Prognostic Significance of Applying the European Society of Cardiology Consensus Algorithm for Heart Failure With Preserved Systolic Function Diagnosis

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ABSTRACT

Background: The diagnosis of heart failure with preserved left ventricular ejection fraction (HFpEF) is challenging. Although diagnostic criteria have been proposed, limited information exists concerning its implication on prognosis. We aimed to evaluate the prognostic significance of applying the European Society of Cardiology algorithm for HFpEF diagnosis, namely the tissue Doppler imaging information, in patients with acute heart failure (HF).

Hypothesis: The application of the European Society of Cardiology algorithm for HFpEF diagnosis, identifies a group of HF patients with high morbidity and mortality.

Methods: Consecutive patients admitted due to acute HF were recruited. The European Society of Cardiology algorithm was used in the HFpEF diagnosis. Patients were followed for a 6-month period and mortality and rehospitalization due to HF were recorded.

Results: A total of 491 patients were included in this registry. Mean patient age was 78 years and 63% were women; 177 patients had HFpEF and 314 had HF with reduced ejection fraction (HFrEF). Of the HFpEF patients, 44.8% had an E/E' ratio >15 and 1.8% had an E/E' ratio <8. Patients with HFpEF and those with HFrEF had a similarly dismal prognosis when considering all-cause mortality, and morbidity and mortality, but there was a trend for better survival when HF death was the outcome in analysis (hazard ratio 1.63 [95% confidence interval: 0.95–2.80, $P = 0.08$]).

Conclusions: The use of objective criteria for diagnosis of HFpEF identifies patients with similar outcomes as patients with HFrEF; this observation increases the robustness of the diagnostic criteria for HFpEF. The use of objective criteria for the diagnosis of HFpEF identifies patients with a similarly ominous prognosis as patients with HFrEF; this observation increases the robustness of the diagnostic criteria for HFpEF. Identifying these patients based on objective criteria, as we did, is an important step for future investigation, namely drugs, warranted to the HFpEF approach.

Introduction

Over the last decades, a growing interest has been dedicated to heart failure with preserved ejection fraction (HFpEF).^{1–5}

Epidemiological and clinical studies reported prevalences of HFpEF between 13% and 60% in heart failure (HF) patients.^{5–7} The observed discrepancy in HFpEF prevalence

across studies is probably due to several factors, including the populations' characteristics, HF diagnostic criteria, and, most importantly, the definition of HFpEF used. Different definitions of HFpEF have been proposed (Framingham's criteria and European Society of Cardiology [ESC] consensus criteria).^{8,9} Nonuniform diagnostic criteria used in previous studies and registries on HFpEF are one of their major caveats, making the knowledge on clinical presentation and epidemiology of HFpEF somewhat fluid. Epidemiological studies aimed to evaluate HFpEF populations used mainly scoring systems and the Framingham criteria. These diagnostic criteria are known to have a low specificity for HF diagnosis.^{10–12}

A uniform and positive identification of HFpEF patients is crucial to build sound knowledge of the condition and to the

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design of trials aimed to study specific approaches in these patients.

Although previous reports observed that HFpEF patients had a morbidity and mortality similar to that of patients with HF with reduced ejection fraction (HFrEF),^{13,14} a recent meta-analysis reported that the mortality of these patients was lower than that of HFrEF patients, although morbidity was identical.¹⁵

Recently, an ESC consensus panel proposed a diagnostic algorithm for HFpEF identification. This algorithm includes neurohumoral activation (as measured by B-type natriuretic peptide [BNP] or N-terminal pro BNP levels) and invasive or noninvasive evaluation of the diastolic function. To our knowledge, such an algorithm has not yet been fully tested in clinical practice.

We aimed to evaluate the application of the ESC algorithm, namely using BNP levels and tissue Doppler imaging ratio E/E', in the identification of HFpEF in patients admitted to hospital due to acute HF. The prognosis of HFpEF patients positively identified by using these criteria was also studied.

