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Right ventricular ejection fraction <20% is an independent predictor of mortality but not of hospitalization in older systolic heart failure patients

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Abstract

Background—Reduced right ventricular ejection fraction (RVEF) is associated with poor outcomes in patients with chronic systolic heart failure (HF). Although most HF patients are older adults, little is known about the relationship between low RVEF and outcomes in older adults with systolic HF.

Methods—Of the 2008 Beta-Blocker Evaluation of Survival Trial (BEST) participants with systolic HF (left ventricular ejection fraction ≤35%) 822 were ≥65 years and had data on baseline RVEF estimated by gated-equilibrium radionuclide ventriculography. Using RVEF ≥40% (n=308) as reference, we examined association of RVEF 30–39% (n=214), 20–29% (n=206) and <20% (n=94) with outcomes using Cox regression models.

Results—All-cause mortality occurred in 36%, 40%, 39% and 56% of patients with RVEF ≥40%, 30–39%, 20–29% and <20% respectively. Compared with RVEF ≥40%, unadjusted hazard ratios (HR) and 95% confidence intervals (CI) for all-cause mortality associated with RVEF 30–39%, 20–29% and <20% were 1.19 (0.90–1.57; P=0.220), 1.13 (0.84–1.51; P=0.423) and 1.97 (1.43–2.73; P<0.001) respectively. Respective multivariable-adjusted HR's (95% CI's) for all-cause mortality were 1.19 (0.88–1.60; P=0.261), 1.00 (0.73–1.39; P=0.982) and 1.70 (1.14–2.53; P=0.009). Adjusted HR's (95% CI's) associated with RVEF <20% (versus ≥40%) for cardiovascular mortality and HF mortality were 1.79 (1.17–2.76; P=0.008) and 1.97 (1.02–3.83; P=0.045) respectively. RVEF had no independent association with sudden cardiac death, all-cause or HF hospitalization.

Conclusions—Abnormally low RVEF is a significant independent predictor of mortality, but not of HF hospitalization, in older adults with systolic HF.

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Keywords

Heart Failure; Older Adults; Right Ventricle; Mortality; Morbidity

1. Introduction

We have recently demonstrated that in a relatively young (mean age, 60 years) cohort of systolic heart failure (HF) patients, low right ventricular ejection fraction (RVEF) was an independent predictor of increased all-cause mortality and HF hospitalization [1]. In that study, we have also observed that systolic HF patients with reduced RVEF were significantly younger than those with preserved RVEF. Although most HF patients are 65 years or older [2], most prior studies of the association between RVEF and outcomes in HF were conducted in younger HF patients [3–10] and little is known about the specific relationship between reduced RVEF and outcomes in older adults with systolic HF. Therefore, in the current study we examined the relationship between RVEF and outcomes in older adults with advanced chronic systolic HF.

2. Material and methods

2.1. Study design

The Beta-Blocker Evaluation of Survival Trial (BEST) was a randomized clinical trial of the beta-blocker bucindolol in HF conducted at 30 Veterans Administration Hospital (VA) sites and 60 non-VA sites in the United States and Canada between May 1995 and December 1998. The study was funded by the National Heart, Lung, and Blood Institute (NHLBI) and the Department of Veterans Affairs Cooperative Studies Program. The BEST protocol and results have been previously detailed elsewhere [11, 12]. Briefly, 2708 patients with moderate-to-severe chronic systolic HF were randomized to receive bucindolol or placebo and were followed up for a mean of 2 years. All patients gave written informed consent and the protocol was approved by the institutional review board of each site. For the purpose of the current analysis we used a public-use copy of the BEST data obtained from the NHLBI. The public-use version of the data is similar to the original data except for de-identification and that one patient did not consent to be included in these de-identified datasets.

2.2 Patients

Of the 2707 patients in the public-use copy of the data, 2008 had data on baseline RVEF, who were the subjects of our previous study [1]. The current analysis is restricted to the 822 (41%) patients who were 65 years or older at baseline. All patients had a LVEF ≤35%, and were in New York Heart Association (NYHA) functional class III (92%) or IV (8%). The majority was receiving angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers (>90%), diuretics (>90%) and digoxin (>90%).

2.3. Estimation of LVEF and RVEF

All patients underwent a baseline gated-equilibrium radionuclide ventriculographic assessment of LVEF and RVEF during randomization or within 60 days prior to randomization [1]. The lower limit of normal RVEF by gated-equilibrium radionuclide ventriculography is 40% [13, 14]. Patients were categorized into four RVEF groups: ≥40% (n=308 or 37%), 30–39% (n=214 or 26%), 20–29% (n=206 or 25%) and <20% (n=94 or 11%).

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2.4. Study outcomes

The primary end point for the current analysis was all-cause mortality which was also the primary end point in BEST and was centrally adjudicated. Secondary outcomes included cardiovascular and HF mortality, and all-cause and HF hospitalization.

