Prognosis in Women With Myocardial Ischemia in the Absence of Obstructive Coronary Disease

Results From the National Institutes of Health–National Heart, Lung, and Blood Institute–Sponsored Women's Ischemia Syndrome Evaluation (WISE)

B. Delia Johnson, PhD; Leslee J. Shaw, PhD; Steven D. Buchthal, PhD; C. Noel Bairey Merz, MD; Hee-Won Kim, PhD; Katherine N. Scott, PhD; Mark Doyle, MD; Marian B. Olson, MS; Carl J. Pepine, MD; Jan den Hollander, MD; Barry Sharaf, MD; William J. Rogers, MD; Sunil Mankad, MD; John R. Forder, PhD; Sheryl F. Kelsey, PhD; Gerald M. Pohost, MD

Background—We previously reported that 20% of women with chest pain but without obstructive coronary artery disease (CAD) had stress-induced reduction in myocardial phosphocreatine–adenosine triphosphate ratio by phosphorus-31 nuclear magnetic resonance spectroscopy (abnormal MRS), consistent with myocardial ischemia. The prognostic implications of these findings are unknown.

Methods and Results—Women referred for coronary angiography for suspected myocardial ischemia underwent MRS handgrip stress testing and follow-up evaluation. These included (1) n=60 with no CAD/normal MRS, (2) n=14 with no CAD/abnormal MRS, and (3) n=352 a reference group with CAD. Cardiovascular events were death, myocardial infarction, heart failure, stroke, other vascular events, and hospitalization for unstable angina. Cumulative freedom from events at 3 years was 87%, 57%, and 52% for women with no CAD/normal MRS, no CAD/abnormal MRS, and CAD, respectively ($P<0.01$). After adjusting for CAD and cardiac risk factors, a phosphocreatine–adenosine triphosphate ratio decrease of 1% increased the risk of a cardiovascular event by 4% ($P=0.02$). The higher event rate in women with no CAD/abnormal MRS was primarily due to hospitalization for unstable angina, which is associated with repeat catheterization and higher healthcare costs.

Conclusions—Among women without CAD, abnormal MRS consistent with myocardial ischemia predicted cardiovascular outcome, notably higher rates of anginal hospitalization, repeat catheterization, and greater treatment costs. Further evaluation into the underlying pathophysiology and possible treatment options for women with evidence of myocardial ischemia but without CAD is indicated. **(*Circulation*. 2004;109:2993-2999.)**

Key Words: prognosis ■ women ■ cost-benefit analysis ■ magnetic resonance imaging ■ spectroscopy

Women with signs and symptoms of myocardial ischemia in the absence of obstructive coronary artery disease (CAD) remain a challenge to clinicians. Women present more often than men for the evaluation of chest pain symptoms,[1,2] and half of all women with chest pain undergoing coronary angiography do not have CAD, compared with 17% of men.[2] Comparative data reported over the past 2 decades indicate that this false-positive rate among women has not declined.[2] Gender differences in symptomatic presentation are complex and not well understood, but prior data suggest that symptoms may be equally predictive of adverse prognosis in women and men.[3] These data, combined with the predominance of women with cardiac Syndrome X (signs and symptoms of myocardial ischemia in the absence of CAD), suggest that a female-specific disorder, such as microvascular disease, may provide a unifying explanatory pathophysiology for these findings.[4]

Cardiac catheterization is frequent in women, with 534 000 performed in the United States in the year 2001, which is twice the rate of other procedures such as cholecystectomy or

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From the Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pa (B.D.J., M.B.O., S.F.K.); Atlanta Cardiovascular Research Institute, Atlanta, Ga (L.J.S.); Center for Nuclear Imaging Research, University of Alabama at Birmingham (S.B., J.D.H.); Women's Health Program, Cedars Sinai Hospital, Los Angeles, Calif (C.N.B.M.); the University of Florida, Gainesville (H.W.K., C.J.P., K.N.S.); Veterans Affairs Medical Center, Gainesville, Fla (K.N.S.); Rhode Island Hospital, Providence (B.S.); the University of Alabama at Birmingham Medical Center, Birmingham (W.J.R.); Western Pennsylvania Allegheny Hospital, Pittsburgh (S.M.); and Keck School of Medicine, University of Southern California, Los Angeles (J.R.F., G.M.P.).

