Prognostic Implications of Stress Echocardiography and Impact on Patient Outcomes: An Effective Gatekeeper for Coronary Angiography and Revascularization

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Background: Stress echocardiography is an established technique for diagnosis, risk stratification, and prognosis in patients with known or suspected coronary artery disease. The ability of stress echocardiography to predict clinical outcomes, such as coronary angiography and revascularization, has not been reported previously. The purpose of this study was to evaluate the clinical outcomes of coronary angiography, revascularization, and cardiac events in patients undergoing stress echocardiography.

Methods: A total of 3121 patients (mean age, 60 ± 13 years; 48% men) undergoing stress echocardiography (41% treadmill, 59% dobutamine) were assessed. Follow-up (mean, 2.8 ± 1.1 years) for subsequent coronary angiography, revascularization (percutaneous coronary intervention [PCI] or coronary artery bypass grafting [CABG]), and confirmed hard events (nonfatal myocardial infarction or cardiac death) was obtained.

Results: Stress echocardiographic results were normal (peak wall motion score index [pWMSI], 1.0) in 66% and abnormal (pWMSI > 1.0) in 34% of patients. The pWMSI effectively risk-stratified patients into low-risk (pWMSI, 1.0; 0.8% per year), intermediate-risk (pWMSI, 1.1-1.7; 2.6% per year), and high-risk (pWMSI >1.7; 5.5% per year) groups for future cardiac events ($P < .0001$). Early coronary angiography (30 days following stress echocardiography) was performed in only 35 patients (1.7%) with normal stress echocardiographic results and 267 patients (25.5%) with abnormal stress echocardiographic results ($P < .0001$). Late coronary revascularization (2 years following stress echocardiography) occurred in 80 patients (PCI, 2.8%; CABG, 1.1%) with pWMSI values of 1.0, 123 patients (PCI, 13.5%; CABG, 7.3%) with pWMSI values of 1.1 to 1.7, and 102 patients (PCI, 12.7%; CABG, 9.6%) with pWMSI values > 1.7. Multivariate logistic regression analysis identified pWMSI as a predictor of coronary angiography (relative risk, 2.04; 95% confidence interval, 1.67-2.5), revascularization (relative risk, 1.91; 95% confidence interval, 1.68-2.17), and cardiac events (relative risk, 2.45; 95% confidence interval, 2.09-2.88) (all P values < .0001). Patients with markedly abnormal stress echocardiographic results (pWMSI > 1.7) had a significantly higher cardiac event rate in those who did not undergo coronary revascularization (9.6% per year vs 2.9% per year, $P < .05$).

Conclusions: Stress echocardiography is an effective gatekeeper for coronary angiography and revascularization. Stress echocardiographic results influence clinical decision making in higher risk patients with significantly increased referral to coronary angiography and revascularization. Patients with markedly abnormal stress echocardiographic results (pWMSI > 1.7) were most likely to benefit from coronary revascularization. (J Am Soc Echocardiogr 2010;23:832-9.)

Keywords: Echocardiography, outcome, prognosis, stress

Stress echocardiography is routinely used for diagnosis, risk stratification, and prognosis in patients with known or suspected coronary artery disease (CAD).[1-8] Because coronary angiography is invasive and carries a potential risk for leading to inappropriate coronary revascularization, noninvasive testing strategies that could influence the decision to perform coronary angiography might prove to be cost effective. As such, stress echocardiography can be proposed as a gatekeeper to coronary angiography and coronary revascularization. This concept would be valid if patients with normal stress echocardiographic results are deemed at low risk with an acceptably low cardiac event rate, and few such patients are referred to coronary angiography. Numerous studies have demonstrated that

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Abbreviations

CABG = Coronary artery bypass grafting

CAD = Coronary artery disease

COURAGE = Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation

LV = Left ventricular

MI = Myocardial infarction

PCI = Percutaneous coronary intervention

pWMSI = Peak wall motion score index

patients with normal stress echocardiographic results have a benign prognosis, with a cardiac event rate < 1% per year.[5-7]

The objectives of the present stress echocardiographic study were 4-fold: (1) to reaffirm the prognostic value of stress echocardiography to risk-stratify patients into low-risk (<1% per year), intermediate-risk (1%-5% per year), and high-risk (>5% per year) risk groups for cardiac events; (2) to characterize patients and determine the component variable(s) of stress echocardiography that best predict outcomes of coronary angiography, revascularization, and cardiac events; (3) to evaluate the post–stress echocardiography use of coronary angiography and revascularization as an effective gatekeeper in a large patient population with follow-up; and (4) to examine the influence of stress echocardiographic results on the decision to refer for coronary revascularization and its subsequent impact on cardiac events and prognosis.

