The Importance of Heart Rate Recovery in Patients With Heart Failure or Left Ventricular Systolic Dysfunction

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ABSTRACT

Background: The ability to better predict outcome with exercise testing in patients with heart failure (HF) and left ventricular systolic dysfunction (LVSD) may prove extremely valuable in determining which patients are at increased risk. This study evaluated the ability of heart rate recovery (HRR) to predict outcome in patients with HF and validate previous findings in LVSD.

Methods and Results: HRR was measured at 1-, 2-, 3-, and 5-minute time points after treadmill testing in 2,193 males being evaluated for chest pain at the Palo Alto and Long Beach VA Hospitals. Left ventricular ejection fraction (LVEF) was calculated using biplane ventriculography and patients were considered to have LVSD if they had an LVEF $<50\%$. Angiographic and clinical data was available for all patients. Of the 2,193 patients, 314 patients had LVSD and 109 had a history of HF. Both HF patients and patients with LVSD with a normal HRR at 2 minutes had improved survival compared with patients that had an abnormal HRR at 2 minutes when adjusted for age and β-blocker use (HF adjusted odds ratio 0.25, 95% CI 0.10–0.66, $P < .006$; LVSD alone adjusted odds ratio 0.25, 95% CI 0.13–0.47, $P < .0001$). Stepwise proportional hazard regression analysis revealed that only 2-minute HRR, age, LVEF, and chronic obstructive pulmonary disorder were significant predictors of mortality in patients with LVSD and only HRR at 2 minutes and LV hypertrophy were significant predictors of mortality in patients with HF.

Conclusion: HRR is a significant predictor of mortality in patients with HF and patients with LVSD and may be useful in better determining prognosis.

Key Words: Heart rate recovery, heart failure, left ventricular dysfunction, mortality.

Heart failure (HF) and left ventricular systolic dysfunction (LVSD) are major causes of morbidity and mortality in the United States and the ability to provide accurate prognostic information to both patients and physicians may greatly improve patient care. Heart rate recovery (HRR) after exercise treadmill testing has recently emerged as a powerful predictor of mortality in individuals being evaluated for chest pain[1–3] and in healthy individuals.[4] Although the importance of HRR in predicting mortality has been investigated in patients with LVSD,[5] the importance of HRR in predicting mortality in patients with HF has not been investigated. Although previous studies revealed that HRR was generally decreased in patients with HF[6] and that long-term β blocker (BB) therapy did not improve HRR in patients with HF,[7] mortality in patients with HF has not been evaluated in regards to HRR. The goal of this study was to evaluate the importance of HRR in predicting mortality in patients with HF and to validate the importance of HRR in predicting mortality in patients with LVSD.

Methods

A total of 8000 male patients underwent treadmill testing at 2 Veterans Affairs Medical Centers between 1987 and 1998. Of these, 3454 were evaluated for chest pain with coronary angiography and left ventriculography within 3 months of treadmill testing. Patients with previous cardiac surgery or angiography, valvular heart disease, left bundle branch block, paced rhythms, atrial fibrillation, or Wolff-Parkinson-White on their resting

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electrocardiogram were excluded from the study. This left 2193 patients that qualified for our study. Patients underwent symptom-limited treadmill testing using the US Air Force School of Aerospace Medicine or an individualized ramp treadmill protocol. The physiologic distinction of these protocols is that the patient is subjected to small, frequent increments in workload rather than abrupt increases every 3 minutes. Information gathered from a questionnaire enabled maximal exercise to be reached at approximately 10 minutes. Individuals reached their target HR if their maximum HR on treadmill testing was 85% or higher of their estimated physiologic maximum HR. Patients did not perform a cool-down walk but were placed in a supine position immediately after exercise. Reasons for terminating exercise testing were angina, 2 mm or greater of ST depression, a drop in systolic blood pressure, or ominous cardiac arrhythmias. Abnormal ST-segment depression was defined as 1 mm or more of horizontal or downsloping ST-segment depression. Blood pressure was taken manually and metabolic equivalents were estimated from treadmill speed and grade. No test was classified as indeterminate,[15] medications were not withheld, and maximal HR target was not used as an end point. The exercise tests were performed, analyzed and reported with a standard protocol using a computerized database. Heart rate was measured supine, standing, during each minute of exercise, at maximum exercise and in recovery at 1, 2, 3 and 5 minutes. Heart rate recovery was defined as (maximum HR – HR at specified time period during recovery) and represented the drop in HR during that time interval.