2.5. Statistical analysis

We used chi-square tests and analysis of variance tests, as appropriate, for descriptive analyses to compare baseline characteristics between the four RVEF groups. Kaplan–Meier plots were constructed to determine associations of RVEF groups with all-cause mortality. Associations of various RVEF categories with outcomes were determined using Kaplan–Meier survival analysis and Cox proportional hazard models. RVEF category ≥40% was used as the reference category and dummy variables were used for RVEF categories 30%–39%, 20%–29% and <20%. Variables were entered into the model in multiple steps in the following order: step 1 (unadjusted: dummy variables for RVEF 30–39%, 20–29% and <20%), and step 2 (step 1 plus LVEF), step 3 (step 2 plus demographics), step 4 (step 3 plus medical history), step 5 (step 4 plus medications), step 6 (step 5 plus clinical findings), and step 7 (step 6 plus laboratory findings). The same model was used for all the outcomes. We confirmed the assumption of proportional hazards by a visual examination of the log (minus log) curves. All statistical tests were evaluated using two-tailed 95% confidence levels and tests with p-value <0.05 were considered significant. Data analyses were performed using SPSS for Windows, Rel. 15. 2006. Chicago: SPSS Inc.

3. Results

3.1. Baseline characteristics

Patients had a mean age of 72 (±5) years, 16% were women and 14% were African Americans. Patients in the lower RVEF categories were more likely to be African Americans with characteristics suggesting more advanced HF, including higher NYHA functional class, higher heart rate, lower systolic blood pressure, lower LVEF, and more signs of peripheral or pulmonary congestion (Tables 1 and 2). Mean RVEF was 35% (±13) and its distribution among the participants is displayed in Figure 1.

3.2. Association between RVEF and mortality

Unadjusted rates for all-cause mortality in patients with RVEF ≥40%, 30–39%, 20–29% and <20% were 36%, 40%, 39% and 56%, respectively (Table 3 and Figure 2). When compared to patients with RVEF ≥40%, unadjusted hazard ratios (HR) and 95% confidence intervals (CI) for all-cause mortality for those with RVEF 30–39%, 20–29% and <20% were 1.19 (0.90–1.57; P=0.220), 1.13 (0.84–1.51; P=0.423) and 1.97 (1.43–2.73; P<0.001) respectively. Respective multivariable-adjusted HR's (95% CI's) for all-cause mortality associated with RVEF 30–39%, 20–29% and <20% were 1.19 (0.88–1.60; P=0.261), 1.00 (0.73–1.39; P=0.982) and 1.70 (1.14–2.53; P=0.009) respectively. The associations between RVEF <20% (versus ≥40%) and all-cause mortality were homogenous across various subgroups (Figure 3). Unadjusted and adjusted HR's (95% CI's) for cause-specific mortalities are displayed in Table 4.

3.3. Association between RVEF and hospitalization

Unadjusted rates for HF hospitalization in patients with RVEF ≥40%, 30–39%, 20–29% and <20% were 40%, 40%, 42% and 51%, respectively (Table 4). Compared to patients with RVEF ≥40%, unadjusted HR for HF hospitalization for those with RVEF <20% was 1.82 (95% CI, 1.30–2.54; P<0.001) but lost significance after multivariable-adjustment (1.26,

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95% CI =0.84–1.87; P=0.260). Unadjusted and adjusted HR's (95% CI's) for all-cause hospitalization are displayed in Table 4.

4. Discussion

4.1. Summary and relevance of the key findings

Findings from our study demonstrate that in older adults with advanced systolic HF, compared to normal RVEF (≥40%), those with severely reduced RVEF (<20%) had increased risk of all-cause, cardiovascular and HF mortalities and sudden cardiac death, and all-cause and HF hospitalizations. However, only the association with all-cause, cardiovascular and HF mortalities were independent of other confounders including LVEF. Milder impairment of RVEF (20 to 39%), on the other hand, had no association with mortality or HF hospitalization. These findings suggest that in older adults with systolic HF, a severely reduced RVEF may be used as a marker of poor prognosis and evaluation of RVEF may be considered a part of a comprehensive assessment of these patients. These findings are important because the majority of HF patients are 65 years and older and most of HF-related mortality occurs in these patients [15, 16].

4.2. Potential explanation and mechanism of the key findings

Low RVEF in HF patients with reduced LVEF may occur early as a result of a disease process involving both ventricles but more commonly, it may be the consequence of LVEF impairment through complex hemodynamic, mechanical and neurohormonal ventricular interactions [1, 17–21]. RV failure, in turn, may compromise adequate LV preload and further reduce LV output, which creates a positive loop of feedback enhancing neurohormonal activation and precipitating end-organ hypoperfusion [1, 19]. The association of reduced RVEF with mortality in elderly patients is therefore mechanistically coherent since low RVEF is primarily a long-term consequence of low LVEF and may also lead to further LVEF impairment and disease progression.