Correspondence to Gerald M. Pohost, MD, Division of Cardiovascular Medicine, Keck School of Medicine, University of Southern California, 1355 San Pablo St, AHC 117, Los Angeles, CA 90089-9231. E-mail Pohost@usc.edu

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hip fracture reduction/replacement.[2,5] It is estimated that the excessive rate of angiographically nonobstructive coronary arteries in women undergoing coronary angiography results in an expenditure of more than $280 million annually. This does not include the costs of continued medical evaluation and care for the 50% of women found to have nonobstructed coronary arteries but who continue to have persistent or worsening symptoms, test abnormalities, and disability.[6]

Recent innovations in the application of phosphorus-31 nuclear magnetic resonance spectroscopy (MRS) have provided a means for monitoring changes in the myocardial high-energy phosphates phosphocreatine (PCr) and adenosine triphosphate (ATP) after stress. We have previously reported a transient decrease in myocardial PCr/ATP ratio during handgrip exercise (abnormal MRS) in 20% (7 of 35) of women with chest pain but no CAD.[7] Evidence of reduced high-energy phosphates suggests a shift toward anaerobic metabolism or myocardial ischemia.[7] The myocardial PCr/ATP ratio at rest has been shown to predict cardiovascular death in patients with dilated cardiomyopathy.[8] The prognostic implications of these findings among women without CAD are unknown. The aim of the present report is to evaluate whether an abnormal MRS predicts cardiovascular outcome in symptomatic women without CAD.

Methods

Study Population

The study population consisted of participants in the Women's Ischemia Syndrome Evaluation (WISE), 74 without CAD undergoing MRS, and a reference group of 352 WISE women with CAD (≥50% stenosis in ≥1 coronary artery). Among the reference women with CAD, 13 underwent MRS. WISE is a National Heart, Lung, and Blood Institute–sponsored, 4-center study of women undergoing clinically ordered coronary angiography for chest pain or suspected myocardial ischemia.[1] A small subpopulation of WISE women from two of the sites (University of Florida, Gainesville; University of Alabama at Birmingham), without contraindication for MRI and primarily without CAD were asked to participate in the MRS study. All subjects provided informed consent by using forms and procedures in accordance with institutional guidelines and approved by the institutional review board at each WISE clinical site.

Baseline Evaluation

Extensive baseline data were collected, including CAD risk factors, clinical history, and laboratory variables. All angiograms were quantitatively evaluated by the WISE angiographic core laboratory that scored each angiogram on a coronary disease severity index, based on stenosis severity weighted by proximal location.[9] The complete design and methodology of the WISE study have been previously described.[1]

Phosphorus-31 MRS

Studies were performed on a 1.5-T Philips Gyroscan ACS or General Electric Signa MR spectrometer. A 10-cm, transmit-receive surface coil was positioned over the heart. An image-selective in vivo spectroscopy (ISIS) sequence[10] was used in the Philips system and the oblique depth-resolved spectroscopy (DRESS)[11] with a modified FIDCSI sequence from a 25-mm-thick slice was used in the General Electric system. MRS data were acquired from a region that maximized signal from the heart muscle while minimizing that from skeletal muscle. Each spectrum consisted of 128 averages, with a repetition time of every third heartbeat.

After obtaining a spectrum at rest, a spectrum was obtained with the patient exercising by isometric squeezing of a hydraulic or mechanical handgrip at 30% of predetermined maximum effort. Work output was monitored. MRS data acquisition commenced 1 minute after onset of exercise. After a 3-minute rest period, 2 postexercise recovery spectra were obtained. Blood pressure and pulse rate were measured every 2 minutes. Spectroscopy data were quantified by the Fitmasters computer program (Philips Medical Systems), which fits spectral raw data in the time domain.[12] Data from the GE platform were converted (using NMR-1) to a format that the Fitmasters program could analyze. The PCr/ATP ratios were corrected for T_1 differences and for blood pool contamination.