METHODS

Study Population

We identified 3121 nonconsecutive patients referred for exercise or pharmacologic stress echocardiography between March 21, 2000, and December 31, 2007, to St Luke's-Roosevelt Hospital Center (New York, NY). Successful follow-up (100%) for cardiac events ≥1 year after testing was obtained. Patients with nonischemic cardiomyopathy were excluded (n = 35).

Exercise Echocardiographic Protocol

Exercise was the preferred stress modality in patients who were able to exercise to an adequate workload (≥85% of age-adjusted maximal predicted heart rate and 5 metabolic equivalents). Maximal exercise treadmill testing was performed using a standard Bruce protocol. Patients exercised to general fatigue, with premature termination for severe angina, ventricular tachycardia, hemodynamically significant arrhythmias, or hemodynamic instability. Postexercise echocardiographic images were acquired within 30 to 60 seconds after the termination of treadmill exercise.

Dobutamine Echocardiographic Protocol

Dobutamine was administered intravenously beginning at a dose of 5 to 10 μg/kg/min and increased by 10 μg/kg/min every 3 minutes up to a maximum of 40 μg/kg/min, or until a study end point was achieved. The end points for termination of the dobutamine infusion included the development of new segmental wall motion abnormalities, the attainment of >85% of age-predicted maximum heart rate, or the development of significant adverse effects related to the dobutamine infusion. Atropine was administered intravenously in 0.25-mg to 0.5-mg increments up to a maximum dose of 2.0 mg if a study end point was not achieved.

During both types of stress, transthoracic echocardiographic images were obtained using standard views with commercially available ultrasound equipment (Acuson Sequoia, Siemens Medical Solutions USA, Inc, Mountain View, CA; Sonos 5500, Hewlett-Packard Corporation, Andover MA). Echocardiographic images were acquired at baseline, with each increment of dobutamine infusion (if pharmacologic stress), and during the recovery phase.

Echocardiographic Image Analysis

The left ventricle was divided into 16 segments, as recommended by the American Society of Echocardiography,[9] and a score was assigned to each segment at baseline, with each stage of stress (dobutamine only), and during recovery. Each segment was scored as follows: 1 = normal, 2 = mild to moderate hypokinesis (reduced wall thickening and excursion), 3 = severe hypokinesis (markedly reduced wall thickening and excursion), 4 = akinesis (no wall thickening and excursion), and 5 = dyskinesis (paradoxical wall motion away from the center of the left ventricle during systole).[10] All echocardiograms were interpreted by two experienced echocardiographers who were blinded to patients' treatment and outcomes. Stress echocardiographic studies of poor image quality (<13 of 16 left ventricular [LV] segments visualized) were excluded (approximately 5%). Contrast (Definity; Lantheus Medical Imaging, North Billerica, MA) was used in approximately 13% of stress echocardiographic studies for endocardial border delineation both at rest and during stress.

A normal response to stress was defined as normal wall motion at rest, with increases in wall thickening and excursion during stress. An abnormal (ischemic) response to stress was defined as (1) an LV wall segment that did not increase in thickening and excursion during stress (lack of a hyperdynamic wall motion response) or (2) a deterioration in LV wall segment thickening and excursion during stress (increase in wall-motion score of ≥1 grade) and (3) a biphasic response with dobutamine stress. Maximal severity was the score of the LV wall segment(s) with the greatest value (worst wall motion grade) at postexercise stress (range, 0-5). Peak wall motion score index (pWMSI) following stress was derived from the cumulative sum score of 16 LV wall segments divided by the number of visualized segments. Resting ejection fraction used in the study analysis was an average visual estimation[11] from two experienced echocardiographers.