Interestingly, in contrast to the patients with systolic HF in general [1], RVEF was not associated with HF hospitalization in this older cohort with systolic HF. Potential explanations for increased mortality without associated increase in hospitalization include sudden death or death not associated with acute exacerbation of symptoms. However, RVEF <20% in our study was not association with sudden cardiac death. This is also unlikely to be explained by small sample size or event size, as the number of events for HF hospitalization (51%) in those with RVEF <20% was similar to that for total mortality (56%) and CV mortality (49%), both of which were significantly increased. Finally, an alternative explanation might be that this association occurred by chance.

4.3. Comparison with findings from relevant published literature

Several studies have reported the prognostic value of RVEF in HF using different techniques of assessment of RVEF [3–10]. However, patients included in these studies had a mean age of 50 to 60 years, and many were based exclusively on candidates for heart transplant [4, 5, 9]. In contrast, our previous report of the relationship between RVEF and outcomes was the largest, was based on ambulatory systolic HF patients, and nearly half of the patients were older adults. To the best of our knowledge, this is the first report of the effect of RVEF on the natural history of systolic HF in ambulatory older adults. The findings from the current study suggest that RVEF may provide useful prognostic information in ambulatory older adults with systolic HF and whenever possible RVEF should be estimated as a part of the comprehensive evaluation of HF in these patients. Radionuclide ventriculography has been extensively validated for the estimation of RVEF. However, echocardiographic assessment of the right ventricle using the apical 4-chamber view can also provide overall qualitative

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assessments of right ventricular size and function [22]. Finally, three-dimensional echocardiography appears very promising in RVEF measurement [23].

4.4. Clinical and public health importance

The management of RV failure in patients with chronic systolic HF is poorly understood and remains largely empirical [17]. The presence of reduced RVEF may be used in a near future not only to assess prognosis but also to refine the therapeutic management of these patients. Preliminary data from patients with nonischemic hear disease suggest that those with low RVEF are less likely to experience an increase in LVEF from beta-blocker therapy [24]. Patients with low RVEF are also less likely to respond to cardiac resynchronization therapy [25] but more likely to respond to therapy with sildenafil [26]. Cardiac resynchronization therapy has been shown to be associated with a slight improvement in RVEF (by about 2%; P=0.016) after a mean follow-up of 9 months [25]. Data from patients with systolic HF and pulmonary hypertension also suggest that therapy with sildenafil may also improve RVEF [26].

4.5. Potential limitations and future direction

Several limitations of our study must be acknowledged. RVEF may have changed during follow-up resulting in regression dilution and potential underestimation of the observed associations between RVEF and outcomes [27]. Radionuclide ventriculography has now been replaced by cardiac magnetic resonance imaging (MRI) as the gold standard for measuring RVEF [28]. However, routine use of MRI in the assessment of HF patients is still limited by lack of availability, costs and the wide use of devices that are not MRI-compatible yet. Also, RVEF is an imperfect measure of RV systolic function as it is dependent on loading conditions [17, 28], and thus may be affected by volume status, pulmonary pressure, and tricuspid regurgitation, none of which was specifically evaluated in our study. However, the same limitations also apply to many other measurements of RV systolic function. Finally, BEST participants were not receiving beta-blockers approved for HF, which may limit generalizability of these findings to contemporary patients with systolic HF.

4.6. Conclusions

In conclusion, in older adults with advanced chronic systolic HF, severely reduced RVEF (<20%) is an independent predictor of increased mortality but had no association with hospitalization. Measurement of RVEF should be considered in these patients, and when available, should be used to stratify patients for prognostic and therapeutic purposes. Future studies need to develop and test new therapies to improve outcomes in older adults with systolic HF and low RVEF.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [29].