Follow-Up Procedures

Follow-up was conducted by telephone interview at 6 weeks and then yearly thereafter. Follow-up consisted of a scripted interview by an experienced nurse or physician. Because of the experimental nature of MRS ^{31}P spectroscopy, the patients, study nurses, physicians, and the patients' referring physicians were not informed of the MRS results. Each patient was queried for the occurrence of cardiovascular events and hospitalizations. Patients were also asked for detailed information on repeat angiograms and myocardial revascularization procedures, current medication use, comorbid conditions, and a description of any recurrent symptoms. The median follow-up time was 36.5 months. Freedom from events was defined as absence of death, myocardial infarction, congestive heart failure, stroke, other vascular events, or hospitalization for unstable angina. "Other vascular events" included hospitalization for peripheral artery disease, and so forth, but not cardiovascular procedures such as revascularization. When a major cardiovascular event was identified, the referring physician was contacted for confirmation, dates, and documentation of the occurrence. In the event of death, a death certificate was obtained.

Statistical Analysis

MRS results were expressed as percent change of the PCr/ATP ratio from rest to handgrip stress. Additionally, on the basis of our pilot study findings,[7] a decrease in the PCr/ATP ratio of ≥20% was defined as abnormal, regardless of the actual rest or stress values.

Because of skewed distributions, continuous variables were expressed as medians and interquartile ranges, and probability values were derived from the nonparametric Wilcoxon rank-sum test. Categorical measures were expressed as percentages, and probability values were obtained by χ^2 or Fisher exact tests where appropriate.

The Duke Activity Status Index (DASI), completed at baseline, year 1, and year 2, was scored to yield a predicted maximal oxygen consumption (or $\dot{V}$Omax)[13] and divided by 3.5 to estimate peak metabolic equivalents (METs). We compared the DASI-derived scores among 3 groups (no CAD/normal MRS, no CAD/abnormal MRS, and CAD reference) by using the nonparametric Kruskal-Wallis test.

The Kaplan-Meier method was used to compare the 3-year freedom from events rate among the same 3 groups (no CAD/normal MRS, no CAD/abnormal MRS, CAD reference). With the use of stepwise procedures, multivariable Cox proportional hazards regression models, which included risk factors, clinical history, and laboratory variables, were developed to estimate freedom from events. Untransformed values as well as logarithmic transformations were entered for variables violating the normality assumption. Participants without a cardiovascular event were censored at either 3 years or the last date of follow-up before 3 years.

Cost Analysis

Detailed resource utilization was assessed by tracking clinical outcomes, major cardiovascular procedure use, and medication use. Costs were calculated as median global charges, adjusted by median (urban and rural) state-specific, cost-charge ratios[14] and supplemented by available published cost data.[15–17] Redbook prices were used to estimate medical therapy costs.[18] Diagnostic costs included MRS (using charges for MRS) and coronary angiography. Follow-up costs included the use of antiischemic or risk factor modification drug therapy, coronary revascularization procedures, and cardiovas-

TABLE 1. Demographic and Risk Factor Characteristics by Diagnostic Category

Characteristic	No CAD/Normal MRS (−18.5 to +22.8) (n=60)	No CAD/Abnormal MRS (−20.6 to −49.6) (n=14)	CAD (n=352)	P*
Age, y	56 (50–63)	57 (48–65)	64 (54–71)†	0.72
CAD severity score	5.0 (5.0–7.0)	5.0 (5.0–11.2)	23.8 (14.2–36.5)	0.45
Maximum % stenosis	0 (0–34)	0 (0–30)	79 (62–100)	0.63
<20% Stenosis, %	63	64	0	0.91
Body mass index ≥30, %	30	50	38	0.21
Diabetes mellitus, %	18	7	38‡	0.44
History of hypertension, %	59	36	68§	0.11
Family history of CAD, %	78	43	67	0.02
History of dyslipidemia, %	49	25	69‡	0.13
Ever smoked, %	48	78	56	0.04
Prior HT use, %	66	86	44†	0.20
Current HT use, %	52	64	32‡	0.43

Medians (interquartile ranges) or percent. HT indicates hormone therapy.

*P values comparing no CAD/normal MRS vs no CAD/abnormal MRS, with Wilcoxon rank-sum tests used for continuous measures, and χ^2 or Fisher exact tests for categorical variables.