Coronary artery narrowing was visually estimated and expressed as percent lumen diameter stenosis. Patients with a 50% diameter narrowing of the left main, left anterior descending, left circumflex, or right coronary arteries or their major branches were considered to have significant angiographic CAD. Severe CAD was defined as 3-vessel disease, 2-vessel disease if the proximal left anterior descending was involved, or left main disease. Left ventricular ejection fraction (LVEF) was estimated from biplane left ventricular angiograms and patients with a LVEF ≤50% were considered to have LVSD. Patients were considered to have HF if they had previous symptoms of HF (pulmonary edema or an S3 gallop) and were New York Heart Association Class I or greater. Decisions for cardiac catheterization were consistent with clinical practice. The social security death index was used to match all of the patients' names to their social security numbers. The index was updated weekly, and the most current records were used. Death status was determined as of October 2004 and was 100% complete. No other information regarding hospitalizations, cardiac interventions or cause of death during the follow-up was known.

Student t-test analysis and analysis of variance for continuous variables and chi-squared analysis for categorical variables was performed to compare patient subgroups. Results are shown as mean ± standard deviation. Receiver operating characteristic curves were calculated to determine which cut-points should be used for HRR. Survival analysis was performed using Kaplan-Meier curves to compare variables and cut-points in different patient subgroups. Unadjusted and adjusted odds ratios were calculated to determine the strength of heart rate recovery cut-points in predicting mortality in patient subgroups. Stepwise Multivariate proportional hazard regression analysis was performed to determine which variables significantly predict mortality and how they rank in comparison with other variables. Number Crunching Statistical System 2001 (Salt Lake City, UT) was used for all statistical analyses and P values less than .05 were considered significant.

Results

Of the 2193 patients in our study, 109 patients (5%) composed the HF subgroup. Of the 1916 patients that had LVEF data, 314 patients (16.4%) had a LVEF ≤50% and composed our LV dysfunction subgroup. Twenty-five of the 109 patients (23%) with HF and 126 of the 314 patients (40%) with LVSD were on BB therapy at the time of treadmill testing. Of the 109 patients with HF, 46 had a LVEF ≤50%, 49 of had an LVEF >50%, and 14 patients did not have angiographic data. Table 1 provides a comparison of clinical, angiographic, and treadmill data of 49 patients that had HF alone, the 268 that LVSD alone, the 46 that had both HF and LVSD, and the 1551 without HF or LVSD. Among clinical variables, significant differences between the groups exist in age, diabetes, prior myocardial infarction, digitalis use, BB use, death, and left ventricular hypertrophy. Among angiographic variables, significant differences between the groups exist in significant CAD, severe CAD, 3-vessel disease, and obviously LVEF. Finally, significant differences between the groups exist in 2-, 3-, and 5-minute HRR, METs, and other treadmill variables. Additionally, HRR at 3 and 5 minutes had a strong correlation with HR reserve ($r^2 = 0.57$, $P < .0001$ and $r^2 = 0.65$, $P < .0001$, respectively) and though included in the different analyses, HRR at 3 and 5 minutes did not perform as well as HRR at 2 minutes.