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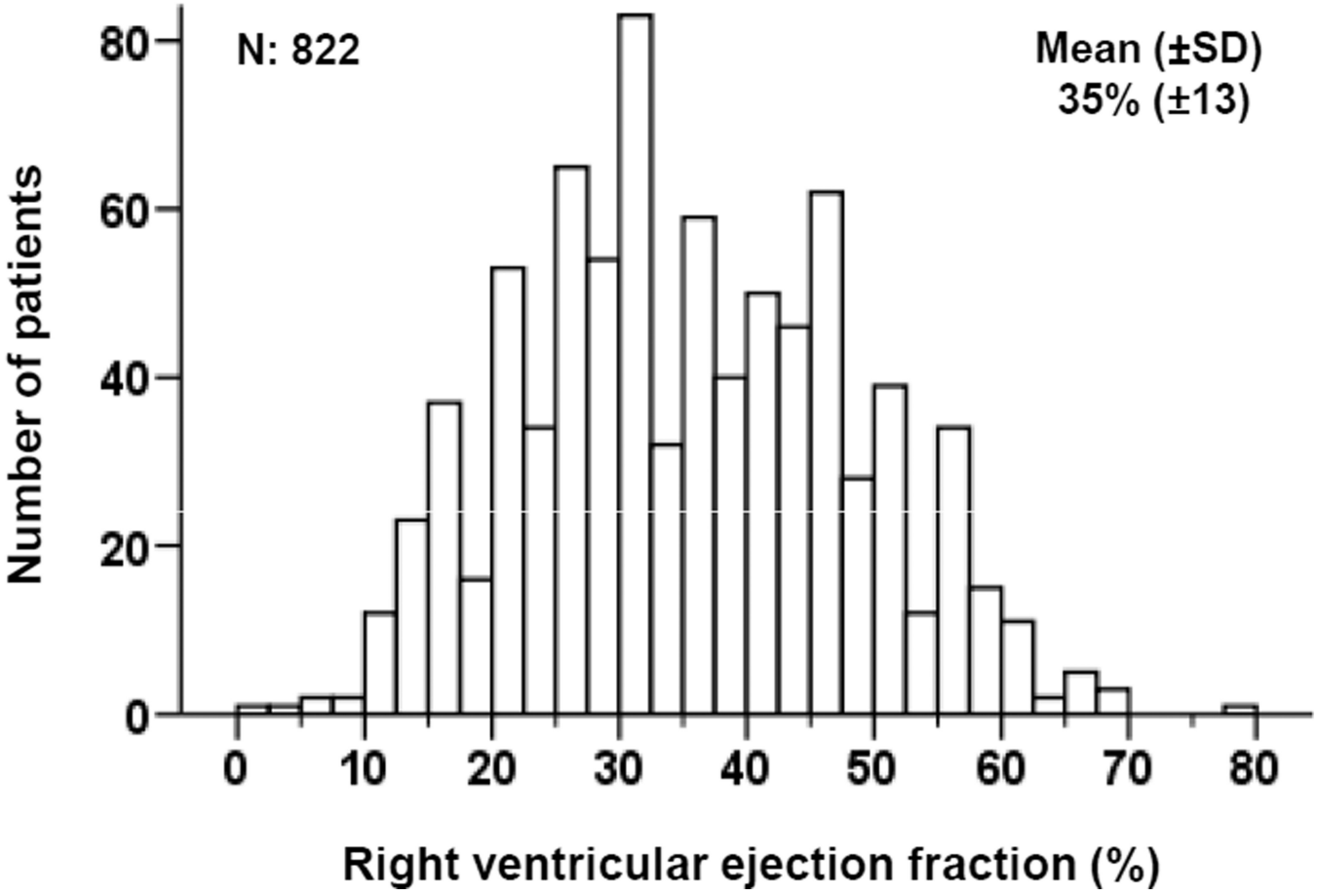

Figure 1.
Histogram displaying frequency distribution of right ventricular ejection fraction (%)

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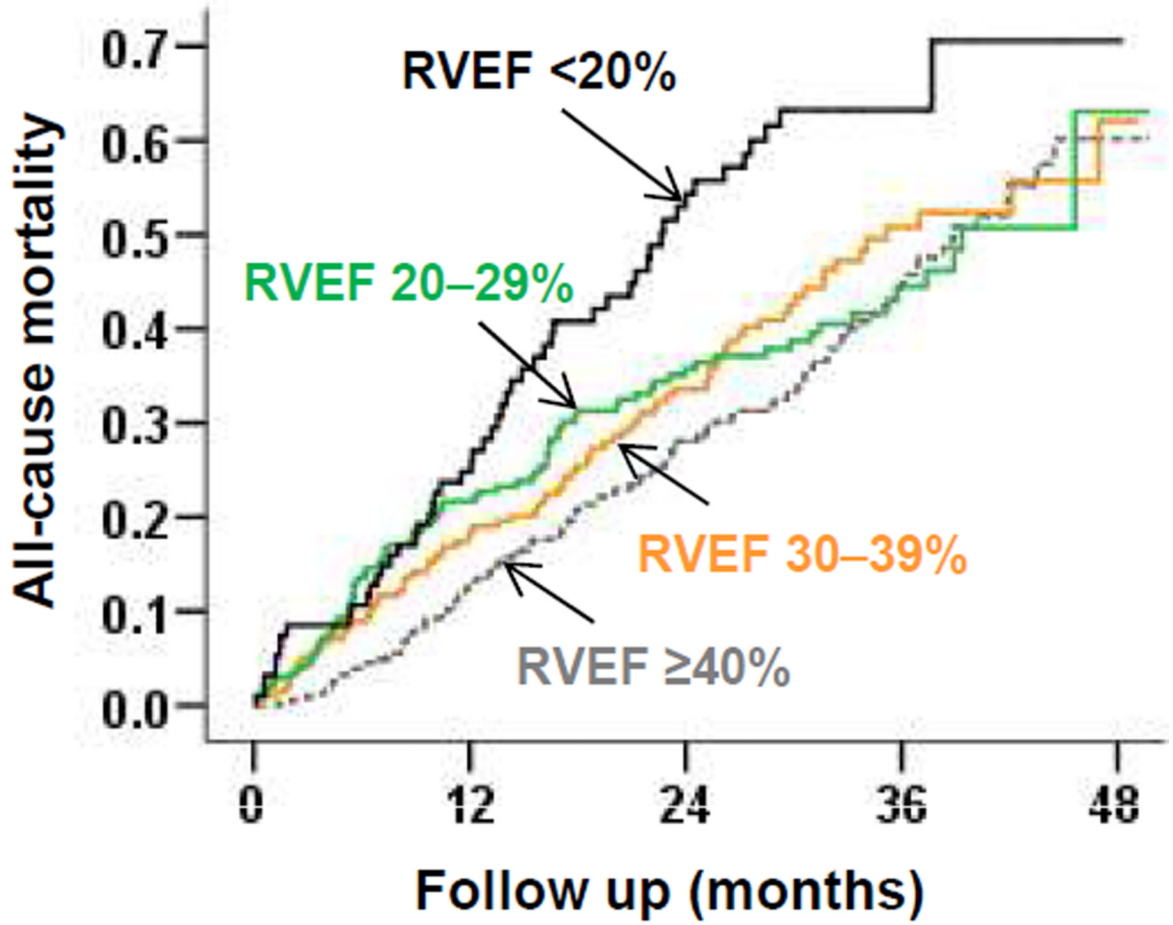