Methods

During a 20-month period, all patients admitted to our internal medicine department due to acute HF, whether worsening or de novo HF, with an admission BNP >200 pg/mL were eligible for inclusion in a registry of acute HF (risk assessment of acute heart failure, RAAHF).

Patients with acute coronary syndromes and patients having other conditions leading to symptoms, as considered by the attending internist, were excluded from the registry. Patients with HF of valvular etiology were excluded from the analysis. Patients without structural or functional cardiac abnormalities, despite admission due to acute dyspnea and both the emergency department and the attending physician considering HF as the most probable cause, were also excluded from the registry, but they were considered a control group for echocardiography parameters.

The ESC guidelines were used for the diagnosis of HFpEF and of HF with systolic dysfunction.¹⁶ Arterial hypertension was defined as the presence of previous diagnosis, record of antihypertensive pharmacological treatment, or blood pressure >140/90 mm Hg. Diabetes mellitus was defined as either a history of diabetes, the current prescription of either an oral hypoglycemic agent or insulin, a fasting venous blood glucose >126 mg/dL, or a random glucose >200 mg/dL. Coronary heart disease was defined as history of angina or acute myocardial infarction, history or electrocardiographic evidence of ischemia, or significant coronary heart disease confirmed by coronary angiography.

A fasting venous blood sample was collected between 8 and 9 A.M. within 48 hours of admission.

An echocardiogram was performed within 72 hours of admission. All images were obtained with a standard ultrasound machine (System 6; GE Vingmed, Horten, Norway) with a 2.5-MHz probe. Standard techniques were used to obtain M-mode, 2D, and Doppler measurement in accordance with American Society of Echocardiography guidelines. Left ventricular (LV) end-systolic and end-diastolic volumes along with the left ventricular ejection fraction (LVEF) were calculated by the biplane Simpson's

method from apical 4- and 2-chamber views. Left atrial volume was also calculated with the biplane Simpson's method. Tissue Doppler-derived peak systolic (s'), early (e'), and late diastolic (a') velocities were derived from the medial and septal mitral annulus. The average from the medial and lateral mitral annular e' diastolic velocities was used for calculation of the E/E' ratio.

Patients were followed for a 6-month period. Adverse outcomes analyzed were all-cause mortality, mortality due to HF, and the combined endpoint of admission due to worsening HF or HF death. Follow-up data were obtained by consulting the hospital records for each patient and by telephone contact. One patient was lost during follow-up.

All patients provided written informed consent to participate in the study. The study protocol conforms to the ethical guidelines of the Declaration of Helsinki.

Statistical Analysis

Continuous variables are presented as mean (SD) or median (interquartile range) if nonnormally distributed; categorical variables are presented as counts and proportions. Comparisons between patients with HFpEF and those with HFrEF were made by use of a χ^2 test for categorical variables, independent samples *t* test for normally distributed continuous variables, and the Mann-Whitney *U* test when the distribution was skewed.

We used univariate Cox regression analysis to quantify the association of independent variables with the outcome in the whole group of patients and in each of the groups created according to systolic function. Outcomes studied were the isolated endpoints all-cause death or death due to HF and the combined endpoint of hospitalization or death due to HF. As a trend toward lower HF death in the HFpEF group was observed, a multivariate Cox regression model was used to determine the independent prognostic value of having HFpEF instead of HFrEF. The prognostic value of E/E' >15 (the median E/E' of the study population) in both patients with HFpEF and HFrEF was adjusted for left atrial volume index (LAVI), the other echocardiographic parameter prognostic associated.

All the analyses were conducted using SPSS 13.0 (SPSS Inc., Chicago, IL). A *P* value <0.05 was considered to be statistically significant.