Comparing CAD vs no CAD: †$P<0.0001$; ‡$P<0.001$; §$P<0.05$.

cular-related hospitalizations. Societal economic cost for cardiac death was based on nationwide average hospitalization estimates.[15] Total costs were calculated as the sum of diagnostic and follow-up costs and were age-adjusted. All costs were inflation-corrected to year 2002, using rates set by the Medicare Trust Fund,[19] and discounted at an annual rate of 5%. Cost data were compared among groups by using a nonparametric Kruskal-Wallis statistic. Sensitivity analysis was used to vary the cost for chest pain admissions within a range of $5956 to $14 660.[13,15]

Results

Population Characteristics

The median age of the women undergoing MRS was 56 years, and 22% were racial minorities, primarily black. Although only 15% of the women had CAD, 49% had 2 or more risk factors including diabetes (17%), hypertension (55%), a family history of coronary disease (72%), dyslipidemia (52%), a history of smoking (54%), and obesity (median body mass index, 27.7). When compared with the reference WISE women with CAD (Table 1), members of the MRS population without CAD were significantly younger (56 versus 64 years, $P<0.0001$) and had lower rates of diabetes (16% versus 38%, $P=0.0002$), hypertension (55% versus 68%, $P=0.02$), and dyslipidemia (45% versus 69%, $P=0.0002$). They also had a significantly higher frequency of hormone therapy use (70% versus 44%, $P<0.0001$).

Among women without CAD, 14 of the 74 women (19%) had an abnormal PCr/ATP decrease of ≥20% (Table 1). Women with abnormal MRS were more likely to be smokers (78% versus 48%, $P=0.04$) and less likely to have a family history of premature coronary disease (43% versus 78%, $P=0.02$) than those with normal MRS. They did not differ in angiographic CAD severity, age, menopausal status, racial or socioeconomic variables, self-reported stress levels, or other CAD risk factors, although they tended to have a lower prevalence of diabetes, hypertension, and dyslipidemia (P=NS).

Despite the use of handgrip stress (a mild stressor), a 42% increase in rate-pressure product was observed during testing. However, there were no significant differences in heart rate, blood pressure, or rate-pressure product among women with normal versus abnormal MRS. Reproductive hormones (estrone, estradiol, progesterone, luteinizing hormone, follicle-stimulating hormone, n=70), lipids (total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, n=68), and inflammatory markers (high-sensitivity C-reactive protein and interleukin-6, n=60) were measured in a majority of patients undergoing MRS but were not related to percent change in PCr/ATP ratio after handgrip stress or binary classification of normal versus abnormal MRS.

Functional Status Outcomes

DASI-predicted METs at baseline were 5.9, 5.3, and 4.7, respectively, for women with no CAD/normal MRS, no CAD/abnormal MRS, and CAD reference ($P=0.09$). During the follow-up period, DASI-predicted METs among women with no CAD/abnormal MRS were more similar to women with CAD (P=NS) than to women with no CAD/normal MRS (Figure 1). At year 1, women with no CAD/normal MRS had functional capacity measures ≈1 MET ($P=0.11$) higher than women with CAD or an abnormal MRS, a difference that increased to 1.8 METs by year 2 ($P=0.02$).

Cardiovascular Outcomes

Among the 74 women without CAD undergoing MRS, a total of 14 (19%) had a cardiovascular event during the 3 years of follow-up. These included no deaths, no myocardial infarctions, 1 heart failure admission, no cerebrovascular accidents, 2 other vascular events (hospitalization for peripheral thrombosis, carotid endarterectomy), and 12 unstable angina admissions.

Figure 2 plots the freedom-from-event rates for the 3 groups. Women with no CAD/normal MRS had the highest

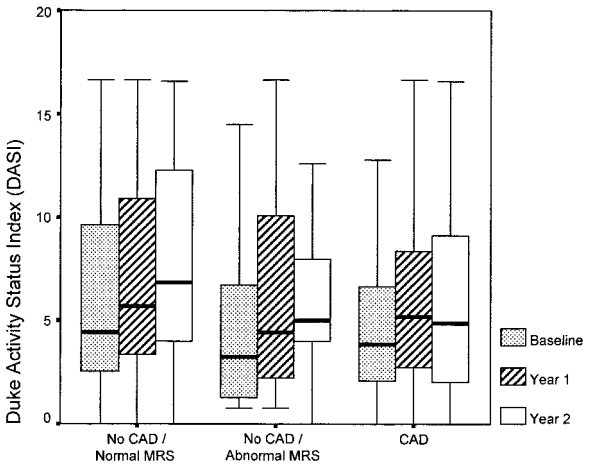

Figure 1. Estimated METs, based on the DASI, by diagnostic category.

