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ORIGINAL RESEARCH

Prognostic Value of Exercise Echocardiography in Patients With Left Bundle Branch Block

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OBJECTIVES Our aim was to evaluate the role of exercise echocardiography for predicting outcome in a cohort of patients with left bundle branch block (LBBB).

BACKGROUND Although the prognostic value of exercise echocardiography has been well established in several subgroups of patients, it has not been specifically assessed in patients with LBBB.

METHODS Of the 8,050 patients who underwent treadmill exercise echocardiography, 618 demonstrated complete LBBB. Nine patients were lost to follow-up and 609 patients were included in this study. Wall motion score index (WMSI) was evaluated at rest and at peak exercise, and the difference (ΔWMSI) was calculated. Ischemia was defined as the development of new or worsening wall motion abnormalities with exercise. End points were all-cause mortality and major cardiac events (including cardiac death, myocardial infarction, or cardiac transplantation). Mean follow-up was 4.6 $\pm$ 3.4 years.

RESULTS Mean age was 66 $\pm$ 10 years, and 331 patients (54%) were men. A total of 177 patients (29%) developed ischemia with exercise. During follow-up, 124 deaths occurred, and 74 patients had a major cardiac event before any revascularization procedure. Patients with ischemia had a greater 5-year mortality rate (24.6% vs. 12.6%, $p < 0.001$) and 5-year major cardiac events rate (18.1% vs. 9.7%, $p = 0.003$). In multivariate analysis, ΔWMSI remained an independent predictor of mortality (hazard ratio: 2.42, 95% confidence interval: 1.21 to 4.82, $p = 0.012$) and major cardiac events (hazard ratio: 3.38, 95% confidence interval: 1.30 to 8.82, $p = 0.013$). Exercise echocardiographic results also provided incremental value over clinical, resting echocardiographic, and treadmill exercise data for the prediction of mortality ($p = 0.014$) and major cardiac events ($p = 0.017$).

CONCLUSIONS Exercise echocardiography provides significant prognostic information for predicting outcome in patients with LBBB. As compared to patients with normal exercise echocardiograms, patients with abnormal results are at increased risk of mortality and major cardiac events. (J Am Coll Cardiol Img 2009;2:251–9) © 2009 by the American College of Cardiology Foundation

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Left bundle branch block (LBBB) has been found to be associated to a greater risk of mortality and major cardiac events, particularly in patients with coronary artery disease (CAD) (1–5). Noninvasive stress testing may provide useful prognostic information. Patients with LBBB and suspected CAD traditionally have been referred for nuclear imaging; however, its specificity in patients with LBBB is poor as a result of a high proportion of false-positive results, although it improves significantly when vasodilators are used (6,7). Pharmacological stress echocardiography has good sensitivity and specificity for the detection of CAD in patients with LBBB (6) and provides incremental prognostic information in patients without previous myocardial infarction (8). Exercise echocardiography (EE) has similar diagnostic accuracy in patients with LBBB (9) and is preferable to pharmacological stress echocardiography in patients who are able to exercise (10). The prognostic value of EE has been well established in several subgroups of patients (11–18); however, it has not been specifically evaluated in patients with LBBB so far. The aim of this study was to assess the value of EE for predicting long-term outcome in patients with LBBB.

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

EE = exercise echocardiography

LBBB = left bundle branch block

MACE = major adverse cardiac events

WMSI = wall motion score index

METHODS

Patients. Between March 1, 1995, and November 30, 2007, a total of 8,050 patients underwent 9,010 treadmill EE evaluations at our institution. Of them, we identified 618 patients with complete LBBB at the time of EE. In case of repeated studies, the first one was selected. Nine patients (1.5%) were lost to follow-up and were excluded. Thus, 609 patients were finally included in the study. Demographic and clinical data, as well as the results of stress testing, were entered in our prospective database at the time of the tests. All patients gave informed consent before testing.