Results

During the study period, 643 eligible patients had an echocardiogram performed within 72 hours of admission. From these, 152 patients were excluded from the analysis: 126 (19.6%) because they had significant valve disease and the etiology of HF was considered valvular (moderate to severe primary mitral insufficiency, moderate to severe aortic insufficiency or stenosis), and 26 because the echocardiogram did not show structural or functional cardiac abnormalities sustaining HF diagnosis. A total of 491 patients were included in the study.

Heart failure patients were older (median age, 78 years) and 260 of them (63%) were women. The median LVEF was 34%. One hundred and seventy-seven (36%) of the patients had HFpEF and 314 (64%) had HFrEF.

Table 1. Clinical and Echo Doppler Characteristics of the Study Population

Characteristics	All Patients (N = 491)	HFpEF (n = 177)	HFrEF (n = 314)	P Value
Clinical characteristics				
Age, y, median (IQR)	78 (70–84)	81 (74–87)	76 (66–83)	<0.001
Male sex, n (%)	231 (47.0)	53 (29.9)	178 (56.7)	<0.001
Hypertension, n (%)	368 (77.0)	146 (84.4)	222 (72.8)	0.005
DM, n (%)	204 (44.1)	75 (44.6)	129 (43.7)	0.93
AF, n (%)	216 (44.6)	91 (52.3)	125 (40.3)	0.01
CHF, n (%)	423 (87.9)	152 (87.4)	271 (88.3)	0.88
CHD, n (%)	227 (46.3)	66 (37.3)	161 (51.4)	0.003
NYHA class IV at admission, n (%)	297 (60.9)	100 (57.5)	197 (62.7)	0.30
BMI (kg/m ²), median (IQR)	25.2 (22.7–27.9)	25.4 (22.6–28.3)	25.0 (22.8–27.7)	0.49
SBP, mm Hg, median (IQR)	132 (115–153)	140 (120–158)	128 (112–149)	0.001
Admission laboratory parameters				
Hemoglobin, g/dL, median (IQR)	11.7 (10.4–13.4)	11.4 (9.8–12.8)	12.0 (10.8–13.7)	0.001
Serum sodium, mEq/L, median (IQR)	139 (136–141)	139 (135–142)	139 (136–141)	0.47
Plasma creatinine, mg/dL, median (IQR)	1.38 (1.11–1.81)	1.30 (1.08–1.80)	1.40 (1.15–1.82)	0.05
BNP, pg/mL, median (IQR)	1627.8 (954.0–2765.3)	1191.5 (684.6–2038.2)	2008.9 (1085.2–3066.0)	<0.001
Echo Doppler parameters				
EF, %, median (IQR)	34.0 (22.5–53.5)	57.8 (52.5–61.5)	26.0 (19.0–33.5)	<0.001
LAVI, mL/m ² , median (IQR)	48.4 (37.7–60.6)	46.3 (35.6–60.6)	50.0 (38.7–60.6)	0.17
LVEDVI mL/m ² , median (IQR)	74.5 (55.6–102.3)	57.8 (45.4–67.8)	93.5 (69.5–115.6)	<0.001
LVMI g/m ² , median (IQR)	129.1 (106.8–158.3)	115.1 (90.4–145.8)	135.3 (113.8–164.8)	<0.001
E/E' ratio	17 (13–22)	15 (12–21)	18 (13–22)	<0.001
E/E' ratio >15	265 (57.9)	73 (44.8)	192 (65.1)	<0.001
Abbreviations: AF, atrial fibrillation; BMI, body mass index; BNP, B-type natriuretic peptide; CHD, coronary heart disease; CHF, chronic heart failure; DM, diabetes mellitus; E/E' ratio, relation of the E atrial wave measure by pulsed wave transmitral Doppler and early diastolic velocity E' by pulsed-wave tissue Doppler imaging; EF, ejection fraction; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; IQR, interquartile range; LAVI, left atrial volume index; LVEDVI, left ventricular end-diastolic volume index; LVMI, left ventricular mass index; NYHA, New York Heart Association; SBP, systolic blood pressure; SD, standard deviation.				

