td>
<td>0.12</td>
</tr>
<tr>
<td>LA Vol</td>
<td>1.09 (1.03–1.15)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

CL indicates confidence limits; FMR, functional mitral regurgitation (qualitative); LA Vol, left atrial volume; LVDD, left ventricular diastolic dysfunction; LVEF, Left ventricular ejection fraction; MVDT, mitral valve deceleration time; PH, pulmonary hypertension; and PSP, pulmonary systolic pressure. *Clinical variables: Charlson index of comorbidities (including diabetes mellitus) and symptoms.

Subgroup Analyses
Separate subgroup analyses by PSP<45 and ≥45 mm Hg for common variables of risk were also undertaken to assess their individual effect on mortality risk. Age above and below median for the cohort (<73 and ≥73 years), sex, presence of symptoms, Charlson index, absence (none-trivial) versus presence of FMR, and presence of diabetes mellitus at the time of index D-E evaluation were evaluated (Figure 3). Older age was associated with increased risk of all-cause mortality, but the presence of PH superimposed a separate significant effect on risk, particularly high in the younger patients (age <73 years: HR, 1.64; 95% CL, 1.32–2.04; P<0.001 and age ≥73 years: HR, 1.26; 95% CL, 1.07–1.50; P=0.007). Sex had minimal effect overall on outcome, but the presence of PH independently affected risk (women: HR, 1.38; 95% CL, 1.12–1.72; P=0.003 and male: HR, 1.42; 95% CL, 1.20–1.69; P<0.001). Incident symptoms influenced mortality outcome, but PSP≥45 mm Hg resulted in a poorer and independent outcome with symptoms (HR, 1.29; 95% CL, 1.03–1.62; P=0.030) or without symptoms (HR, 1.38; 95% CL, 1.17–1.63; P<0.001). This was also
Mechanisms of PH in LVSD

We have previously reported on the contribution of LVDD as a significant predictor for the presence of PH in clinically stable patients. The current analysis emphasizes that even though parameters of diastolic dysfunction and other clinical variables are highly predictive of PH, PH is a distinct risk factor for mortality independent of LVDD or severity of LVSD. The lack of association of PH with the severity of LVSD (low LVEF) has been previously reported, but our findings show that PH confers a severe influence on LVSD by its independent association to poor survival after diagnosis. This finding is also independent of the presence and severity of FMR, which is by itself linked to outcome. By quantifying the FMR, which is poorly assessed by standard qualitative methods, we ensured that through the matching process patients with and without PH had similar degrees of FMR so that we could ascertain for the first time that the PH link to morality is not a surrogate for FMR. Furthermore, our subgroup analysis, which could not be performed in previous studies because of lack of FMR ascertainment, shows that PH is equally predictive of excess mortality with or without FMR, confirming the independent role of PH in predicting survival. Similarly, although an independent link between LVDD and mortality is not entirely established, by obtaining quantitative measures of LVSD, we were also able for the first time to demonstrate that PH is not a surrogate of LVDD. Thus, our comprehensive quantitative imaging assessment allows for the conclusion that PH is truly an independent marker of excess mortality.

Prognostic Significance and Clinical Implications of PH in LVSD

Although age, comorbidities, symptoms, FMR, and to some extent sex negatively influence outcomes and likely dilute the overall effect of PH on mortality, PH imposes a singular contribution to worsening outcome. In addition, as demonstrated in our analysis, even in those patients without symptoms or FMR, the identification of PH was associated with increased mortality risk. The development of PH in these patients with no or few symptoms or physical findings arguably puts these patients at high risk because of the absence of risk markers and, therefore, a possible reduced vigilance as to the presence of PH. This emphasizes the need for a focused imaging and also therapy approach in patients with evidence of LVSD. PSP should
be systematically evaluated in all patients with LVSD, and patients should also be followed closely to identify the development of PH as a marker of disease progression that initially may be clinically silent. Furthermore, this should support a need for more intense and novel treatments to reduce the risk associated with PH in LVSD in otherwise stable outpatients without recent events.

Limitations
In interpreting these data, the retrospective nature of the study needs to be considered. Pulmonary pressures were calculated from D-E-derived data, which reflects current clinical practice; the noninvasive methodology has been well established for the assessment of PSP.1,2,15,34–36 The matched nature of the study design and patient cohort limits heterogeneity and accounts for many, if not all, commonly associated clinical variables that otherwise confound data interpretation. It should be noted that not all eligible patients were included in the final analysis as a result of the matching process (1384 patients included of 3106 eligible). Also, patients with right ventricular systolic dysfunction were excluded, and, therefore, the results do not apply to patients with combined LV and RV systolic dysfunction. However, the results of this study reflect observations from standard clinical outpatient practice with a design to control for the confounding influence of common clinical variables on the interpretation of the effect of PH with LVSD.

Conclusions
In this large cohort of matched ambulatory outpatients with LVSD, with and without PH, PH was demonstrated to be a powerful factor contributing to mortality independent from the severity of diastolic or systolic LV dysfunction, presence of FMR, and clinical variables of age or comorbidities. Notable from this analysis is the observation that the absence of symptoms or FMR in outpatients without recent hospitalizations or acute episodes of decompensation did not mitigate the effect of PH on poor outcomes. These findings, if confirmed in prospective analyses, support the benefit of routine PH-focused D-E imaging evaluations in patients with LVSD and PH-directed therapy aimed at preventing the clinical progression and excess mortality associated with LVSD.

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Disclosures
None.

References


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**CLINICAL PERSPECTIVE**

Doppler-echocardiography provides quantitative imaging of systolic and diastolic left ventricular (LV) function, functional mitral regurgitation (FMR), and pulmonary hypertension (PH) in patients with LV systolic dysfunction. Whether PH is linked to survival independently of LV features and FMR in symptomatic and asymptomatic patients is unknown. In this analysis, a cohort of patients (n=1384) with LV systolic dysfunction (LV ejection fraction ≤40%) with quantitative Doppler-echocardiography assessment of FMR and PH were matched between those with (estimated pulmonary artery systolic pressure, ≥45 mm Hg) and without (estimated pulmonary artery systolic pressure, <45 mm Hg) PH for age, sex, LV ejection fraction, and quantified FMR severity and analyzed for long-term survival after diagnosis. In multivariate analysis, PH demonstrated increased mortality risk independent of age, sex, severity of diastolic and systolic LV dysfunction, FMR, comorbidities, and symptoms. PH is not a surrogate for the severity of LV systolic dysfunction or FMR. In asymptomatic or symptomatic patients with or without FMR, PH is a critical marker for poor outcomes. PH-focused Doppler-echocardiography evaluations in patients with LV systolic dysfunction are warranted to identify high-risk patients.
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