cumulative 3-year freedom from event (87%). Women with no CAD/abnormal MRS and WISE reference women with CAD had significantly poorer freedom-from-events rates (57%, $P=0.009$ and 52%, $P<0.0001$, respectively). Freedom-from-event rates were similar for women with no CAD/abnormal MRS and WISE reference women with CAD (57% versus 52%, $P=0.42$). Detailed analysis of events (Table 2) reveals that the most frequent cardiovascular event was hospitalization for unstable angina. In the population of women with chest pain but without CAD, there were no deaths, myocardial infarction, stroke, or coronary bypass surgery. However, those with abnormal MRS had a higher rate of hospitalization for angina (36% versus 12%, $P<0.05$) and repeat angiography (21% versus 3%, $P<0.05$) compared with those with normal MRS. These rates were comparable to those of WISE reference women with CAD (34% and 30%, respectively, $P=$NS).

Multivariate Cox proportional hazards models (Table 3), calculated for all women undergoing MRS (including 13 with CAD), demonstrate that the percent change in PCr/ATP ratio after handgrip stress was a significant independent predictor of cardiovascular events ($P=0.02$). The risk ratio of 0.96 in the linear model means that, after controlling for the presence of CAD and cardiac risk factors, a PCr/ATP decrease of 1% increased the risk of a subsequent cardiovascular event by 4%

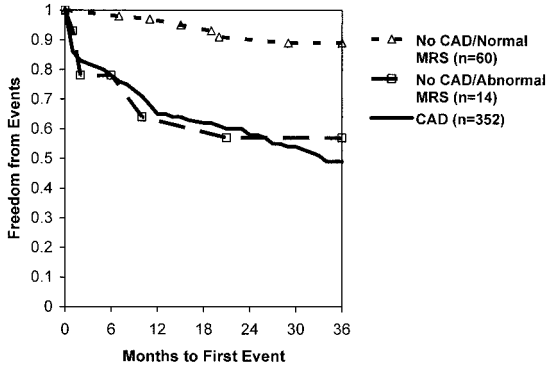

Figure 2. Freedom from events by diagnostic category.

($P=0.02$). Other independent predictors included the presence of CAD ($P<0.0001$) and (log) serum triglyceride levels ($P=0.04$). Age, hyperlipidemia, hypertension, diabetes, cigarette smoking, obesity, a family history of premature CAD, typical angina or frequency of chest pain symptoms at baseline, nitrate consumption, and DASI-predicted METs were not statistically significant. A log-linear transformation of %PCr/ATP change was a better fit of the relation between MRS results and events ($P=0.001$). Figure 3 indicates an accelerating risk beyond a PCr/ATP change score of −20%. The strong statistical relation between PCr/ATP change was not altered when adding or eliminating the other potential explanatory or confounding variables listed above, thus indicating a robust relation.

Cost Outcomes

As expected, the WISE reference women with CAD had significantly higher 3-year total costs, including antiischemic therapy, revascularization, and cardiovascular events (Table 4) compared with those without CAD ($P<0.0001$). However, for women with no CAD/abnormal MRS, the cardiovascular event costs were similar to those with CAD ($11 102 versus $14 495, $P=$NS), and total costs ($16 975) were intermediate between those with no CAD/normal MRS ($7995) and those with CAD ($34 836, $P<0.0001$). Sensitivity analysis revealed that this difference in total costs was a result of higher rates of hospitalization for unstable angina and depended on the cost estimate for unstable angina.[13,15] Women with no CAD/abnormal MRS were 3 times more likely to have "typical angina" (versus atypical, nonanginal, or no symptoms) by year 3 compared with women with no CAD/normal MRS and 4.5 times more likely than women with CAD (36%, 12%, 8% respectively, $P=0.04$). These women also had a higher rate of nitroglycerin use than those with no CAD/normal MRS and those with CAD (36%, 7%, and 25%, respectively, $P=0.003$).

Discussion

Women without angiographic CAD but with persistent anginal symptoms present a challenge for diagnosis and treatment. Tests that suggest myocardial ischemia have typically included ECG, myocardial perfusion imaging, and ventricular function studies,[20] often with limited utility due to technical artifacts specific to women. Cardiovascular MRS provides a new strategy for evaluating women with myocardial ischemia. We have previously noted that ≈20% of women with suspected ischemia in the absence of CAD had evidence of abnormal stress-induced myocardial high-energy phosphate metabolism measured by MRS.[7] The current analysis reveals that such women continue to have persistent symptoms leading to increased rehospitalization, repeat coronary angiography, and greater functional limitations over a 3-year follow-up evaluation, with associated increased healthcare costs. This is true despite the similarity in coronary disease risk factor profiles among women with abnormal and normal MRS.