Because the number of patients with HF was small, we only assessed the role of BB therapy in the group of 109 patients with HF while we assessed the role of BB therapy in the 268 patients with LVSD alone. Among patients without HF or LVSD, patients taking a BB (n = 499) had more hypertension (60% versus 48%, $P < .0001$), CAD (76% versus 66%, $P < .0001$), hypercholesterolemia (48% versus 39%, $P < .002$), and family history of CAD (46% versus 39%, $P < .01$), but a decreased HRR at 2 minutes (30 versus 35, $P < .0001$), 3 minutes (38 versus 44, $P < .0001$), and 5 minutes (39 versus 47, $P < .0001$), a decreased maximum HR (115 beats/min versus 133 beats/min, $P < .0001$), resting HR (69 beats/min versus 78 beats/min, $P < .0001$), maximum systolic blood pressure (159 mm Hg versus 170 mm Hg, $P < .0001$), resting systolic blood pressure (124 mm Hg vs 128 mm Hg, $P < 0.004$), achievement of target HR (16% versus 44%, $P < .0001$), and less were taking digitalis (1% versus 4%, $P < .02$) compared with patients not taking a BB (n = 1052). Among the 268 patients with LVSD alone, patients taking a BB (n = 117) had decreased age (58 versus 61, $P < 0.005$), target HR achievement (12% versus 45%, $P < .0001$), maximum HR (114 versus 131, $P < .0001$), resting HR (72 versus 81, $P < .0001$), maximum SBP (147 versus 159, $P < .0004$), resting SBP (117 versus 122, $P < .03$), and HRR at 2 minutes (28 versus 33, $P < .0006$), 3 minutes (34 versus 42, $P < .0001$), and 5 minutes (36 versus 45, $P < .0001$) compared with patients not taking a BB (n = 151). Among patients with HF, patients taking a BB had significantly decreased maximum

Table 1. Comparison of Clinical Variables, Treadmill Data, and Angiographic Findings for Patients With HF Alone, LVSD Alone, Both HF and LVSD, and Neither

Clinical Variables	Normal (n = 1551)	LVSD Alone (n = 268)	CHF Alone (n = 49)	CHF + LVSD (n = 46)	*P* Value
Age (years)	59 ± 10	60 ± 10	64 ± 9	63 ± 11	<0.0007
BMI (kg/m^2)	28 ± 10	27 ± 4	29 ± 5	27 ± 4	0.28
Hypertension	52%	51%	59%	65%	0.23
Hypercholesterolemia	42%	36%	37%	28%	0.07
Diabetes	15%	16%	22%	37%	<0.0003
Chronic obstructive pulmonary disease	6%	6%	6%	11%	0.61
History of smoking	66%	72%	59%	57%	0.08
Family history of CAD	42%	45%	45%	24%	0.07
Prior MI	36%	72%	53%	76%	<0.0001
Prior stroke	4%	4%	2%	11%	0.10
Digitalis use	3%	6%	18%	33%	<0.0001
β-blocker use	32%	44%	24%	20%	<0.0003
Death	25%	35%	45%	54%	<0.0001
LV hypertrophy	2%	6%	8%	13%	<0.0001
Exercise Treadmill Data					
Standing HR (bpm)	75 ± 15	77 ± 15	76 ± 13	82 ± 15	<0.003
Maximum HR (bpm)	127 ± 23	123 ± 21	125 ± 20	127 ± 20	0.11
HR reserve	52 ± 21	47 ± 19	49 ± 21	44 ± 18	<0.0001
Standing systolic BP	127 ± 20	120 ± 19	125 ± 22	120 ± 21	<0.0001
Maximum systolic BP	166 ± 29	154 ± 29	167 ± 31	150 ± 32	<0.0001
METs	7.2 ± 3.1	6.3 ± 2.7	5.8 ± 2.4	5.3 ± 2.1	<0.0001
ST deviation ≥ 1 mm	38%	46%	37%	39%	0.11
Target HR achievement	35%	31%	41%	35%	0.39
1-minute HR recovery	12.7 ± 7.9	12.4 ± 7.3	11.5 ± 6.9	10.5 ± 8.0	0.18
2-minute HR recovery	34 ± 13	31 ± 13	32 ± 13	27 ± 16	<0.0005
3-minute HR recovery	42 ± 14	39 ± 15	41 ± 14	36 ± 15	<0.0001
5-minute HR recovery	45 ± 15	41 ± 14	45 ± 16	39 ± 15	<0.0007
Angiographic Data					
Ejection fraction	66 ± 9%	41 ± 8%	64 ± 8%	34 ± 9%	<0.0001
Significant CAD	69%	88%	65%	76%	<0.0001
Severe CAD	37%	63%	41%	59%	<0.0001
1-vessel CAD	25%	24%	18%	22%	0.69
2-vessel CAD	23%	26%	29%	22%	0.59
3-vessel CAD	20%	38%	18%	33%	<0.0001

HF, heart failure; LVSD, left ventricular systolic dysfunction; CHF, congestive heart failure, BMI, body mass index; CAD, coronary artery disease; MI, myocardial infarction; HR, heart rate; bpm, beats per minute; BP, blood pressure.