Patient Follow-Up

Follow-up was obtained in all patients by means of physician-directed telephone interviews using a standardized questionnaire. Early coronary angiography was defined as occurring <3 months after the stress echocardiographic study. Late coronary revascularization was defined as occurring <2 years after the stress echocardiographic study. Coronary angiography and revascularization reports were reviewed in detail and obtained from outside institutions when known. The hard endpoints of the study were nonfatal myocardial infarction (MI) or cardiac death. Nonfatal MI was documented when diagnostic changes in cardiac enzymes (troponin) were accompanied by appropriate clinical symptoms, electrocardiographic findings, or both. Cardiac death was confirmed by review of hospital medical records, death certificate, or both. Autopsy records were reviewed when available. The adjudication of MI and cardiac death was done by physicians who were blinded to clinical and stress echocardiographic results of the patients.

Statistical Analysis

Continuous data are expressed as the mean ± SD. Differences in categorical variables among groups were assessed using χ^2 analysis.

Table 1 Patient characteristics, stress echocardiographic results, and follow-up cardiac events

Variable	Stress echocardiographic results (WMSI) Normal 1.0 (n = 2072)	Abnormal 1.1-1.7 (n = 593)	Abnormal >1.7 (n = 456)
Age (y)	58 ± 13	63 ± 12*	63 ± 12*
Men	879 (43%)	301 (51%)‡	314 (69%)‡
History of MI	170 (8%)	125 (21%)‡	215 (47%)‡
History of PCI	18 (5%)	57 (12%)*	65 (16%)*
History of CABG	60 (4%)	69 (15%)*	79 (20%)*
History of hypertension	1304 (64%)	425 (72%)*	316 (70%)†
History of diabetes	446 (23%)	171 (31%)§	174 (40%)§
Number of cardiac risk factors	1.8 ± 1.1	2 ± 1.1*	2.1 ± 1.2*
Abnormal rest electrocardiographic results	743 (37%)	280 (49%)‡	324 (74%)‡
% maximal heart rate (beats/min)	92 ± 11	90 ± 10	81 ± 15†
pWMSI	1.0	1.3 ± 0.2‡	2.7 ± 0.6‡
Number of new ischemic wall motion abnormalities	0	3.5 ± 2‡	8.5 ± 3.9‡
Ejection fraction (%)	58 ± 4.7	54 ± 7.7‡	32 ± 14‡
MI	33 (0.6%)	24 (1.5%)*	19 (1.5%)*
Cardiac death	13 (0.2%)	19 (1.1%)*	51 (4.0%)*

Data are expressed as mean ± SD or as number (percentage).
*$P < .0001$ versus normal stress echocardiographic results.
†$P < .05$ versus normal stress echocardiographic results.
‡$P < .0001$ versus both groups.
§$P < .05$ versus both groups.

Multiple comparisons of continuous variables were made using single-factor analysis of variance, and when significant, differences between pairs were tested using Bonferroni's correction for the confidence limit. Univariate analysis was performed to determine the relationship between clinical and echocardiographic variables separately with coronary angiography and coronary revascularization. Univariate variables that were separately predictive of coronary angiography and coronary revascularization were considered in multivariate logistic regression analysis. Statistical significance was defined as $P < .05$. All analyses were performed using commercially available statistical software (SPSS for Windows version 10.0.5; SPSS, Inc, Chicago, IL).

RESULTS

Patient Characteristics and WMSI

From the entire study cohort of 3121 patients, 1293 (41%) underwent treadmill exercise, and 1828 (59%) underwent pharmacologic stress. The patient characteristics and stress echocardiographic results are listed in Table 1. Patients with abnormal stress echocardiographic results (pWMSI, 1.1-1.7 or >1.7) more often were older and male; had histories of MI; had undergone percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG); and had hypertension, diabetes, greater numbers of cardiac risk factors, abnormal rest electrocardiographic results, higher pWMSI values, greater numbers of new ischemic wall motion abnormalities, lower ejection fractions, and higher cardiac event rates compared with patients with pWMSI values of 1.0. Patients with abnormal stress echocardiographic results and pWMSI values > 1.7 more often were male; had histories of MI; and had diabetes, abnormal rest electrocardiographic results, lower achieved percentage maximal heart rate, higher pWMSI values, greater numbers of new ischemic wall motion abnormalities, and lower ejection fractions compared with patients with pWMSI values of 1.1 to 1.7.