Number of patients at risk

RVEF ≥40	308	244	147	66
RVEF 30-39	214	152	100	36
RVEF 20-29	206	149	96	38
RVEF >20	94	67	33	9

Figure 2.
Kaplan–Meier plots for all-cause mortality by right ventricular ejection fraction (RVEF)

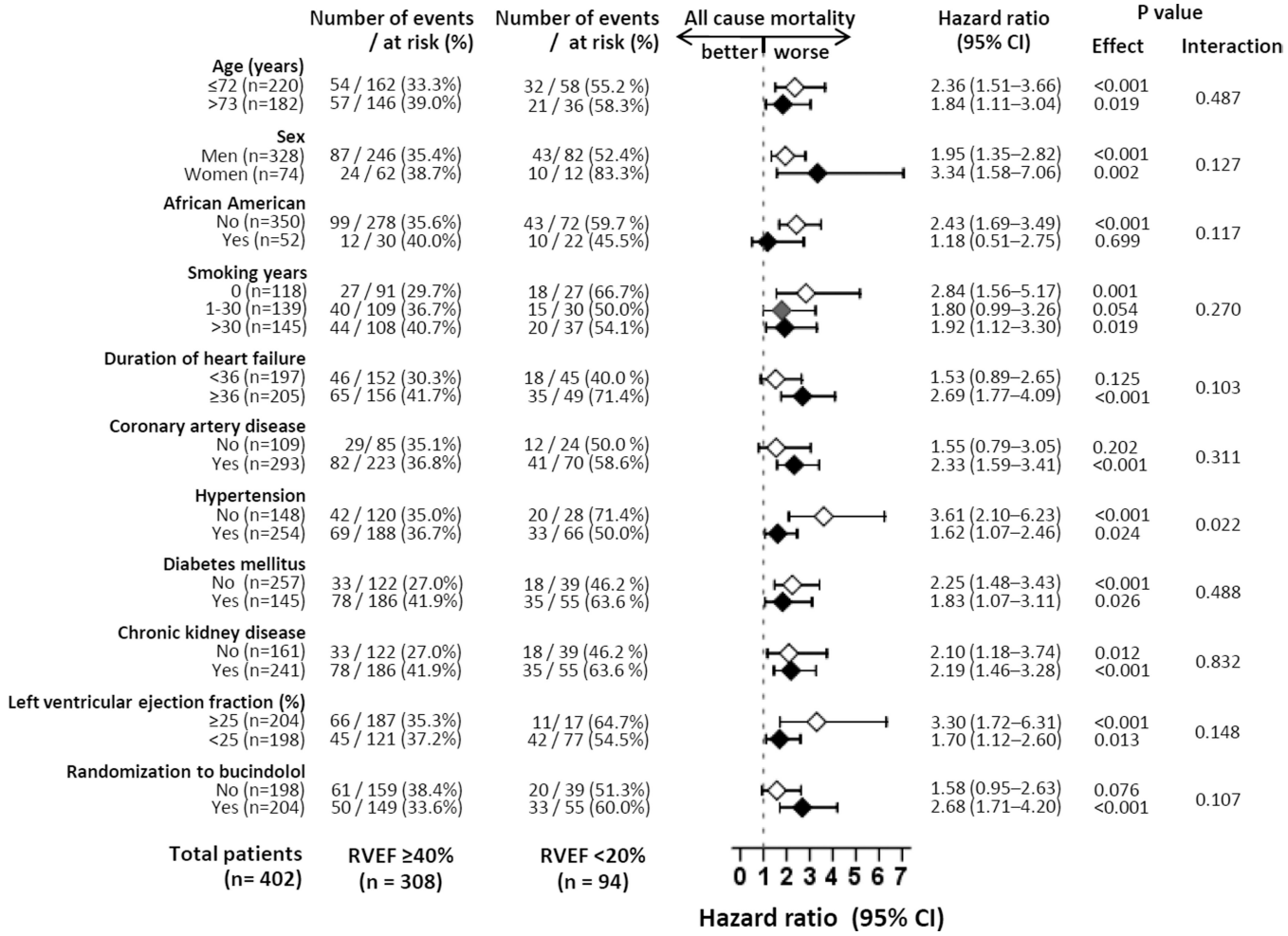

Figure 3.

Association of right ventricular ejection fraction (RVEF) <20% (versus RVEF ≥40%) with all-cause mortality in various patient subgroups (CI = confidence interval)

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Table 1

Baseline patient characteristics by right ventricular ejection fraction (RVEF) categories

n (%) or mean (±SD)	**RVEF ≥40% (n=308)**	**RVEF 30 to 39% (n=214)**	**RVEF 20 to 29% (n=206)**	**RVEF <20% (n=94)**	**P-value**
Age, years	73 (±5)	71 (±5)	72 (±5)	72 (±5)	0.014
Female	62 (20)	31 (15)	27 (13)	12 (13)	0.099
African American	30 (10)	29 (14)	37 (18)	22 (23)	0.003
Veteran	127 (41)	92 (43)	91 (44)	34 (36)	0.601
Current smoker	40 (13)	20 (9)	22 (11)	6 (6)	0.269
New York Heart Association class III	281 (91)	196 (92)	176 (85)	74 (79)	0.002
Body mass index, kg/m^2	34 (±7)	35 (±7)	33 (±6)	33 (±7)	0.025
Heart rate, beats per minute	77 (±12)	77 (±11)	79 (±12)	83 (±11)	<0.001
Systolic blood pressure, mm Hg	123 (±19)	118 (±17)	115 (±18)	114 (±19)	<0.001
Diastolic blood pressure, mm Hg	69 (±10)	69 (±10)	68 (±10)	69 (±11)	0.514
Left ventricular ejection fraction, %	26 (±6.3)	24 (±6.4)	21 (±7.1)	18 (±5.8)	<0.001
Past medical history					
Duration of heart failure, months	52 (±48)	57 (±52)	64 (±57)	58 (±61)	0.099
Idiopathic dilated cardiomyopathy	66 (21)	43 (20)	35 (17)	15 (16)	0.318