HR (113 versus 129, $P < .0002$), resting HR (72 versus 81, $P < .006$), and target HR achievement (20% versus 44%, $P < .03$) compared with patients not taking a BB.

Patients with data on LVEF were separated into different groups based on their LV function and whether or not they used a BB and the mean HRR at 1, 2, and 5 minutes was compared between the different groups using analysis of variance. As seen in Table 2, patients with reduced LV function had significantly reduced HRR at 2 and 5 minutes compared with patients with normal LV function regardless of the BB status. Additionally, patients taking a BB had significantly reduced HRR at 2 and 5 minutes regardless of their LV function ($P < .001$).

Cutpoint analysis was performed using receiver operating characteristic curves for 1, 2, and 5 minutes HRR on patient with HF, LVSD alone, or neither and separated depending on BB use. As seen in Table 3, HRR at 1 minute was considered abnormal if less than 9 beats for HF and

Table 2. Comparison of HR recovery After 1 Minute, 2 Minutes, and 5 Minutes After Exercise Treadmill Testing in Patients Based on Their EF using ANOVA

Variables	BB Use	EF ≤40% (No BB = 86 BB = 46)	EF 41-50% (No BB = 102 BB = 80)	EF ≥51% (No BB = 1089 BB = 512)	*P* Value
HRR at 1 minute (beats)	No BB	11.1 ± 6	12.7 ± 7.3	12.6 ± 8.1	.20
	BB	12.7 ± 8.4	12.1 ± 8.4	12.9 ± 7.5	.72
HRR at 2 minutes (beats)	No BB	29.9 ± 13.8	34.8 ± 13.7	34.9 ± 12.9	<.003
	BB	26.8 ± 12.3	28.1 ± 11.5	30.5 ± 12	<.05
HRR at 5 minutes (beats)	No BB	42 ± 14.4	46 ± 14.5	47.1 ± 15	<.009
	BB	35.4 ± 13.4	36 ± 12.1	39.2 ± 14.2	<.05

HR, heart rate; EF, ejection fraction; ANOVA, analysis of variance; BB, β blocker; HRR, heart rate recovery.

Table 3. Cutpoint Selection Using Receiver Operating Characteristic Curves for Abnormal HR Recovery at 1, 2, and 5 Minutes After Exercise in Patients With LVSD, HF, or neither

1-Minute HRR	Cutpoint	Predictive Accuracy	Sensitivity	Specificity
LVSD alone + no BB (151)	Abnormal <9	61%	35%	78%
LVSD alone + BB (117)	Abnormal <9	62%	44%	72%
HF + no BB (84)	Abnormal <9	69%	65%	73%
HF + BB (25)	Abnormal <9	72%	64%	79%
Neither + no BB (1052)	Abnormal <10	63%	54%	66%
Neither + BB (499)	Abnormal <10	64%	52%	68%
2 Minute HRR				
LVSD alone + no BB	Abnormal <27	69%	48%	82%
LVSD alone + BB	Abnormal <23	70%	56%	78%
HF + no BB	Abnormal <24	64%	51%	78%
HF + BB	Abnormal <23	64%	45%	79%
Neither + no BB	Abnormal <24	71%	31%	86%
Neither + BB	Abnormal <17	77%	25%	94%
5 Minute HRR				
LVSD alone + no BB	Abnormal <33	65%	30%	88%
LVSD alone + BB	Abnormal <30	69%	51%	79%
HF + no BB	Abnormal <37	65%	54%	78%
HF + BB	Abnormal <36	60%	55%	64%
Neither + no BB	Abnormal <32	72%	21%	90%
Neither + BB	Abnormal <32	67%	43%	75%

See Tables 1 and 2 for definitions.

LVSD alone regardless of BB use and abnormal if less than 10 regardless of BB use in patients with neither LVSD nor HF. The cutpoint was generally lower for HRR at 2 and 5 minutes for patients taking a BB compared with those not taking a BB.