Left bundle branch block was defined as a QRS duration ≥120 ms, with predominantly upright complexes and slurred R-waves in leads I, V_5, and V_6, and QS or rS pattern in V_1. Whenever possible, beta-blockers were discontinued at least 48 h before testing; however, 28 patients (4.6%) were under the influence of beta-blockers at the time of their tests. In addition, 178 patients (29.2%) were on nitrates and 98 patients (16.1%) were on calcium channel blockers.

Exercise echocardiography. Heart rate, blood pressure, and a 12-lead electrocardiogram (ECG) were obtained at baseline and at each stage of the exercise protocol. Patients were encouraged to perform a treadmill exercise test until they reached an end point. Exercise end points included physical exhaustion, severe angina, significant arrhythmia, severe hypertension (systolic blood pressure >240 mm Hg or diastolic blood pressure >110 mm Hg), or severe hypotensive response (a decrease of >20 mm Hg in systolic blood pressure from baseline). Exercise protocols included the standard Bruce protocol (88.2%), modified Bruce (4.9%), modified Bruce for sportive people (4.6%) (19), and the Naughton protocol (2.3%).

Two-dimensional echocardiography was performed at baseline, at peak exercise (20), and immediately after exercise. Peak imaging was performed with the patient still exercising, when signs of exhaustion were present or an end point was achieved. The patient was asked to walk quickly rather than run, to decrease body and respiratory movements. The transducer was firmly positioned on the cardiac apex to obtain the apical views by applying slight pressure to the patient's back with the left hand, so maintaining the patient between the transducer and the left hand, to avoid movement. Finally, the transducer was positioned in the parasternal region to obtain the parasternal views. Peak and post-exercise images were obtained with continuous imaging capture. Image acquisition was performed online and stored on an optical disk. The images corresponding to each view having the best quality at peak and post-exercise imaging were chosen for comparison with rest images.

Echocardiographic analysis. Echocardiographic 2-dimensional analysis was performed on a digital quadscreen display system. Regional wall motion was evaluated with a 16-segment model of the left ventricle (21). Each segment was graded on a 4-point scale, with normal wall motion scoring = 1, hypokinetic = 2, akinetic = 3, and dyskinetic = 4. Wall motion score index (WMSI) was calculated at rest and at exercise as the sum of the scores divided by the number of segments. The change in WMSI from rest to peak exercise (ΔWMSI) also was calculated, and all segments were available for analysis. Resting and exercise left ventricular ejection fraction were estimated visually (22).

Ischemia was defined as the development of new or worsening wall motion abnormalities with exercise (ΔWMSI >0). An abnormal EE was defined as the presence of wall motion abnormalities at rest or the development of an ischemic response during exercise (10). Isolated septal asynchronous motion was not considered abnormal (23); instead, worsening septal wall thickening was the criterion for ischemia.

Follow-up and end-points. Follow-up was obtained by review of hospital databases, medical records, and death certificates, as well as by telephone interviews when necessary. The end points were major adverse cardiac events (MACE) and all-cause mortality; MACE included cardiac death, myocardial infarction, and cardiac transplantation. Cardiac death was defined as death due to acute myocardial infarction, congestive heart failure, life-threatening arrhythmias, or cardiac arrest; unexpected sudden death without an identified noncardiac cause also was considered cardiac death. Myocardial infarction was defined as the appearance of new symptoms of myocardial ischemia accompanied by increases in markers of myocardial necrosis.

Statistical analysis. Categorical variables were reported as percentages and comparison between groups based on the chi-square test. Continuous variables were reported as mean ± standard deviation and differences were assessed with the unpaired *t* test or Mann-Whitney *U* test as appropriate.

Intra- and interobserver variabilities for the assessment of resting wall motion abnormalities and ischemia were evaluated by 2 independent observers in a sample of 20 randomly selected tests.

Survival free of the end point of interest was estimated by the Kaplan-Meier method, and survival curves were compared with the log-rank test. For the MACE analysis, patients were censored at the time of a coronary revascularization procedure or noncardiac death.