Coronary artery disease	223 (72)	153 (72)	153 (74)	70 (75)	0.904
Coronary artery stenosis >70%	171 (56)	116 (54)	123 (60)	51 (54)	0.666
Angina pectoris	180 (58)	121 (57)	115 (56)	59 (63)	0.689
ST segment elevation myocardial infarction	122 (40)	85 (40)	87 (42)	44 (47)	0.610
Anterior ST segment elevation myocardial infarction	69 (22)	32 (15)	35 (17)	19 (20)	0.155
Lateral ST segment elevation myocardial infarction	28 (9)	16 (8)	21 (10)	9 (10)	0.800
Inferior-posterior ST segment elevation myocardial infarction	45 (15)	38 (18)	26 (13)	16 (17)	0.480
Coronary artery bypass surgery	111 (36)	90 (42)	87 (42)	36 (38)	0.419
Percutaneous coronary interventions	54 (18)	35 (16)	26 (13)	10 (11)	0.251
Hypertension	188 (61)	139 (65)	128 (62)	66 (70)	0.394
Diabetes mellitus	107 (35)	82 (38)	65 (32)	38 (40)	0.360
Hyperlipidemia	145 (47)	102 (48)	76 (37)	37 (39)	0.061

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n (%) or mean (±SD)	RVEF ≥40% (n=308)	RVEF 30 to 39% (n=214)	RVEF 20 to 29% (n=206)	RVEF <20% (n=94)	P-value
Atrial fibrillation	90 (29)	77 (36)	78 (38)	23 (25)	0.043
Peripheral arterial disease	69 (22)	52 (24)	38 (18)	15 (16)	0.263
Chronic kidney disease*	186 (60)	107 (50)	120 (58)	55 (59)	0.115
Medications					
Bucindolol	149 (48)	105 (49)	94 (46)	55 (59)	0.223
Angiotensin-converting enzyme inhibitors / angiotensin II receptor blockers	291 (95)	202 (94)	195 (95)	88 (94)	0.987
Digitalis	274 (89)	197 (92)	190 (92)	91 (97)	0.103
Diuretics	288 (94)	197 (92)	196 (95)	94 (100)	0.040
Vasodilators	157 (51)	111 (52)	95 (46)	48 (51)	0.637
Anticoagulants	166 (54)	142 (66)	119 (58)	48 (51)	0.018