Table 2 Clinical characteristics of patients with cardiac events and no events

Variable	Cardiac events (n = 159)	No events (n = 2962)	*P*
Age (y)	67 ± 12	60 ± 13	.0001
Men	86 (54%)	1413 (48%)	.07
History of MI	62 (39%)	446 (15%)	.0001
History of hypertension	120 (77%)	1929 (66%)	.002
History of diabetes	69 (45%)	804 (28%)	.0001
Abnormal rest electrocardiographic results	52 (33%)	513 (17%)	.0001
Treadmill exercise	23 (14%)	1272 (67%)	.0001
pWMSI	1.9 ± 1	1.3 ± 0.6	.0001
Number of new ischemic wall motion abnormalities	4.7 ± 3.5	1.7 ± 1.7	.0001
Ejection fraction (%)	43 ± 19	54 ± 11	.0001

Data are expressed as mean ± SD or as number (percentage).

Stress Echocardiography and Follow-Up Cardiac Events

Patients were followed for up to 5 years (mean, 2.8 ± 1.1 years), and 100% were followed for ≥1 year. Among the total study cohort of 3121 patients, 159 coronary events (5.1%) occurred during the follow-up period. These included 76 nonfatal MIs (2.4%) and 83 cardiac deaths (2.7%). There were 23 cardiac events among patients who underwent treadmill stress and 136 events among patients who underwent dobutamine stress (1.8% per year vs 7.4% per year, $P < .0001$).

Characteristics of Patients With and Without Cardiac Events

Descriptive patient characteristics and exercise and stress echocardiographic variables in patients with and without cardiac events on follow-up are shown in Table 2. Patients with cardiac events on follow-up were older; had more frequent histories of MI, hypertension, and diabetes; had abnormal rest electrocardiographic results; and were less likely to undergo treadmill exercise compared with those without cardiac events. With respect to echocardiographic variables, patients with cardiac events had higher pWMSI values, greater numbers of new ischemic wall motion abnormalities, and lower ejection fractions.

pWMSI and Cardiac Event Rate

The annual cardiac event rate[7] increased as a function of the extent and severity of wall motion abnormalities during stress and increasing pWMSI (Figure 1). Normal stress echocardiographic results (pWMSI, 1.0) were associated with a benign prognosis (0.8% per year), whereas mild to moderate (pWMSI, 1.1-1.7) and markedly abnormal (pWMSI > 1.7) stress echocardiography results were associated with higher cardiac event rates (2.6% per year and 5.5% per year, respectively, $P < .0001$ vs normal stress echocardiographic results).

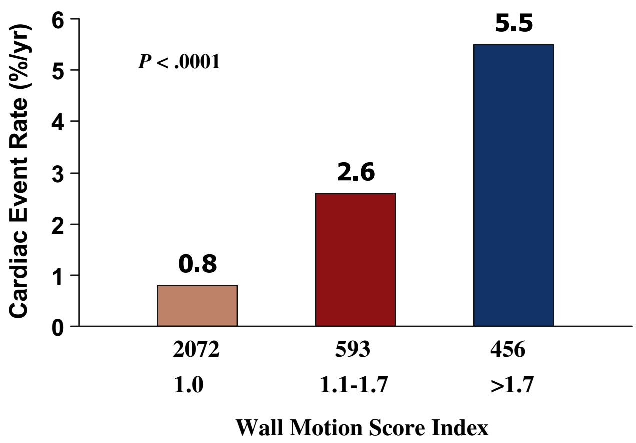

Figure 1 Cardiac event rate per year as a function of WMSI. The number of patients within each WMSI category is shown beneath each column. Statistical significance increases as a function of WMSI result.