Univariable and multivariable associations of clinical, exercise, and EE variables with the end points were assessed with Cox's proportional hazard models. Variables were selected in a stepwise forward selection manner, with entry and retention set at a significance level of 0.05. Hazard ratios with 95% confidence intervals were estimated.

The incremental value of EE results over clinical, resting echocardiographic and exercise treadmill testing variables was assessed in 4 modeling steps in the same order as in clinical practice. The first step was based on clinical data. Resting echocardiographic data was then added in the following step. The third step consisted of hemodynamic data obtained during exercise. In the final step, the EE data were added. The chi-square value of each model and the incremental value of adding the different variables were estimated (24). Statistical analysis was performed with the use of SPSS software, version 15.0 (SPSS Inc., Chicago, Illinois).

RESULTS

Baseline characteristics. Mean age was 66 ± 10 years, and 331 patients (54%) were men. Clinical and demographic characteristics of the 609 patients are summarized in Table 1. The main reasons for performing the tests were typical chest pain in 31 patients (5.1%), probable angina in 307 patients (50.4%), nonischemic chest pain in 84 patients (13.8%), dyspnea in 42 patients (6.9%), and risk stratification in 145 patients (23.8%).

Exercise echocardiographic characteristics. There were no complications during the tests. Of the 609 patients, 177 (29%) developed ischemia and 335 (55%) had an abnormal EE; 82 patients (13.5%) had normal echocardiograms at rest but developed ischemia with exercise; in 158 patients (25.9%), there were resting wall motion abnormalities without ischemia; the remaining 95 patients (15.6%) had wall motion abnormalities at rest that impaired with exercise.

Patients with ischemia (with or without resting wall motion abnormalities) were older and were more likely to be male or to have a history of myocardial infarction or coronary revascularization; these patients presented more frequently with typical chest pain (Table 1). Hemodynamic and echocardiographic data obtained during the tests are presented in Table 2.

Intraobserver and interobserver variability. There was 95% intraobserver agreement (kappa = 0.88 ± 0.12) and 90% interobserver agreement (kappa = 0.73 ± 0.18) for the diagnosis of resting wall motion abnormalities. The intra- and interobserver agreement for the detection of ischemia were 90% (kappa = 0.74 ± 0.17) and 90% (kappa = 0.69 ± 0.21), respectively.

Outcomes. During a mean follow-up of 4.6 ± 3.4 years (interquartile range 1.8 to 7.3 years), 124 deaths occurred. Five-year mortality rate was 24.6% in the group of patients with ischemia versus 12.6% in the group without ischemia ($p < 0.001$) (Fig. 1A).

Overall, 80 patients underwent revascularization procedures, 38 within 3 months and 42 beyond 3 months after the EE. Seventy-four patients had a MACE before any revascularization procedure, including 57 cardiac deaths, 15 nonfatal myocardial infarctions, and 2 cardiac transplantations. Nineteen patients who had a MACE after a revascularization

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Table 1. Baseline Characteristics of 609 Patients With Left Bundle Branch Block