Patient characteristics and comparison between the ones with HFpEF and those with HFrEF are shown in Table 1. During the 6-month period, 94 (9.2%) patients died, and 78 of the deaths were attributed to HF; the combined endpoint of death due to HF or admission due to worsening HF occurred in 162 patients (33.1%).

The HFpEF patients were older and more often women; prevalence of hypertension was higher and prevalence of coronary artery disease was lower. Admission BNP levels were lower in patients with HFpEF. Significant differences in echocardiographic parameters were also noted: LAVI and E/E' were significantly higher in patients with systolic dysfunction.

The median E/E' of the HFpEF patients was 15 (interquartile range, 11–21). Using the criteria of the ESC algorithm for the diagnosis of HFpEF—BNP levels

>200 pg/mL and E/E' >8—all but 3 (1.8%) patients accomplished a positive diagnosis. More than half (53.4%) of the HFpEF patients had an E/E' between 8 and 15. In 6.7%, E/E' ratio determination was not possible.

Using 15 as the E/E' cutoff for HFpEF diagnosis, sensitivity was 44.8% and the specificity was 95.8%. The area under the receiver operating characteristic curve for the accuracy for E/E' to diagnose HFpEF was 0.88, with the best suggested cutoff of 12.5. Using 12.5 as the E/E' cutoff, HFpEF diagnosis sensitivity would be 69.3% with 4.8% false-positive diagnosis; test specificity using this cutoff would be 95.2%. That is, in patients without systolic dysfunction, an E/E' >12.5 has a 98.2% positive predictive value in HFpEF diagnosis and an E/E' <12.5 has a negative predictive value of 36.3%. If 10 is used as the E/E' cutoff for HFpEF diagnosis, test sensitivity would be 82.8% with 19% false-positive tests.

Table 2. Variables Associated in an Univariate Approach With All-Cause Mortality, Heart Failure Mortality, and Heart Failure Mortality and Morbidity in Patients With HFpEF and in Those With HFrEF