Characteristics of Patients With and Without Coronary Angiography and Revascularization

The characteristics of patients who underwent coronary angiography and revascularization are listed in Table 3. Patients who underwent coronary angiography and revascularization more often were older and male; had histories of PCI or CABG; and had hypertension, diabetes, greater numbers of cardiac risk factors, and lower achieved percentage maximal heart rate. With respect to echocardiographic variables, patients with cardiac events had higher pWMSI values, greater numbers of new ischemic wall motion abnormalities, and lower ejection fractions.

Post–Stress Echocardiography Referral for Coronary Angiography and Coronary Revascularization

Referral to early coronary angiography increased as a function of the extent and severity of abnormal wall motion response during stress and increasing pWMSI (Figure 2A). Normal stress echocardiographic results (pWMSI, 1.0) were associated with low referral to coronary angiography (1.7%), whereas mild to moderate (pWMSI, 1.1-1.7) and markedly abnormal (pWMSI > 1.7) stress echocardiographic results were associated with higher referral to coronary angiography (22.9% and 41.9%, respectively, $P < .0001$ vs normal stress echocardiographic results).

Referral to late coronary revascularization increased as a function of the extent and severity of abnormal wall motion response during stress and increasing pWMSI (Figure 2B). Normal stress echocardiographic results (pWMSI, 1.0) were associated with low referral to coronary revascularization (PCI, 2.8%; CABG, 1.1%), whereas mild to moderate (pWMSI, 1.1-1.7) and markedly abnormal (pWMSI > 1.7) stress echocardiographic results were associated with higher referral to coronary revascularization (PCI, 13.5% and 12.7%; CABG, 7.3% and 9.6%; $P < .0001$ vs normal stress echocardiographic results).

Predictors of Cardiac Events

Univariate predictors of coronary angiography and revascularization are shown in Table 4. Clinical and echocardiographic variables significant by univariate analysis were considered in multivariate analysis. By multivariate logistic regression analysis, diabetes (relative risk [RR], 1.44; 95% confidence interval [CI], 1.15-1.80; $P = .002$) and pWMSI (RR, 1.78; 95% CI, 1.04-3.04; $P = .03$) were predictors of coronary angiography. By multivariate logistic regression analysis, diabetes (RR, 1.59; 95% CI, 1.17-2.16; $P = .003$), ejection fraction (RR, 0.98; 95% CI, 0.97-0.99; $P < .0001$), and pWMSI (RR, 1.13; 95% CI, 1.06-1.20; $P < .0001$) were predictors of coronary revascularization.

Post–Stress Echocardiography Referral for Coronary Revascularization and Subsequent Cardiac Event Rate

The annual cardiac event rate and referral for coronary revascularization increased as a function of the extent and severity of wall motion abnormalities during stress and increasing pWMSI (Figure 3). Normal stress echocardiographic results (pWMSI, 1.0) were associated with a benign prognosis regardless of coronary revascularization (0.7% per year vs 0.0% per year, $P =$ ns). Patients with mild to moderate abnormal stress echocardiographic results (pWMSI, 1.1-1.7) had no significant difference in cardiac event rate with or without (2.3% per year vs 2.6% per year, $P =$ ns) coronary revascularization. Patients with markedly abnormal stress echocardiographic results (pWMSI > 1.7) had a significantly higher cardiac event rate in those who did not undergo coronary revascularization (9.6% per year vs 2.9% per year, $P < .05$).

DISCUSSION

This study reaffirms the known risk stratification and prognostic value of stress echocardiography. Normal stress echocardiographic results confer an excellent prognosis. Stress echocardiography can effectively risk-stratify patients not only into high-risk (>5% per year) and low-risk (<1% per year) groups but also into an intermediate-risk (1%-5% per year) group. Multivariate logistic regression analysis identified pWMSI as the strongest predictor of coronary angiography, revascularization, and future cardiac events. Furthermore, referral to coronary angiography and revascularization increased in parallel with the extent and severity of abnormal stress echocardiographic results. Importantly, patients with markedly abnormal stress echocardiographic results (pWMSI > 1.7) and at the highest risk for adverse events were also most likely to benefit from coronary revascularization.

When a test is first introduced into clinical practice, it is heavily scrutinized for its diagnostic and prognostic abilities. Once a test is well established, its impact on clinical outcomes is then examined.