	All Patients (n = 609)	No Ischemia (n = 432)	Ischemia (n = 177)	p Value
Male, n (%)	331 (54.4)	211 (48.8)	120 (67.8)	<0.001
Age, yrs	65.7±10.2	64.8 ± 10.5	68.1 ± 8.9	<0.001
Current smokers, n (%)	101 (16.6)	67 (15.5)	34 (19.2)	0.27
Diabetes, n (%)	104 (17.1)	61 (14.1)	43 (24.3)	0.002
Hypertension, n (%)	311 (51.1)	220 (50.9)	91 (51.4)	0.91
Hypercholesterolemia, n (%)	261 (42.9)	175 (40.5)	86 (48.6)	0.07
Family history of MI, n (%)	67 (11.0)	46 (10.6)	21 (11.9)	0.66
Previous MI, n (%)	79 (13.0)	39 (9.0)	40 (22.6)	<0.001
≤30 days before EE	26 (4.3)	15 (3.5)	11 (6.2)	0.13
>30 days before EE	55 (9.0)	26 (6.0)	29 (16.4)	<0.001
Previous coronary revascularization, n (%)	61 (10.0)	31 (7.2)	30 (16.9)	<0.001
PCI	38 (6.2)	21 (4.9)	17 (9.6)	0.03
CABG	26 (4.3)	11 (2.5)	15 (8.5)	0.001
Typical chest pain, n (%)	31 (5.1)	9 (2.1)	22 (12.4)	<0.001
Dyspnea	42 (6.9)	38 (8.8)	4 (2.3)	0.004
Atrial fibrillation, n (%)	26 (4.3)	17 (3.9)	9 (5.1)	0.52
Medication, n (%)				
Beta-blockers	28 (4.6)	19 (4.4)	9 (5.1)	0.71
Calcium channel blockers	98 (16.1)	67 (15.5)	31 (17.5)	0.54
Nitrates	178 (29.2)	109 (25.2)	69 (39)	0.001
Aspirin	46 (7.6)	36 (8.3)	10 (5.6)	0.26
ACE inhibitors	217 (35.6)	141 (32.6)	76 (42.9)	0.016
Digoxin	28 (4.6)	21 (4.9)	7 (4.0)	0.63
Diuretics	93 (15.3)	60 (13.9)	33 (18.6)	0.14

ACE = angiotensin-converting enzyme; CABG = coronary artery bypass grafting; EE = exercise echocardiography; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Table 2. Exercise Echocardiographic Data of the 609 Patients

	All Patients (n = 609)	No Ischemia (n = 432)	Ischemia (n = 177)	p Value
Systolic blood pressure, mm Hg				
Rest	138 ± 21	137 ± 22	140 ± 19	0.22
Peak	167 ± 30	168 ± 32	164 ± 26	0.06
Heart rate, beats/min				
Rest	80 ± 15	81 ± 15	80 ± 14	0.64
Peak	145 ± 22	147 ± 21	141 ± 22	0.001
Rate-pressure product, $\times 10^3$ mm Hg beats/min				
Rest	11.09 ± 2.64	11.05 ± 2.65	11.18 ± 2.63	0.59
Peak	24.38 ± 6.07	24.90 ± 6.31	23.11 ± 5.25	<0.001
Chest pain, n (%)	93 (15.3)	36 (8.3)	57 (32.2)	<0.001
Metabolic equivalents	8.1 ± 3.0	8.5 ± 2.9	7.1 ± 2.9	<0.001
Left ventricular ejection fraction, %				
Rest	47.5 ± 12.9	47.8 ± 13.2	46.8 ± 12.1	0.38
Peak	49.1 ± 15.8	52.7 ± 15.4	40.4 ± 13.0	<0.001
Wall motion score index				
Rest	1.31 ± 0.43	1.30 ± 0.43	1.35 ± 0.42	0.01
Peak	1.40 ± 0.46	1.27 ± 0.41	1.72 ± 0.40	<0.001

procedure (14 of 177 patients in the ischemic group and 5 of 432 patients in the nonischemic group) were censored at the time of the procedure for the MACE analysis. Five-year MACE rate was 18.1% in the ischemic group versus 9.7% in the nonischemic group ($p = 0.003$) (Fig. 2A).

When resting wall motion abnormalities also were considered, patients with normal EE had a 5-year mortality rate of 8.3% as compared with 22% in patients with abnormal EE ($p < 0.001$) (Fig. 1B). Five-year MACE rate also was significantly lower in the group of patients with normal EE (4.6% vs. 18%, $p < 0.001$) (Fig. 2B). Patients with wall motion abnormalities at rest and ischemia during exercise were at greater risk of events (5-year mortality rate of 35.8% and 5-year MACE rate of 22.7%).