	All-Cause Mortality in HFpEF HR (95% CI)	HF Mortality in HFpEF HR (95% CI)	HF Mortality and Morbidity in HFpEF HR (95% CI)	All-Cause Mortality in HFrEF HR (95% CI)	HF Mortality in HFrEF HR (95% CI)	HF Mortality and Morbidity in HFrEF HR (95% CI)
Clinical characteristics						
Age (per year)	1.03 (0.99–1.08)	1.06 (1.00–1.13) ^a	1.02 (0.99–1.05)	1.04 (1.01–1.06) ^a	1.03 (1.01–1.05) ^a	1.02 (1.00–1.03) ^a
Male sex	0.90 (0.40–2.04)	1.01 (0.39–2.63)	1.80 (1.03–3.16) ^a	0.88 (0.54–1.43)	0.99 (0.59–1.67)	1.12 (0.77–1.63)
Hypertension	0.41 (0.18–0.93) ^a	0.37 (0.14–0.96) ^a	0.63 (0.31–1.26)	0.58 (0.35–0.98) ^a	0.62 (0.36–1.07)	0.94 (0.61–1.42) ^a
DM	0.84 (0.56–1.23)	0.84 (0.52–1.33)	1.12 (0.84–1.49)	0.78 (0.59–1.01)	0.83 (0.63–1.09)	1.00 (0.82–1.21)
AF	1.30 (0.60–2.81)	1.23 (0.49–3.05)	1.36 (0.76–2.42) ^a	2.06 (1.25–3.38) ^a	2.35 (1.38–4.00) ^a	1.51 (1.04–1.20) ^a
CHD	1.01 (0.48–2.13)	0.55 (0.20–1.51)	1.14 (0.65–2.00)	1.46 (0.89–2.40)	1.48 (0.87–2.50)	1.97 (1.34–2.91) ^a
SBP (per mm Hg)	0.99 (0.98–1.00)	0.98 (0.96–1.00) ^a	1.00 (0.99–1.01)	0.97 (0.96–0.98) ^b	0.97 (0.96–0.98) ^b	0.98 (0.98–0.99) ^b
Laboratory parameters						
Hemoglobin (per g/dL)	0.85 (0.72–1.01)	0.92 (0.75–1.12)	0.97 (0.88–1.07)	0.92 (0.82–1.03)	0.90 (0.80–1.01)	0.89 (0.82–0.96) ^a
Serum sodium (per mEq/L)	0.97 (0.90–1.04)	0.97 (0.90–1.06)	0.93 (0.88–0.97) ^a	0.94 (0.90–0.99) ^a	0.95 (0.90–1.00) ^a	0.96 (0.92–1.00) ^a
Plasma creatinine (per mg/dL)	0.92 (0.58–1.46)	0.99 (0.59–1.65)	1.16 (0.89–1.52)	1.34 (1.07–1.66) ^a	1.38 (1.10–1.72) ^a	1.34 (1.13–1.59) ^a
BNP (per 100 pg/L)	1.05 (1.01–1.09) ^a	1.06 (1.02–1.11) ^a	1.05 (1.02–1.08) ^a	1.02 (1.01–1.03) ^b	1.02 (1.01–1.03) ^b	1.02 (1.01–1.02) ^b
Echocardiographic parameters						
EF (per 1%)	1.01 (0.95–1.08)	1.02 (0.94–1.10)	1.01 (0.96–1.05)	0.97 (0.94–1.00) ^a	0.96 (0.94–0.99) ^a	0.98 (0.96–1.00)
LAVI (per mL/m ²)	1.01 (0.99–1.02)	1.01 (0.99–1.03)	1.01 (1.00–1.03)	1.02 (1.01–1.03) ^b	1.02 (1.01–1.03) ^b	1.02 (1.01–1.02) ^b
LVMI (per 10 gr/m ²)	1.00 (0.90–1.10)	1.00 (0.88–1.14)	0.99 (0.91–1.07)	1.02 (1.00–1.03) ^a	1.02 (1.00–1.03) ^a	1.01 (1.00–1.02)
E/E' ratio	1.02 (0.97–1.08)	1.01 (0.94–1.08)	1.02 (0.98–1.07)	1.06 (1.03–1.09) ^b	1.07 (1.04–1.10) ^b	1.04 (1.01–1.06) ^a
E/E' ratio >15	1.58 (0.72–3.48)	1.37 (0.56–3.38)	1.25 (0.70–2.23)	2.31 (1.23–4.34) ^a	2.26 (1.17–4.38) ^a	1.28 (0.84–1.92)
Abbreviations: AF, atrial fibrillation; BNP, B-type natriuretic peptide; CHD, coronary heart disease; CI: confidence interval; DM, diabetes mellitus; E/E' ratio, relation of the E atrial wave measure by pulsed-wave transmitral Doppler and early diastolic velocity E' by pulsed-wave tissue Doppler imaging; EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HR: hazard ratio; LAVI, left atrial volume index; LVMI, left ventricular mass index; SBP, systolic blood pressure. ^a <i>P</i> < 0.05. ^b <i>P</i> < 0.001.						

Variables predicting all-cause mortality and HF mortality (data not shown) were older age, absence of history of hypertension, atrial fibrillation history, lower admission systolic blood pressure, lower admission sodium, worse renal function, higher admission BNP, higher E/E' and higher LAVI. Lower hemoglobin predicted worse outcome only when all-cause mortality was the endpoint under consideration.