*Estimated glomerular filtration rate <60 mL/min per 1.73 m^2 of body surface area

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Table 2

Baseline clinical and laboratory characteristics by right ventricular ejection fraction (RVEF) categories

n (%) or mean (±SD)	**RVEF ≥40% (n=308)**	**RVEF 30 to 39% (n=214)**	**RVEF 20 to 29% (n=206)**	**RVEF <20% (n=94)**	**P-value**
Clinical findings					
Elevated jugular venous pressure at 30 degrees	141 (46)	98 (46)	123 (60)	49 (52)	0.009
S3 gallop	122 (40)	85 (40)	90 (44)	45 (48)	0.439
S4 gallop	53 (17)	45 (21)	27 (13)	14 (15)	0.172
Pulmonary rales	57 (19)	37 (17)	51 (25)	28 (30)	0.029
Hepatomegaly	32 (10)	29 (14)	30 (15)	19 (20)	0.093
Lower extremity edema	80 (26)	64 (30)	73 (35)	40 (43)	0.010
Chest x-ray findings					
Pulmonary edema	21 (7)	16 (8)	32 (16)	28 (30)	<0.001
Cardiothoracic ratio	54.5 (±7.1)	54.7 (±7.0)	57.3 (±7.3)	59.5 (±7.0)	<0.001
Electrocardiographic findings					
Left ventricular hypertrophy	54 (18)	37 (17)	39 (19)	20 (21)	0.830
Right ventricular hypertrophy	1 (0.3)	2 (1)	2 (1)	3 (3)	0.105
Atrial fibrillation	38 (12)	41 (19)	40 (19)	8 (9)	0.015
Left bundle branch block	94 (31)	64 (30)	56 (27)	27 (29)	0.869
Right bundle branch block	19 (6)	23 (11)	22 (11)	9 (10)	0.203
Q-T interval (corrected)	443 (±45)	452 (±45)	455 (±45)	444 (±45)	0.014
Laboratory values					
Creatinine, mg/dL	1.38 (±0.43)	1.31 (±0.41)	1.38 (±0.37)	1.40 (±0.39)	0.192
Potassium, mEq/L	4.4 (±0.2)	4.4 (±0.3)	4.4 (±0.2)	4.4 (±0.3)	0.818
Sodium, mEq/L	139 (±3.4)	139 (±3.5)	139 (±3.5)	139 (±3.2)	0.250
Magnesium, mg/dL	1.8 (±0.2)	1.8 (±0.3)	1.8 (±0.2)	1.8 (±0.3)	0.279
Blood urea nitrogen, mg/dL	27 (±15.0)	29 (±17.0)	30 (±15.6)	32 (±20.8)	0.046
Glucose, mg/dL	137 (±77)	139 (±76)	124 (±67)	126 (±69)	0.099
Uric acid, mg/dL	7.84 (±2.25)	8.05 (±2.22)	8.55 (±2.37)	8.95 (±2.34)	<0.001
Total cholesterol, mg/dL	193 (±42)	191 (±57)	180 (±41)	179 (±42)	<0.002

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n (%) or mean (±SD)	RVEF ≥40% (n=308)	RVEF 30 to 39% (n=214)	RVEF 20 to 29% (n=206)	RVEF <20% (n=94)	P-value
Triglycerides, mg/dL	222 (±170)	226 (±208)	157 (±143)	145 (±104)	<0.001
Albumin, g/dL	4.1 (±0.38)	4.0 (±0.37)	4.0 (±0.38)	3.9 (±0.44)	0.004
Norepinephrine, pg/mL (n=1580)	510 (±232)	526 (±235)	620 (±335)	671 (±449)	<0.001
Hemoglobin, g/dL	13.6 (±1.6)	13.7 (±1.6)	14.0 (±1.7)	14.0 (±1.8)	0.048
White blood cell count, $10^3/\mu L$	7.5 (±1.98)	7.5 (±2.98)	7.2 (±1.91)	7.2 (±1.92)	0.240
Platelet count, $10^3/\mu L$	209 (±58)	211 (±62)	295 (±59)	203 (±44)	0.017

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Table 3

Associations of right ventricular ejection fraction (RVEF) and all-cause mortality