Prognostic Value of pWMSI: Effective Risk Stratification

After adjusting for clinical factors, the most powerful variable of stress echocardiography was pWMSI. This study confirms that increasing extent and severity of wall motion abnormalities provide incremental prognostic value, and this was consistent across both exercise and dobutamine stress. We have also previously demonstrated that stress echocardiography provides incremental prognostic value over clinical and stress electrocardiographic variables.[12,13]

The diagnosis of CAD is the initial step in the evaluation of patients with anginal symptoms. However, additional information on risk stratification and prognosis is essential for guiding appropriate management decisions. Normal stress echocardiographic results are associated with a benign prognosis for up to 18 months.[12] This low event rate of 0.8% per year approaches that of a normal age-matched population and also of patients with normal coronary angiographic results.[14] The higher cardiac event rate in patients undergoing dobutamine stress is related to worse clinical characteristics of these

Table 3 Patient characteristics

Variable	Coronary angiography			Coronary revascularization		
	No (n = 2581)	Yes (n = 540)	*P*	No (n = 2817)	Yes (n = 304)	*P*
Age (y)	59 ± 14	62 ± 11	.0001	60 ± 13	63 ± 11	.0001
Men	1167 (45%)	332 (62%)	.0001	1301 (46%)	198 (65%)	.0001
History of MI	343 (13%)	70 (13%)	.30	392 (16%)	119 (42%)	.0001
History of PCI	141 (7%)	71 (15%)	.0001	143 (6%)	68 (27%)	.0001
History of CABG	137 (7%)	72 (16%)	.0001	137 (6%)	71 (28%)	.0001
History of hypertension	383 (72%)	1666 (66%)	.003	1832 (66%)	217 (72%)	.01
History of diabetes	668 (27%)	209 (40%)	.0001	684 (26%)	109 (38%)	.0001
Number of cardiac risk factors	1.9 ± 1.1	2.3 ± 1	.0001	1.8 ± 1.1	2.3 ± 1.1	.0001
Abnormal rest electrocardiographic results	805 (31%)	236 (44%)	.0001	934 (33%)	107 (35%)	.50
% maximal heart rate (beats/min)	91 ± 12	87 ± 13	.0001	91 ± 12	87 ± 13	.0001
pWMSI	1.2 ± 0.5	1.7 ± 0.8	.0001	1.3 ± 0.6	1.7 ± 0.8	.0001
Number of new ischemic wall motion abnormalities	1.3 ± 2	4.8 ± 4.4	.0001	1.6 ± 1.2	4.7 ± 3.4	.0001
Ejection fraction (%)	55 ± 10	48 ± 14	.0001	54 ± 11	50 ± 13	.0001

Data are expressed as mean ± SD or as number (percentage).

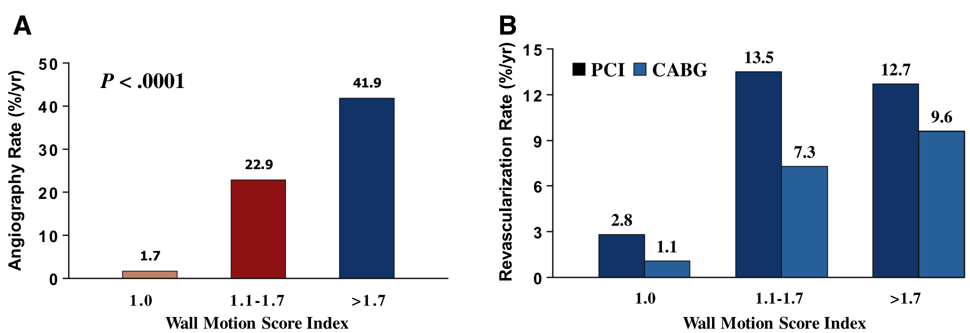

Figure 2 **(A)** Coronary angiography percentage as a function of WMSI. **(B)** Coronary revascularization percentage as a function of WMSI and type of coronary revascularization (CABG or PCI).

patients. The results also compare favorably with those of normal myocardial perfusion studies, which are similarly associated with a benign prognosis.[15] The pWMSI is derived from the interpretation of stress echocardiography and incorporates both the extent and the severity of wall motion abnormalities at peak stress. In this study, pWMSI was able to effectively risk-stratify patients into 3 groups: those at low (0.8% per year), intermediate (2.6% per year), and high (5.5% per year) risk.