Stepwise multivariate Cox proportional hazard regression analysis was performed to determine which clinical, angiographic, and exercise treadmill variables present in Table 1 predicted mortality in patient subsets. As seen in Table 4, HRR at 2 minutes and the presence of LV hypertrophy were the only significant predictors of mortality in patients with HF that were not taking a BB. When performing this analysis in patients with LVSD alone, only HRR at 2 minutes, age, and the presence of chronic obstructive pulmonary disease were significant predictors of mortality in patients not taking a BB, whereas HRR at 2 minutes and EF were significant predictors in patients taking a BB. Additionally, HRR at 2 minutes is a strong predictor of mortality in patients without LVSD and HF regardless of BB use and is the strongest predictor of mortality if patients are not separated based on BB status ($P < .0001$). We also looked at the 132 patients in our study with an EF ≤ 40% and found that HRR at 2 minutes (Z-score 3.07, $P < .003$) and age (Z-score 2.56, $P < .01$) were the only significant predictors of mortality.

Using the cutpoints established for HRR at 1 and 2 minutes, Kaplan-Meier survival curves were calculated for patients with HF depending on whether or not they used a BB. As seen in Fig. 1, patients with HF had significantly decreased survival if they had a HRR at 1 minute <9 regardless of whether or not they were taking a BB. The 8-year survival in patients on a BB was 30% for patients with an HRR at 1 minute <9 compared with 80% for patients with a HRR at 1 minute ≥9 ($P < .05$) and remained significant. For patients not taking a BB, 3, 5, and 10-year survival was significantly decreased if they had an abnormal HRR at 1 minute compared with a normal HRR at 1 minute (74% versus 93%, $P < .01$; 56% versus 89%, $P < .001$; 38% versus 73%, $P < .001$). Additionally, patients with HF not taking a BB had significantly decreased survival if they had a HRR at 2 minutes <24 compared with patients that had a HRR at 2 minutes ≥24 (3-year survival: 68% versus 96%, $P < .001$, 5-year survival: 55% versus 87%, $P < .001$, 10-year survival: 34% versus 69%, $P < .001$). We did not include patients taking a BB in this analysis from the low number but a trend for decreased survival existed if they had a HRR at 2 minutes <23 ($P = .09$). Age-adjusted odds ratios were calculated for patients with HF and demonstrated significant improvement in survival for patients with normal HRR at 1 minute compared with abnormal HRR at 1 minute (odds ratio 0.26, 95% CI 0.08–0.81, $P < .02$). Additionally, there was a significant improvement in survival with normal HRR at 2 minutes compared with an abnormal HRR at 2 minutes when adjusting for age and BB use (odds ratio 0.25, 95% CI 0.10–0.66, $P < .006$).

Figure 2 demonstrates that patients with LVSD alone not taking a BB had significantly decreased survival if they had a HRR at 2 minutes <27 compared with patients that had a HRR at 2 minutes ≥27 (3-year survival: 73% versus 95%, $P < .001$, 5-year survival: 67% versus 92%, $P < .001$, 10-year survival: 37% versus 78%, $P < .001$). Patients with LVSD alone taking a BB had significantly decreased survival if they had a HRR at 2 minutes <23 compared with patients that had a HRR at 2 minutes ≥23 (3-year survival: 70% versus 93%, $P < .01$, 5-year survival: 63% versus 89%, $P < .01$, 10-year survival: 27% versus 74%, $P < .001$). Age-adjusted odds ratios were calculated for patients with LVSD alone demonstrated significant improvement in survival for patients with

Table 4. Stepwise Multivariate Proportional Hazard Regression Analysis

A. Which variables present in table 1 predict mortality in patients with HF depending on BB use

	HF + No BB (n = 84)		HF + BB (n = 25)	
Variable	Z-score	*P* Value	Z-score	*P* Value
2-minute HR recovery	3.66	<.0003		
LVH	2.59	<.01		

B. Variables that predict mortality in patients with LVSD alone depending on BB use

	LVSD alone + No BB (n = 151)		LVSD alone + BB (n = 117)	
Variable	Z-score	*P* Value	Z-score	*P* Value
Ejection fraction			3.76	<.0002
2-minute HR recovery	4.33	<.0001	2.52	<.02
Age	2.68	<.008		
COPD	2.41	<.02		

C. Variables that predict mortality in patients without LVSD or HF depending on BB use

	Normal + No BB (n = 1052)		Normal + BB (n = 499)	
Variable	Z-score	*P* Value	Z-score	*P* Value
METs	6.68	<.0001		
Stroke	4.86	<.0001	2.71	<.007
2-minute HR recovery	4.57	<.0001	3.78	<.0002
Age	4.05	<.0001	5.28	<.0001
COPD	3.15	<.002		
Number of vessels diseased	2.27	<.03		
LVH			2.77	<.006
Prior MI			2.27	<.03

See previous tables for definitions.