	Hazard ratio (95% confidence interval); P-value			
	RVEF ≥40% (n=308)	**RVEF 30 to 39% (n=214)**	**RVEF 20 to 29% (n=206)**	**RVEF <20% (n=94)**
Unadjusted mortality, n (%)	111 (36%)	86 (40%)	81 (39%)	53 (56%)
Step 1: Unadjusted	1.00 (Reference)	1.19 (0.90–1.57); P=0.220	1.13 (0.84–1.51) P=0.423	1.97 (1.43–2.73) P<0.001
Step 2: Step 1 + LVEF*	1.00 (Reference)	1.15 (0.87–1.52); P=0.323	1.06 (0.79–1.43) P=0.700	1.77 (1.26–2.51) P=0.001
Step 3: Step 2 + demographics**	1.00 (Reference)	1.18 (0.89–1.56); P=0.246	1.10 (0.81–1.48) P=0.555	1.80 (1.27–2.57) P=0.001
Step 4: Step 3 + medical history***	1.00 (Reference)	1.15 (0.86–1.52); P=0.348	1.08 (0.79–1.47) P=0.631	1.83 (1.27–2.65) P=0.001
Step 5: Step 4 + medications****	1.00 (Reference)	1.15 (0.87–1.53); P=0.336	1.08 (0.79–1.48) P=0.621	1.80 (1.12–2.62) P=0.002
Step 6: Step 5 + clinical findings*****	1.00 (Reference)	1.17 (0.88–1.57); P=0.284	0.93 (0.67–1.27) P=0.636	1.67 (1.14–2.46) P=0.008
Step 7: Step 6 + laboratory findings******	1.00 (Reference)	1.19 (0.88–1.60); P=0.261	1.00 (0.73–1.39) P=0.982	1.70 (1.14–2.53) P=0.009

* LVEF=left ventricular ejection fraction

** Demographics: age, sex, and race.

*** Medical history: duration of smoking, duration of heart failure, New York Heart Association class, coronary artery disease, angina pectoris, diabetes mellitus, hypertension, hyperlipidemia, peripheral vascular disease, atrial fibrillation, >70% coronary artery stenosis, positive stress perfusion test

**** Medications: bucindolol, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers, digitalis, diuretics, and anticoagulants

***** Clinical findings: body mass index, heart rate, systolic and diastolic blood pressure, S3 gallop, pulmonary râles, and x-ray findings of cardiothoracic ratio and pulmonary edema

****** Laboratory findings: creatinine, potassium, sodium, magnesium, blood urea nitrogen, glucose, uric acid, total cholesterol, albumin, hemoglobin, white blood cells, and platelets

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Table 4

Associations of right ventricular ejection fraction (RVEF) and cause-specific outcomes

	Events, n (%)	Unadjusted hazard ratio (95% confidence interval); P-value	Adjusted hazard ratio* (95% confidence interval); P-value
Cardiovascular mortality			
RVEF ≥40%	90 (29%)	1.00 (Reference)	1.00 (Reference)
RVEF 30 to 39%	61 (29%)	1.05 (0.76–1.44); P=0.789	1.00 (0.71–1.40); P=0.987
RVEF 20 to 29%	64 (31%)	1.11 (0.80–1.53); P=0.544	0.97 (0.68–1.39); P=0.867
RVEF <20%	46 (49%)	2.09 (1.47–2.97); P<0.0001	1.79 (1.17–2.76); P=0.008
Heart failure mortality			
RVEF ≥40%	37 (12%)	1.00 (Reference)	1.00 (Reference)
RVEF 30 to 39%	25 (12%)	1.01 (0.61–1.66); P=0.971	1.06 (0.61–1.85); P=0.836
RVEF 20 to 29%	29 (14%)	1.12 (0.68–1.85); P=0.651	0.93 (0.53–1.61); P=0.783
RVEF <20%	21 (22%)	2.27 (1.34–3.85); P=0.002	1.97 (1.02–3.83); P=0.045
Sudden cardiac death			
RVEF ≥40%	41 (13%)	1.00 (Reference)	1.00 (Reference)
RVEF 30 to 39%	33 (15%)	1.26 (0.80–1.98); P=0.327	1.15 (0.70–1.87); P=0.586
RVEF 20 to 29%	28 (14%)	1.10 (0.67–1.79); P=0.711	0.95 (0.55–1.65); P=0.860
RVEF <20%	23 (25%)	2.26 (1.36–3.75); P=0.002	1.61 (0.86–3.00); P=0.135
All-cause hospitalization			
RVEF ≥40%	205 (67%)	1.00 (Reference)	1.00 (Reference)
RVEF 30 to 39%	148 (69%)	1.09 (0.88–1.34); P=0.443	1.07 (0.86–1.34); P=0.543
RVEF 20 to 29%	135 (66%)	1.02 (0.82–1.28); P=0.838	0.92 (0.72–1.17); P=0.496
RVEF <20%	68 (72%)	1.44 (1.09–1.89); P=0.009	1.19 (0.86–1.63); P=0.292
Heart failure hospitalization			
RVEF ≥40%	122 (40%)	1.00 (Reference)	1.00 (Reference)
RVEF 30 to 39%	86 (40%)	1.11 (0.85–1.46); P=0.451	1.06 (0.79–1.42); P=0.706
RVEF 20 to 29%	87 (42%)	1.20 (0.91–1.58); P=0.209	0.92 (0.67–1.26); P=0.590
RVEF <20%	48 (51%)	1.82 (1.30–2.54); P<0.001	1.26 (0.84–1.87); P=0.260

*Multivariable model based on model 7 from Table 3.