Impact of Stress Echocardiography on Patient Management

This study demonstrates a parallel between coronary angiography and coronary revascularization referral and cardiac event rate after stress echocardiography. Despite physician self-referral incentives for coronary angiography, stress echocardiography was an effective gatekeeper for an invasive management strategy. Patients with normal stress echocardiographic results (pWMSI, 1.0) had uniformly low referral rates for early coronary angiography (1.7% at 30 days) and late revascularization (PCI, 2.8%; CABG, 1.1% at 2 years). The frequency of referral to coronary angiography and revascularization increased in proportion to magnitude of the extent and severity of abnormal stress echocardiographic results. In addition, other authors[16,17] have also demonstrated that referral to revascularization increases with increasing ischemia. The fact that only a minority of patients with abnormal stress echocardiographic results were referred to coronary angiography and revascularization implies that such decisions are often complex, incorporating variables of high risk markers, comorbidities, and other factors into a decision whether to refer for further invasive testing. These findings are consistent with low referral for coronary angiography and revascularization following abnormal nuclear scintigraphic results.[18-20]

In this study, the presence of normal wall motion (pWMSI, 1.0) during stress echocardiography conferred a benign prognosis. These low-risk patients generally only require counseling with regard to lifestyle and risk factor modification. Patients with mild to moderate abnormal stress echocardiographic results (pWMSI, 1.1-1.7) had an intermediate risk for cardiac events. The ideal management strategy for these patients is unclear. Rather than an invasive management strategy of coronary angiography and revascularization with its inherent risks, patients with intermediate risk may be subject to lowering of cardiac risk by aggressive risk factor modification and referral to coronary angiography only if symptoms are refractory. Patients with intermediate cardiac risk (pWMSI, 1.1-1.7) in this study had no significant difference in cardiac event rate, with or without coronary revascularization. Although not examined in this study, an initial noninvasive management strategy may be cost effective and avoid unnecessary invasive procedures.[16]

Table 4 Univariate and multivariate predictors

Variable	Coronary angiography RR	Coronary angiography 95% CI	Coronary angiography *P*	Coronary revascularization RR	Coronary revascularization 95% CI	Coronary revascularization *P*
Univariate predictors						
Age	1.14	1.05-1.24	.002	1.24	1.13-1.36	.0001
Diabetes mellitus	1.71	1.36-2.15	.0001	1.63	1.28-2.09	.0001
History of MI	1.87	1.45-2.41	.0001	3.34	2.61-4.27	.0001
% maximal heart rate	0.98	0.97-0.98	.0001	0.98	0.97-0.98	.0001
Ejection fraction	0.96	0.96-0.97	.0001	0.98	0.97-0.99	.0001
pWMSI	2.93	2.46-3.51	.0001	1.91	1.68-2.17	.0001
Number of new ischemic wall motion abnormalities	1.28	1.25-1.32	.0001	1.24	1.20-1.28	.0001
Multivariate predictors						
Diabetes mellitus	1.44	1.15-1.80	.002	1.59	1.17-2.16	.003
Ejection fraction				0.98	0.97-0.99	<.0001
pWMSI	1.78	1.04-3.04	.03	1.13	1.06-1.20	<.0001

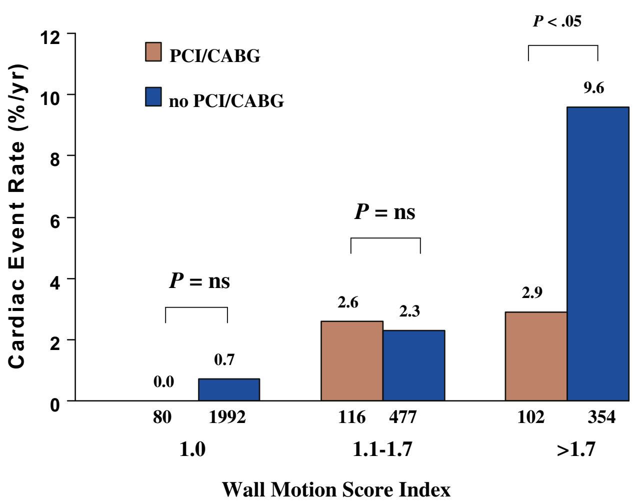

Figure 3 Cardiac event rate per year as a function of WMSI and coronary revascularization. The number of patients within each category is indicated beneath each column.