Predictors of outcome. Mortality and MACE were associated with age, male sex, smoking, history of myocardial infarction, atrial fibrillation and typical chest pain, and also were more common in patients who had resting wall motion abnormalities or ischemic results on EE. Univariate associations with mortality and MACE are reported in Table 3. In the multivariate analysis, resting WMSI and ΔWMSI were independent predictors of both total mortality and MACE (Tables 4 and 5).

Incremental prognostic value of stress echocardiography. The global chi-square of the clinical model for predicting all-cause mortality was 72 ($p < 0.001$); the addition of resting echocardiographic data (resting WMSI) increased the global chi-square to 119 ($p < 0.001$); the inclusion of metabolic equivalents (but not rate-pressure product) added significantly to the model (chi-square 138, $p < 0.001$); the subsequent addition of the EE results (ΔWMSI) to the clinical, resting echocardiographic and treadmill exercise data also provided incremental information for predicting total mortality (chi-square 143, $p = 0.014$).

The global chi-square of the clinical model for predicting MACE was 40 ($p < 0.001$); after adding the resting WMSI, the global chi-square increased to 94 ($p < 0.001$); treadmill exercise data did not add significantly to the initial model and were not included; finally, the addition of the EE results increased the global chi-square to 101 ($p = 0.017$).

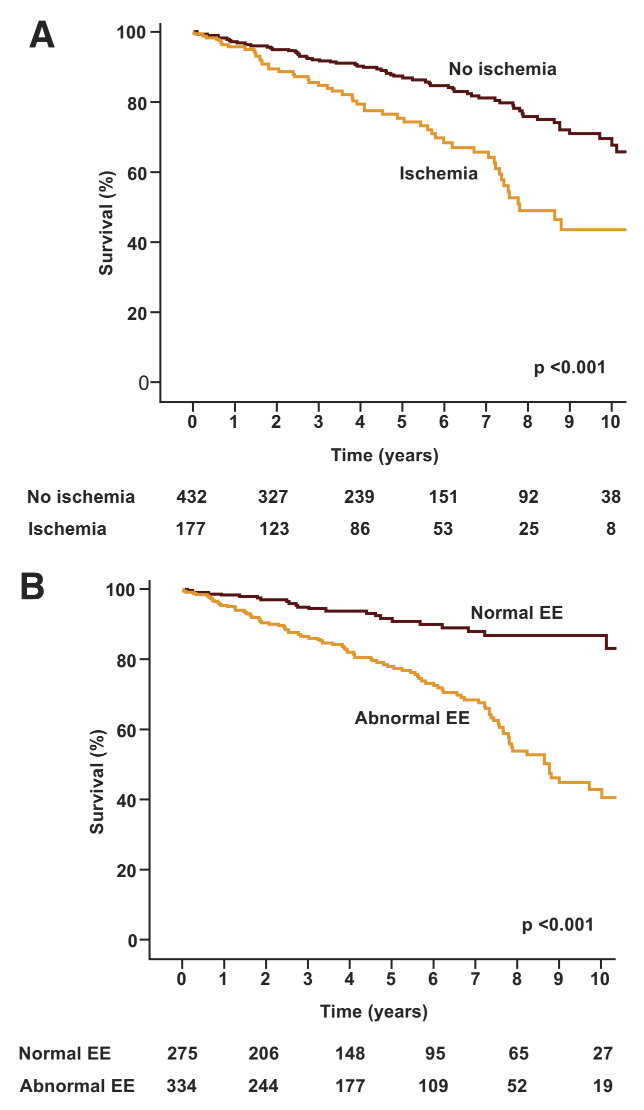

Figure 1. Overall Survival Curves

(A) Overall survival curves for patients with versus without ischemia and **(B)** with normal versus abnormal exercise echocardiography. Ischemia was defined as the development of new or worsening wall motion abnormalities with exercise, whereas an abnormal exercise echocardiography (EE) was defined as the presence of wall motion abnormalities at rest or the development of ischemia during exercise.

DISCUSSION

To our knowledge, the present study is the first to assess the prognostic implications of EE in patients with LBBB, and the largest reported to date on the role of noninvasive imaging studies for detection of CAD in this group of patients. Our study shows that EE provides significant prognostic information for the prediction of mortality and cardiac events in these patients.