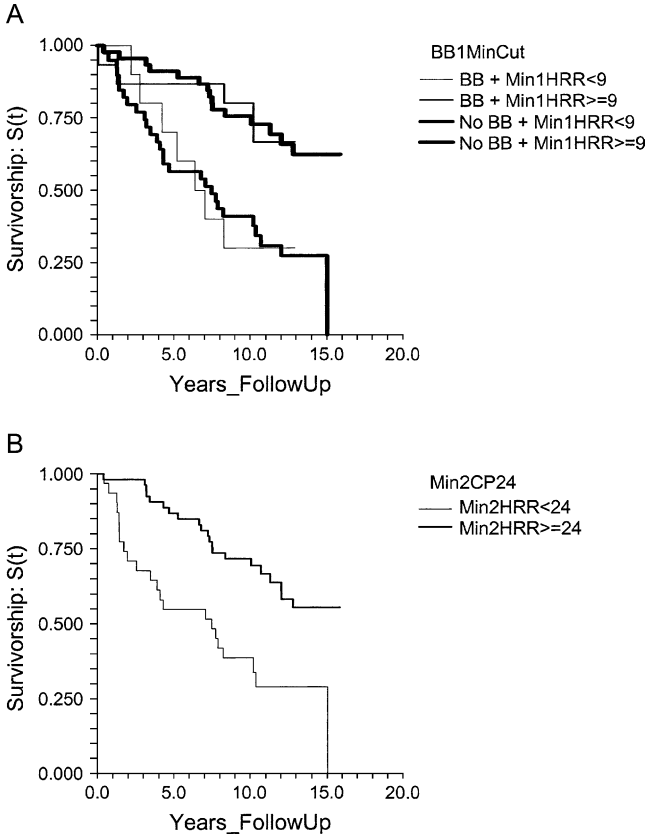

Fig. 1. (A) Kaplan-Meier survival analysis on patients with heart failure (HF) either taking or not taking a BB comparing survival between abnormal and normal heart rate recovery (HRR) at 1 minute. Patients with abnormal HRR at 1 minute had decreased survival regardless of BB use. (B) Kaplan-Meier survival analysis on patients with HF not taking a BB demonstrates better survival for normal HRR compared with abnormal HRR at 2 minutes (Min2HRR <24).

normal HRR at 2 minutes compared with abnormal HRR at 2 minutes (BB group odds ratio 0.31, 95% CI 0.11–0.89, $P < .03$; no BB group odds ratio 0.30, 95% CI 0.12–0.72, $P < .008$). Interestingly, Kaplan-Meier survival analysis was performed on patients with LVSD alone did not have improved survival with a normal HRR at 1 minute compared with an abnormal HRR at 1 minute (<9), regardless of whether they were taking a BB ($P = .12$) or not taking a BB ($P = .10$).

Kaplan-Meier survival analysis was performed for patients without LVSD and HF and revealed that patients with abnormal HRR at 2 minutes had increased mortality compared with patients that had a normal HRR at 2 minutes regardless of BB use. As seen in Fig. 3, patients without LVSD and HF not taking a BB had a decreased 3-, 5-, and 10-year survival if they had a HRR at 2 minutes <24 (88% versus 95%, $P < .005$; 81% versus 92%, $P < .001$; 60% versus 82%, $P < .001$, respectively). Patients without LVSD and HF taking a BB had a decreased 3-, 5-, and 10-year survival if they had a HRR at 2 minutes <17 (87% versus 97%, $P < .03$; 80% versus 92%, $P < .01$; 47% versus 82%, $P < .001$ respectively). Age-adjusted odds ratios were calculated for patients without LVSD and HF and demonstrated significant improvement in survival for patients with normal HRR at 2 minutes compared with abnormal HRR at 2 minutes (BB group odds ratio 0.25, 95% CI 0.14–0.45, $P < .0001$; No BB group odds ratio 0.47, 95% CI 0.33–0.67, $P < .0001$).