The HFrEF patients had similar all-cause mortality, and morbidity and mortality, due to HF—hazard ratio (HR) 1.28 (95% confidence interval [CI]: 0.82–1.98, *P* = 0.28) and 1.29 (95% CI: 0.92–1.78, *P* = 0.14), respectively—when compared with those with HFpEF. The HFpEF patients showed a trend toward better survival when death due to HF was considered, even when adjustments were made to variables also associated with worse prognosis. The HRs of HF death adjusted for age, atrial fibrillation, hypertension history, admission systolic blood pressure, plasma creatinine, and sodium up to 6 months in patients with HFrEF was 1.63 (95% CI: 0.95–2.80, *P* = 0.08) when

compared with those with HFpEF. Table 2 shows variables associated with outcome (all-cause death and the combined endpoint of admission or death due to HF) in patients with HFpEF and in patients with HFrEF. Table 3 shows the multivariate model. The survival adjusted curves according to presence of systolic dysfunction are shown in Figure 1.

Higher E/E' was associated with higher all-cause and HF mortality when all patients were considered; however, this association was only observed for patients with HFrEF and not for patients with HFpEF. The association of higher E/E' with mortality was independent of the LAVI. Figure 2 shows the LAVI and LV mass index adjusted survival curves according to E/E' in patients with HFpEF (left) and in patients with reduced LVEF (right). Patients with HFpEF with E/E' >15 had a LAVI and LV mass index-adjusted HR of HF mortality of 1.23 (95% CI: 0.48–3.231, *P* = 0.68) compared with those with lower E/E'. In patients with HFrEF and an E/E' >15, the LAVI-adjusted HR of HF mortality was 2.02 (95% CI: 1.01–4.01, *P* = 0.046) compared with those with E/E' <15.

Table 3. Multivariate Model of 6-Month Heart Failure Death Predictors

	Hazard Ratio (95% CI)	P Value
HFrEF vs HFpEF	1.63 (0.95–2.80)	0.08
Age (per year)	1.04 (1.02–1.07)	<0.001
AF	1.61 (0.98–2.64)	0.06
Hypertension	0.56 (0.34–0.95)	0.03
SBP (per mm Hg)	0.98 (0.97–0.99)	<0.001
Plasma creatinine (per mg/dL)	1.24 (0.97–1.60)	0.09
Serum sodium (per mEq/L)	0.98 (0.94–1.03)	0.44

Abbreviations: AF, atrial fibrillation; CI, confidence interval; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; SBP, systolic blood pressure.

Figure 1. Mortality due to HF according to left ventricular function. HFpEF patients showed a trend to a better HF survival. Adjustment were made to age, atrial fibrillation, history of hypertension, admission SBP, admission sodium, and creatinine. Abbreviations: HF, heart failure; HFpEF, heart failure with preserved ejection fraction; SBP, systolic blood pressure.

Discussion

Our results in a consecutive group of acute HF patients show that the ESC consensus algorithm based on BNP levels and tissue Doppler imaging ratio E/E' for the diagnosis of HFpEF identifies a group of acute HF patients with a trend to lower HF mortality than HFrEF, but similar all-cause medium-term mortality is identified.

These results using objective criteria for the diagnosis of HFpEF and showing similar prognosis when compared with patients with HFrEF increase the robustness of the diagnostic criteria for HFpEF.

The diagnostic uncertainty of physicians when facing patients with acute dyspnea is well known. In almost two-thirds of patients with acute dyspnea, physicians are uncertain of its cause, as shown in the Breathing Not

Properly Study. In this scenario, the usefulness of natriuretic peptides in the diagnosis of acute HF is now well established and there is robust evidence that its knowledge improves the diagnostic performance of clinicians.^{17,18}

To be considered for inclusion in our registry of acute HF, patients had to have BNP levels >200 pg/mL, no other conditions explaining symptoms, and the demonstration of cardiac structural or functional impairment. The inclusion criteria of our registry made our population an appropriate group in which to evaluate whether the ESC consensus algorithm for HFpEF diagnosis identifies a group of patients with similar prognosis to those with reduced LVEF. The ESC consensus proposed diagnostic criteria for diastolic dysfunction centered on the determination of the E/E' ratio.