Although LBBB may be associated to CAD and other heart diseases, it also may be an isolated finding; thus, diagnostic evaluation and risk stratification of patients with symptoms suggestive of myocardial ischemia are important, given the prognostic implications. Exercise ECG testing is not valid for detecting CAD in these patients (25).

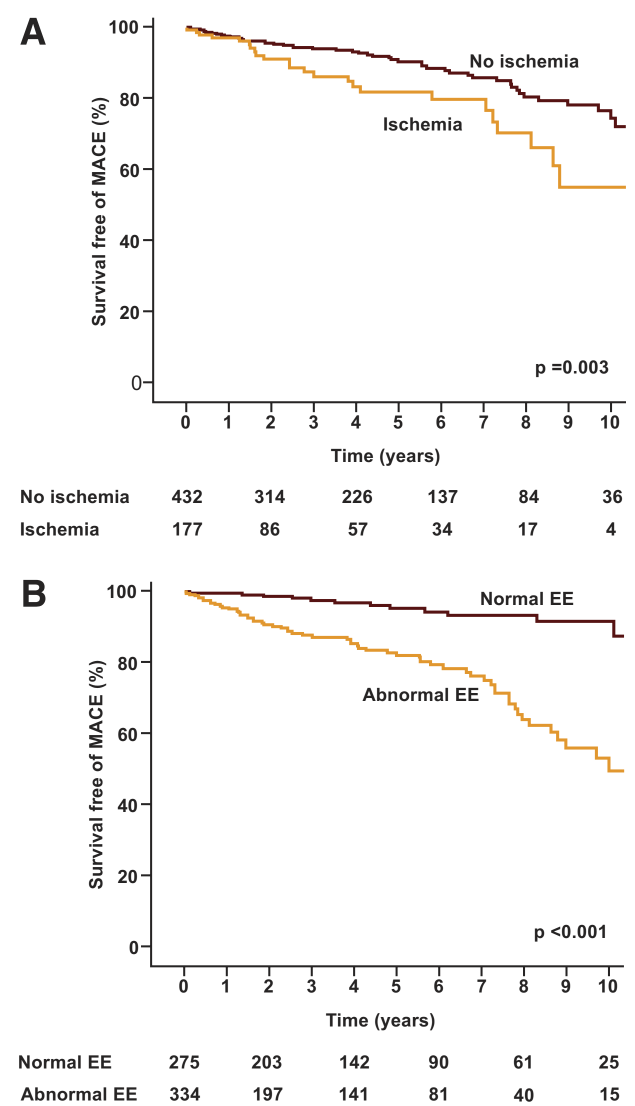

Figure 2. Survival Free of Major Adverse Cardiac Events

(A) Survival free of major adverse cardiac events (MACE) curves in patients with versus without ischemia and **(B)** with normal versus abnormal exercise echocardiography (EE). Ischemia was defined as the development of new or worsening wall motion abnormalities with exercise, whereas an abnormal EE was defined as the presence of wall motion abnormalities at rest or the development of ischemia during exercise.

Single photon-emission computed tomography also has important limitations; although its sensitivity for the diagnosis of CAD is relatively high, its specificity is low as the result of a high incidence of false reversible perfusion defects, especially in the septum. However, its specificity increases significantly when myocardial perfusion is assessed with vasodilators (adenosine or dipyridamole) (6). Stress echocardiography has greater specificity at the expense of lower sensitivity (26–28). Whereas several studies have focused on pharmacological stress echocardiography (23,26–29), only one report (9) has addressed the diagnostic accuracy of EE in patients with LBBB; in that study, sensitivity of exercise-induced new wall motion abnormalities for detection of coronary stenosis was 76%, whereas specificity was 83%; importantly, no patient with multivessel or significant left anterior descending CAD had a normal EE. The main limitation of stress echocardiography in patients with LBBB is septal wall motion analysis, which may not be accurate; instead, worsening of septal wall thickening during stress is a reliable marker of ischemia (23). Even so, overall accuracy for detection of CAD in patients with LBBB seems to be similar for stress echocardiography and myocardial perfusion imaging (6).