Discussion

This study further supports the value of HRR as a prognostic marker and demonstrates that patients with HF or LVSD have increased all-cause mortality if they have a decreased HRR. Additionally, this study supports the value of HRR regardless of whether or not the patient is taking a BB. However, the cutpoints to determine whether

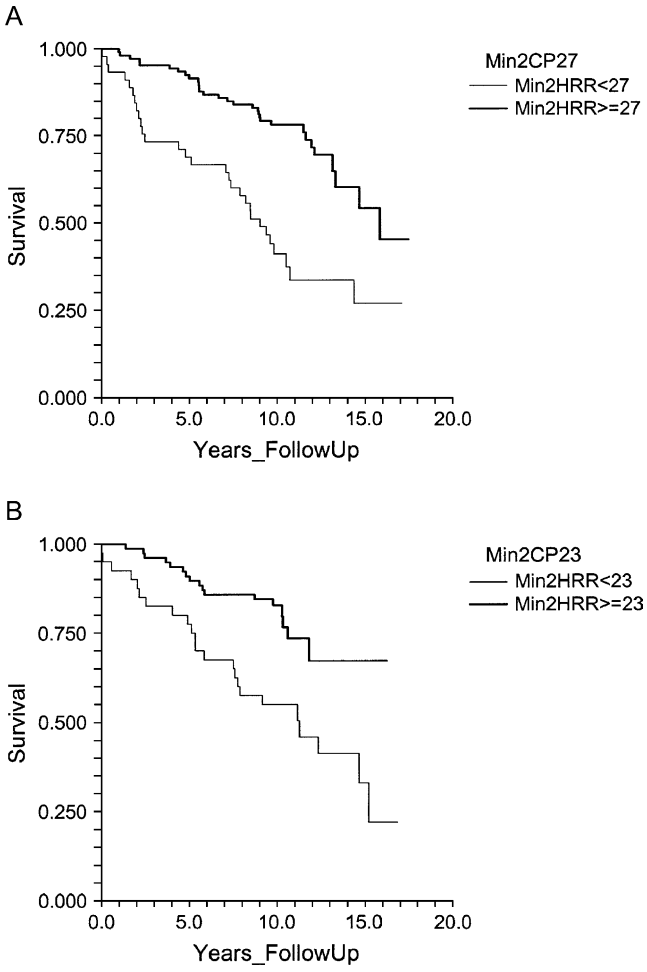

Fig. 2. (A) Kaplan-Meier survival analysis of patients with left ventricular systolic dysfunction (LVSD) alone not taking a BB demonstrates better survival for normal heart rate recovery (HRR) compared with abnormal HRR at 2 minutes (Min2HRR <27) and (B) analysis of patients with LVSD taking a BB demonstrated better survival for normal HRR compared with abnormal HRR at 2 minutes (Min2HRR <23).