According to the ESC consensus statement, patients with an E/E' ratio >15 should be considered to have diastolic dysfunction and those with a ratio <8 should be considered as having normal diastolic function. Patients with a ratio between 8 and 15 represent a grey zone and are considered as possibly having diastolic dysfunction. For patients with BNP levels >200 pg/mL, an E/E' ratio >8 is suggested to be sufficient to consider HFpEF.⁹

The reported prognosis of HFpEF patients has varied widely; however, the recognition of the associated high morbidity and mortality of these patients is becoming unquestionable.^{14,19–21} In the EuroHeart Failure Survey, the incidence of all-cause mortality during a 3-month period was 10% and the need for rehospitalization was 21%.²² A recent systematic review of >40 000 patients observed that patients with HFpEF had a 32% lower risk of death over 3 years compared with those with HFrEF.¹⁵

In our population, and using an E/E' ratio cutoff of 8, we observed similar all-cause mortality and a trend toward lower mortality due to HF in HFpEF patients when compared with patients with HFrEF; this is in line with others' observations in larger registries.²¹ Thus, our results suggest that the use of the proposed E/E' ratio >8 for HFpEF diagnosis clearly identifies a group of patients with an ominous prognosis.

Echocardiography plays a critical role in the HF approach.¹⁶ It is a noninvasive bedside tool able to identify cardiac structure and function abnormalities and can provide relevant prognostic information. Transmittal flow velocity curves and other Doppler variables have been used as noninvasive estimates of intracardiac filling pressures.^{23–25} The E/E' ratio in particular has been shown to correlate with pulmonary capillary wedge pressure in a wide range of cardiac patients.^{24,25} Recent reports evaluating patients with HFpEF, in contrast to patients with reduced LVEF, have shown a weak association of E/E' ratio and pulmonary capillary wedge pressure.²⁶ This observation could substantially limit the interest of E/E' ratio in the identification of HFpEF patients. Our results support the value of E/E' ratio in the diagnostic evaluation of HFpEF. Using the E/E' ratio in patients with signs and symptoms of HF and neurohumoral activation, we could identify a preserved-systolic function HF population at high risk of death. In our study, as well as in another small study,²⁷ the E/E' ratio measured at hospital admission was not associated with prognosis in HFpEF patients, in contrast to patients with reduced LV. The reason for this apparent discrepancy can relay in different aspects. In patients

Figure 2. Heart failure death according to the E/E' ratio in patients with preserved ejection fraction (left) and in patients with reduced ejection fraction (right). Abbreviations: HFrEF, heart failure with reduced ejection fraction.

with reduced LVEF, E/E' ratio mirrors end-diastolic left ventricular pressure, an index of HF severity. In patients with preserved systolic function, E/E' ratio is significantly lower than in patients with reduced LV eventually due to lower left ventricular end-diastolic pressures. The lack of association between E/E' ratio and outcome in HFpEF patients suggests that variables other than the E/E' ratio (disturbances of both LV relaxation and stiffness) are probably relevant in prognostic determination. Other observations found an association between E/E' ratio and outcome in HFpEF patients after clinical stabilization, suggesting that the prognostic value of E/E' may be valid only in normovolemic patients.²⁷ In our population the echocardiogram was performed within 72 hours of admission; that is, still within a period of clinical instability. Thus, in our study the prognostic value of E/E' could be obscured due to lack of therapeutic optimization.

Study Limitations

Our study is a single-center study with a limited number of patients with preserved systolic function, making extrapolation of our results only possible after confirmation by other centers. Follow-up of our patients has been limited to 6 months; longer follow-up would be relevant to expand our observation. Patients included in our registry had BNP levels >200 pg/mL; thus, the study does not allow conclusions in patients with lower BNP levels.

Conclusion

To the best of our knowledge, this is the first report that estimates the prognosis of HFpEF patients as identified using the ESC consensus recommendations. It allowed us to conclude that they in fact identify a group of patients with an ominous prognosis.

A correct and uniform positive identification of HFpEF patients is crucial to the design of trials evaluating interventions in this specific subgroup of HF patients.

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