Few data are available regarding the prognostic value of noninvasive imaging techniques in patients with LBBB. No studies addressing the prognostic role of exercise ECG in these patients have been reported. However, although exercise-induced ST-segment changes are nonspecific for detection of myocardial ischemia in the presence of LBBB, other variables obtained during exercise ECG testing, such as exercise-induced angina, metabolic equivalents, blood pressure response, and heart rate response, may provide valuable prognostic information that cannot be obtained with pharmacological stress (30).

Several studies have shown that myocardial perfusion scintigraphy is useful in risk stratification of patients with LBBB (31–34). Wagdy et al. (34) found that patients with high-risk scans (i.e., those with large fixed or reversible defects and either increased pulmonary uptake or left ventricular ejection fraction <45%) had a 3-year overall survival of 57% and a 3-year survival free of hard events of 55%, as compared with 87% and 93%, respectively, in the low risk group. Nevertheless, these studies did not evaluate separately the prognostic implications of an ischemic response.

Only one study has assessed the prognostic value of stress echocardiography in patients with LBBB; Cortigiani et al. (8) evaluated 387 patients who underwent either dobutamine or dipyridamole stress echocardiography and who were followed up for a mean of 29 months; in this study, 28% of the patients developed an ischemic response; 5-year survival was significantly lower in the ischemic group (77%) than in the nonischemic group (92%, $p = 0.02$). Resting WMSI and ΔWMSI were associated with cardiac death in the multivariate

Table 3. Univariate Predictors of Mortality and Major Cardiac Events

	Total Mortality			Major Cardiac Events		
	HR	95% CI	p Value	HR	95% CI	p Value
Male	2.28	1.53–3.40	<0.001	2.77	1.65–4.67	<0.001
Age (per yr)	1.07	1.05–1.09	<0.001	1.05	1.02–1.07	0.001
Current smokers	1.78	1.13–2.81	0.013	2.42	1.37–4.28	0.002
Diabetes	1.31	0.78–2.19	0.31	1.96	1.08–3.54	0.026
Hypertension	0.88	0.61–1.28	0.52	1.30	0.81–2.11	0.28
Hypercholesterolemia	0.94	0.64–1.38	0.76	0.90	0.54–1.50	0.69
Family history of MI	1.02	0.55–1.91	0.94	1.22	0.58–2.56	0.60
Previous MI	3.02	2.03–4.46	<0.001	2.86	1.69–4.82	<0.001
Previous coronary revascularization	1.51	0.92–2.46	0.10	1.41	0.72–2.75	0.32
Previous CABG	2.33	1.28–4.24	0.006	2.99	1.43–6.27	0.004
Typical chest pain	2.04	1.03–4.02	0.04	2.45	1.06–5.67	0.035
Dyspnea	1.91	1.05–3.47	0.04	2.85	1.49–5.42	0.001
Atrial fibrillation at the time of EE	3.80	2.17–6.66	<0.001	3.78	1.88–7.61	<0.001
Beta-blocker therapy	0.96	0.42–2.19	0.92	0.84	0.26–2.68	0.77
Calcium channel blocker therapy	1.22	0.80–1.87	0.37	1.04	0.59–1.85	0.89
Chest pain during EE	0.83	0.50–1.37	0.47	0.58	0.25–1.33	0.20
Resting RPP (per 10^3 U)	0.99	0.93–1.06	0.74	1.02	0.93–1.11	0.73
Peak heart rate (per beats/min)	0.99	0.98–0.99	<0.001	0.99	0.98–1.00	0.07
Peak systolic blood pressure (per mm Hg)	0.99	0.98–0.99	<0.001	0.99	0.98–0.99	0.004
Peak RPP (per 10^3 U)	0.93	0.90–0.96	<0.001	0.94	0.91–0.98	0.001
Percent of age-predicted maximal heart rate	0.99	0.98–1.00	0.16	0.99	0.97–1.00	0.10
Metabolic equivalents	0.79	0.75–0.85	<0.001	0.84	0.78–0.91	<0.001
Resting LVEF	0.95	0.94–0.96	<0.001	0.94	0.93–0.96	<0.001
Peak LVEF	0.96	0.95–0.97	<0.001	0.95	0.94–0.96	<0.001
Resting WMSI	4.12	2.86–5.94	<0.001	5.94	3.70–9.51	<0.001
Peak WMSI	4.91	3.40–7.09	<0.001	6.34	4.01–10.16	<0.001
ΔWMSI	2.36	1.27–4.41	0.007	2.77	1.09–7.02	0.03
Resting WMA	3.70	2.52–5.42	<0.001	4.15	2.52–6.83	<0.001
Ischemia	2.30	1.61–3.29	<0.001	2.05	1.26–3.33	0.004
Abnormal EE	3.90	2.49–6.09	<0.001	5.30	2.91–9.66	<0.001