Optimal Medical Therapy or Coronary Revascularization for Markedly Abnormal Stress Echocardiographic Results?

Patients with markedly abnormal stress echocardiographic results (pWMSI > 1.7) and at high risk for cardiac events are most often patients with multivessel CAD.[21] This study supports the premise that high-risk patients should be referred for coronary angiography and consideration of revascularization as the best strategy to modify and reduce cardiac risk.[22] This strategy of revascularization in patients with markedly abnormal stress echocardiographic results (pWMSI > 1.7) may improve patient outcome by preventing cardiac events.

The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial was a prospective randomized study that showed that PCI on top of optimal medical therapy did not improve clinical outcome compared to optimal medical therapy alone in patients with stable CAD.[23] However, in the nuclear substudy of the COURAGE trial,[24] the role of myocardial perfusion imaging in identifying subsets of patients with stable CAD with ischemia and changes in ischemic burden following treatment was explored. The main finding was that following treatment, the reduction in percentage ischemic myocardium was greater for PCI plus optimal medical therapy in high-risk patients (≥10% of jeopardized myocardium) compared to optimal medical therapy alone. The authors concluded that these data support myocardial perfusion imaging (stress imaging) as an effective guide to identify patients likely to benefit from PCI (treatment target of ≥5% ischemia reduction).

Stress echocardiography can help clinical decision making by identifying which patients have thresholds of severe ischemia (pWMSI > 1.7) to warrant revascularization. In fact, the underuse of noninvasive testing to document ischemia prior to elective PCI has recently been called into question.[25] Stress echocardiography may serve an important role in the selection of patients for coronary angiography within a strategy based on the identification of patient benefit. Physiologic data from stress echocardiography also have superior clinical impact for revascularization decision making compared to visually defined coronary anatomy.

Study Limitations

This study was retrospective and observational. We have previously demonstrated that stress echocardiographic findings provide incremental prognostic information to baseline clinical parameters,[12,13] but we did not include this analysis in the current report. The prognostic analysis of the study was limited by the study population. Among the 3121 patients included in this study, 2072 (66.4%) had normal responses to stress (pWMSI, 1.0). There were only 159 coronary events (1.8% per year) during the follow-up period. Thus, the study combined analysis of exercise and dobutamine (selection bias with higher percentage of studies) stress echocardiography because of the limited number of hard events. This was probably acceptable, because patients could be individually risk-stratified (abnormal vs normal) by either exercise or dobutamine stress echocardiography. Ejection fraction was not calculated but only visually estimated. A 16-segment model[9] of the left ventricle was used rather than the later proposed 17-segment model, which has an additional apical segment.[26]

The patients in this study were typical in terms of age, gender, and risk factors of a population referred for testing at a tertiary care hospital, and the results may be generalizable to this setting. The subjective nature of wall motion analysis and its dependence on the expertise of the observer presents a limitation with respect to the extrapolation of our results to those of other institutions.[27-29] The referral of patients to coronary angiography and revascularization was subject to referral bias of the practicing physicians. This study did not include a cost analysis of a conservative medical approach compared with catheterization and potential revascularization.

CONCLUSIONS

This study reaffirms the prognostic value of stress echocardiography for risk stratification. The results of this study suggest that referral to coronary angiography and revascularization was proportional to the extent and severity of stress echocardiographic results and their risk for cardiac events. Stress echocardiography can serve as an effective gatekeeper by accurately identifying low-risk patients and appropriately directing the use of invasive procedures. Patients with markedly abnormal stress echocardiographic results (pWMSI $>$ 1.7) were at highest risk for cardiac events and were importantly most likely to benefit from coronary revascularization. Given limited health care resources, the effect of stress echocardiography on patient management and outcomes is important and appropriate.

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