Our working hypothesis is that in women without CAD, an abnormal MRS PCr/ATP response to exercise stress indicates a shift toward greater reliance on anaerobic metabolism consistent with myocardial ischemia. Prior MRS studies have

TABLE 2. Type of Cardiovascular Event by Diagnostic Category

Event Rate (%) at Median 36.5 Months of Follow-Up	No CAD/Normal MRS (n=60)	No CAD/Abnormal MRS (n=14)	CAD (n=352)
Death	0	0	37 (10)‡
Myocardial infarction	0	0	16 (4)
Angina hospitalization	7 (12)	5 (36)§	121 (34)‡
Congestive heart failure	1 (2)	0	22 (6)
Cerebrovascular accident	0	0	11 (3)
Other vascular*	1 (2)	1 (7)	15 (4)
Repeat angiography	2 (3)	3 (21)§	106 (30)‡
PCI	1 (2)	1 (7)	91 (26)‡
CABG	0	0	50 (14)‡
Cardiac surgery	0	0	11 (3)
Any cardiovascular event†	8 (13)	6 (43)§	168 (48)‡

No. (%) of women with cardiovascular events.

*Includes peripheral thrombosis, carotid endarterectomy, transient ischemic attack, and so forth.

†Includes death, myocardial infarction, congestive heart failure, stroke, angina hospitalization, or other vascular event.

‡$P<0.01$, §$P<0.05$ compared with no CAD/normal MRS by χ^2 analysis (or Fisher exact test, where appropriate).

found increased prevalence of abnormal high-energy phosphate metabolism in patients with demonstrated illness, including transplanted hearts and resulting vasculopathy,[21] type I diabetes,[22] valvular disease, and hypertrophic cardiomyopathy.[23] MRS can only evaluate the anterior myocardium; microvascular and metabolic dysfunction is considered a diffuse process and can therefore be captured by interrogation of the anterior myocardium. In women without CAD, the presence of abnormal MRS metabolism suggests that a metabolic dysfunction may be responsible for the signs and symptoms found in these patients.

We found that a large reduction in the PCr/ATP ratio after stress was a significant predictor of poor cardiovascular outcomes, independent of the presence of CAD and CAD risk factors. Although several studies have demonstrated a relation between metabolic abnormalities and the degree of heart failure,[23] our results found no deaths or hospitalizations for myocardial infarction in patients without CAD but abnormal MRS.

In this cohort of WISE women with chest pain and no CAD/abnormal MRS, usual care treatment strategies were not effective for controlling angina pectoris. These women had higher rates of typical angina at follow-up, higher rates of recatheterization, higher rates of rehospitalization for unstable angina, and greater use of nitroglycerin compared with women with no CAD/normal MRS. This higher rate of refractory angina pectoris also led to higher costs for the care of these women. The current study results demonstrate other "costs" to this condition, for example, poor functional capacity (METs) that deteriorated over time. With the self-reported poor functional capacity of these women, even low levels of physical stress (such as handgrip stress) were capable of precipitating myocardial ischemia.

MRS provides a direct clinical means for measuring metabolism, thereby differing from positron emission tomography (^{18}F/perfusion imaging), single-photon emission computed tomography (myocardial perfusion imaging), echocardiography (imaging of change in regional ventricular function), or other noninvasive measures to detect secondary consequences of ischemia.[24] Although flow reductions, inducible perfusion, or wall motion abnormalities have been correlated with prognosis in large cohorts of symptomatic women despite a low frequency of CAD,[25–28] results have tended to be inconsistent. Some investigators have therefore

TABLE 3. Independent Predictors of Cardiovascular Events Among All WISE Women With MRS Testing (n=87)

Predictor	Hazard Ratio	95% Confidence Intervals	*P*
Linear model			
% PCr/ATP change	0.96	0.93–0.99	0.02
Coronary artery disease	7.06	2.79–17.91	<0.0001
Triglycerides (log)	2.62	1.18–5.84	0.04
Logarithmic model			
Log % PCr/ATP change	0.12	0.04–0.44	0.001
Coronary artery disease	7.50	2.92–19.30	<0.0001
Triglycerides (log)	2.99	1.31–6.81	0.009

Cox proportional hazards modeling was used.