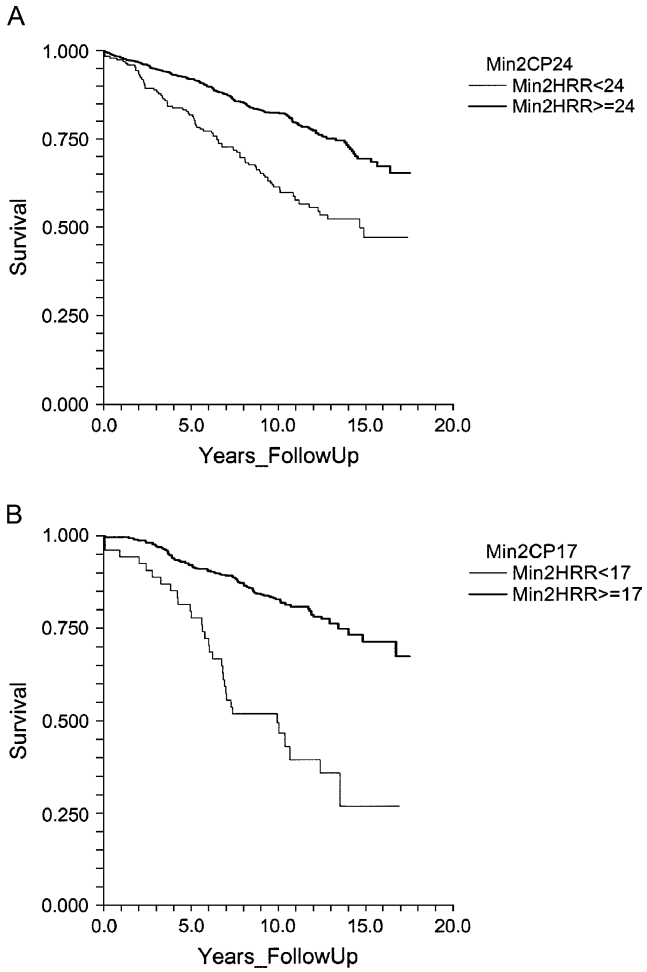

Fig. 3. (A) Kaplan-Meier survival analysis of patients without left ventricular systolic dysfunction (LVSD) and heart failure (HF) not taking a BB demonstrated better survival for normal HRR compared with abnormal heart rate recovery (HRR) at 2 minutes (Min2HRR <24) and (B) analysis of patients without LVSD and HF taking a BB demonstrates better survival for normal HRR compared with abnormal HRR at 2 minutes (Min2HRR <17).

HRR is abnormal are different for patients taking a BB and tend to be lower except for HRR at 1 minute. Although HRR was previously shown to be important in predicting survival in patients with LVSD,[5] prior studies did not evaluate patients with symptoms of HF.[1,2,4,5] This study is therefore the first to investigate the importance of HRR in predicting mortality in patients with HF and demonstrates that HRR at 2 minutes is a better predictor of mortality in patients with HF than age and METs. Therefore, HRR should be evaluated along with METs, age, maximum HR, and other variables to determine which patients with HF and severe LVSD are in greatest need of heart transplantation.[8]

Several methodological differences can be found between the study by Watanabe and colleagues[5] and our current study. The first difference is that EF was estimated in our study from biplane ventriculography, which is considered a more accurate measure of LV function than the used stress echocardiography to estimate EF as performed by Watanabe and colleagues. Another difference is that all patients in our study had angiographic data available to provide information regarding the presence of coronary artery disease, whereas the other study did not. The final major difference between these studies is that we elected to include patients with a history of HF, whereas patients with HF were excluded from the patient population used by Watanabe and colleagues.

HF and LVSD continue to pose a challenge to cardiologists and mortality for these patients remains high. This study shows that HRR is a significant predictor of mortality in patients, especially those with HF or LVSD. Treadmill testing of patients with LVSD or heart failure may provide valuable information regarding their risk of mortality. Patients with HF or LVSD alone not on BB therapy that had an abnormal HRR at 2 minutes had significantly decreased survival ($P < .001$). This study also

demonstrated that HRR at 2 minutes was the strongest predictor of mortality for both patients with HF or LVSD alone that were not taking a BB ($P < .0003$). Therefore, HRR data may enable cardiologist to better identify those patients with HF or LVSD that are at an increased risk of death. A recent study also demonstrated that exercise training improves HRR.[9,10] This raises the question of whether improving HRR by exercise training or cardiac rehabilitation can lead to improvements in survival. This question may be particularly important for patients with HF or LVSD.

The limitations of this study are its retrospective design, an entirely male Veterans Administration population, a different ramp protocol from previous studies, a relatively small sample size for patients with HF, the use of all-cause mortality instead of defining the cause of death, and we did not investigate the influence of HR reserve and its influence on chronotropic incompetence. Another limitation of this study was the lack of New York Heart Classification functional class data for heart failure. We were also unaware of whether the patients underwent revascularization or medical therapy during follow-up. Our inability to censor how patients were managed during follow-up may skew the prognostic data. As would be expected, our study was also limited by workup bias.

In conclusion, HRR is a significant predictor of mortality and may provide valuable prognostic information for patients with HF or LVSD. The ability of HRR to predict mortality may also aid in determining which patients with HF and LVSD will require heart transplantation.

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