CI = confidence interval; HR = hazard ratio; LVEF = left ventricular ejection fraction; RPP = rate-pressure product; WMA = wall motion abnormalities; WMSI = wall motion score index; ΔWMSI = change in wall motion score index; other abbreviations as in Table 1.

analysis, whereas resting WMSI and positive stress echocardiogram were predictors of cardiac events. The stress echocardiographic results provided significant incremental prognostic information over clinical and resting echocardiographic variables for predicting cardiac events in patients without previous myocardial infarction ($p < 0.001$), although it did not reach statistical significance in those with a history of infarction ($p = 0.08$).

Our study shows that patients with LBBB and normal EE have a good long-term prognosis. In this subgroup, the risk of MACE was 0.92% per

Table 4. Multivariate Predictors of Total Mortality

	HR	95% CI	p Value
Male sex	1.97	1.29–3.02	0.002
Age (per yr)	1.05	1.02–1.07	<0.001
Atrial fibrillation	2.24	1.27–3.97	0.006
Resting WMSI	3.12	2.02–4.80	<0.001
Metabolic equivalents	0.88	0.82–0.94	<0.001
ΔWMSI	2.42	1.21–4.82	0.012

Abbreviations as in Table 3.

Table 5. Multivariate Predictors of Major Cardiac Events

	HR	95% CI	p Value
Male sex	2.27	1.31–3.92	0.003
Age (per yr)	1.04	1.01–1.06	0.014
Diabetes	2.26	1.21–4.23	0.011
Atrial fibrillation	2.50	1.22–5.16	0.013
Resting WMSI	5.89	3.55–9.77	<0.001
ΔWMSI	3.38	1.30–8.82	0.013

Abbreviations as in Table 3.

year; although this is greater than the 0.54% annualized event rate reported in a recent meta-analysis in a general population of patients with normal EE (35), the greater age of our population (mean age 64 vs. 56 years) may account, at least in part, for this difference. On the other hand, patients with LBBB and an abnormal EE have a poor outcome, with a mortality rate of 4.4% per year and a MACE rate of 3.6% per year; even if we do not take into account the presence of resting wall motion abnormalities, mortality and MACE rates in the group of patients with ischemia were almost twice as high as for those who did not develop an ischemic response with exercise; these patients, particularly those with extensive ischemia, may significantly benefit from invasive management.

Study limitations. This study has several limitations. First, because patients with ischemic results on EE were more likely to undergo revascularization procedures, the actual prognostic value of the test may have been significantly underestimated. Second, we routinely perform peak imaging in addition to post-exercise imaging since it has shown higher sensitivity (20); therefore, our results could have been different if we had used post-exercise imaging alone.

CONCLUSIONS

EE provides significant prognostic information for predicting outcome in patients with LBBB. Patients with normal EE have a very good prognosis, whereas those with abnormal results are at increased risk of death and major cardiac events.

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