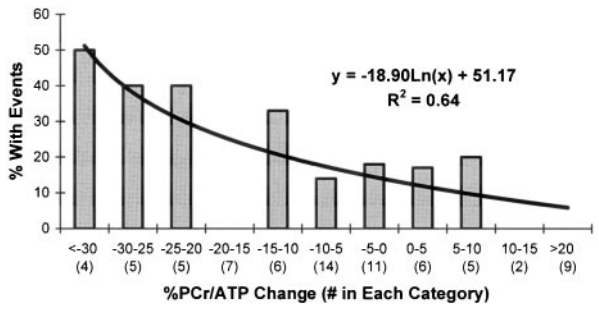

Figure 3. Percentage of women with a cardiovascular event by %PCr/ATP change.

TABLE 4. Age-Adjusted Median Costs of Care at Diagnosis, Medication Costs, and Follow-Up Procedure and Hospitalization Costs by Diagnostic Category

	No CAD/Normal MRS (n=60)	No CAD/Abnormal MRS (n=14)	CAD (n=352)
Baseline costs			
Diagnostic tests	$1717	$ 1717	$ 844
Additional baseline	$4705	$ 4344	$ 4148
Follow-up medication costs			
Antiischemic therapy	$1386	$ 1195	$ 9483
Risk factor treatment	$2399	$ 2571	$ 2920
PCI or CABG	$1041	$ 1543	$ 9459
Cardiovascular event*	$1995	$11 102	$14 495
Total cost	$7995	$16 975	$34 836

*Includes coronary revascularization procedures and cardiovascular-related hospitalizations.

postulated alternative explanations to ischemia for chest pain in women in the absence of CAD. For example, exercise-associated angina pectoris has been ascribed to an increased sensitivity to pain in these women.[29] On the basis of current findings, MRS appears to provide a more sensitive means for detecting ischemia provoked by low levels of stress such as the handgrip used in the present study.

Study Limitations and Potential Solutions

The challenges with the present study include a low level of stress (handgrip exercise at 30% capacity), low strength of the magnet field, and limited sample size. The use of handgrip has become standard practice with ^{31}P studies of the myocardium to induce stress within the limited space of the magnet bore. However, this mild stress stimulus may limit the intensity of myocardial ischemia associated with epicardial coronary artery disease, although it may still reveal those with coronary microvascular dysfunction (which we anticipate to be more diffuse). We have found that women with substantial PCr/ATP decrease using handgrip had worse outcomes than those without such a decrease, independent of angiographic results. In future studies, the use of dobutamine would be anticipated to generate a greater level of stress and make ^{31}P results more sensitive to epicardial and microvascular disease. As a second limitation, our studies were performed at 1.5-T field strength, which is currently being replaced in general use by more powerful magnets. MRS studies at higher ($\geq$3 T) field strengths will improve the spectral resolution and will permit estimation of myocardial P_i resonance and intracellular pH to provide additional confirmation of myocardial ischemia. Finally, the current sample is too small to detect differences in CAD risk factors or in "hard" events such as cardiovascular death or nonfatal myocardial infarction. On the basis of the sample of 60 women with normal MRS versus 14 with abnormal MRS, the cumulative freedom-from-events rates of 0.87 and 0.57, respectively, could be detected with 87% power at a 2-tailed α level of 0.05. The prognostic value of MRS was confirmed despite low statistical power.

The fact that studies were performed on two different platforms should not affect the results. Although partial-volume errors would be anticipated to be different between the two platforms, our data consist of ratios between PCr and ATP. Potential differences between the two approaches would be constant and therefore the ratios are comparable.

Conclusions

Among women with suspected myocardial ischemia in the absence of CAD, the MRS cardiac stress test was able to identify women who were more likely to have persistent and often worsening angina requiring catheterization and hospitalization, resulting in greater functional limitations and higher healthcare costs. These results are consistent with an underlying female-specific disorder, such as microvascular disease, as an underlying cause for the persistent symptoms in these women. Although our current sample is relatively small, our results suggest that MRS can have wide utility in evaluating women with chest pain and reducing the number of women undergoing repeat coronary angiography.

Acknowledgments

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