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The Stress-Recovery Index for the risk stratification of women with typical chest pain

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Abstract

Aim: To prospectively assess the prognostic value of the Stress-Recovery Index (SRI) in women with typical chest pain.
Methods: 165 women without known coronary artery disease, who complained of typical chest pain, were exercise tested and prospectively followed-up for the occurrence of cardiac death and nonfatal myocardial infarction. SRI, defined as the difference in absolute values between the area of heart rate-adjusted ST-segment depression during exercise and recovery, was derived in all. Clinical data, resting ejection fraction, and exercise testing data were entered into a sequential Cox's model; SRI was entered last. Model validation was performed by bootstrap adjusted by the degree of optimism in estimates. Survival curves were set up using Kaplan–Meier method and compared by the log-rank test.
Results: During a median follow-up time of 42 months, 19 events (14 cardiac deaths and 5 nonfatal myocardial infarction) were observed. Age (hazard ratio 3.58, 95% CI 0.87–15) and SRI (hazard ratio 0.62, 95% CI 0.42–0.92) were multivariate predictors of outcome. However, the addition of SRI increased the prognostic power of the model on top of clinical and exercise testing variables, as demonstrated by the significant ($p=0.003$) increase of the area under the ROC curve of the risk function. Survival analysis showed ascending SRI quartiles to identify a significant ($p=0.005$) increase in event-free survival.
Conclusions: SRI is of value in predicting outcome of women with typical chest pain and provides additional prognostic information on the top of clinical and standard exercise testing data.

Keywords: Exercise electrocardiography; Coronary artery disease; Stress testing; Risk stratification in women

1. Introduction

Cardiovascular disease is the leading cause of death among women in the majority of industrialized countries, accounting for the 54% of all cardiovascular deaths in the United States [1]. Cardiovascular mortality among women has been continuously increasing during the last decades; the 49% of this mortality is due to coronary artery disease (CAD) [1]. Moreover, one in nine women between the ages of 45 to 64 and one in three women over 65 years complains of symptoms potentially related to a cardiovascular disease [2]. However, women frequently have more atypical symptoms than men, tend to present late in the process of their disease, and are also less likely to have appropriate diagnostic work-up. Therefore, early recognition of CAD and accurate noninvasive assessment may be the first step towards improving the outcome for at-risk women. Unfortunately, previous research using noninvasive cardiac testing has noted limitations when applied to female subsets of the population. In particular, although exercise electrocardiography (ECG) represents the most popular modality for the noninvasive evaluation of CAD, it is recognized that exercise-induced ST segment depression has less diagnostic value in women than in men, mainly due to high rate of false positive results [3,4]. The diminished diagnostic and prognostic accuracy with noninvasive testing modalities

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have lead to the concept of a sort of sexual discrimination in the use and interpretation of stress testing in women [5]. In addition, due to the limited value of exercise ECG, interest has grown in the use of more expensive and less generally available imaging techniques for assessing CAD in the female population [6].

The Stress-Recovery Index (SRI) has been proposed to improve the diagnostic accuracy of exercise ECG [7]. In addition, it has been shown to provide prognostic information outperforming that of standard ST-segment depression criteria in a variety of clinical settings [8–11]. The aim of the present study was to verify whether SRI may improve the prognostic accuracy of exercise ECG in women complaining of typical chest pain suggestive of myocardial ischemia.

2. Methods

2.1. Study population and standard definitions

The study population consisted of 165 consecutive women with unknown CAD who underwent exercise ECG testing to verify the ischemic origin of a typical chest pain [12]. An informed consent to participate in the study was obtained by all patients before enrolling. The study protocol was approved by the local institutional Ethical Committee.

Hypertension was defined as resting systolic blood pressure >140 mm Hg, resting diastolic blood pressure >90 mm Hg, or treatment with antihypertensive drugs [13]. Diabetes mellitus was diagnosed according to World Health Organization criteria [14]. Hypercholesterolemia was defined as plasma total cholesterol >6.2 mmol/L [15], or treatment with cholesterol-lowering drugs. Resting ejection fraction was obtained by two-dimensional echocardiography using standard methods [16].

Outcome was determined from patient interview, hospital chart reviews and telephone interviews with the patient, his close relative or his referring physician, if necessary. Cardiac mortality and nonfatal myocardial infarction were the elected end points. Death was defined as cardiac if strictly related to proven cardiac causes (fatal myocardial infarction, heart failure resistant to full therapy or malignant arrhythmias) or if sudden and unexpected when occurring outside the hospital. Myocardial infarction was diagnosed according to the international guidelines [17]. The end points were assessed by external reviewers who were unaware of the study hypothesis.

2.2. Exercise ECG test and SRI determination

Exercise testing was performed on an upright, electromagnetically braked cycle ergometer with 25 W incremental loading every 2 min. The 12-lead ECG was continuously monitored throughout the test for rhythm, rate and ST-segment changes using the Mason–Likar exercise adaptation. Blood pressure was measured by arm-cuff sphygmomanometry during the last 30 s of each work stage. Exercise was continued until chest pain, repetitive arrhythmias, significant conduction abnormalities, ST-segment depression >0.3 mV, systolic blood pressure above 230 mm Hg or its drop >20 mm Hg or limiting symptoms (dyspnoea, dizziness, fatigue, cramp in legs) occurred. After exercise, patients recovered in a sitting position. Total work performed (kiloponds per minute) indicated the exercise capacity of the patient. ST-segment deviation was measured 60 ms after the J point using the end of P–R segment as a reference. ECG response was defined as positive in case of horizontal or downsloping deviation >0.1 mV in at least 2 contiguous leads. The ST/Heart Rate (ST/HR) Index was calculated to obtain standard heart rate adjustment of ST-segment depression during exercise only [18].

Beta-blockers and calcium-antagonists were discontinued for at least 5 half-lives before testing; no patient was taking nitrates. Angiotensin-converting-enzyme inhibitors and AT_1 receptor blockers were not withdrawn.

Details on SRI determination have been extensively described elsewhere [7,10]. Briefly, computer-calculated ST-segment amplitudes were obtained every 12 s during exercise and up to five minutes during recovery. At the end of the test, the area subtended to baseline and limited by the ST-segment trend against heart rate during exercise and recovery was calculated in the lead with the greatest ST-segment depression. SRI was defined as the difference in absolute values between the areas referring to the exercise and recovery phase, respectively.

2.3. Statistical analysis

Continuous variables are presented as median with the corresponding interquartile difference. Categorical variables are presented as absolute number with corresponding percentages. Univariate Hazard Ratios refer to the effect of being in the highest as compared to the lowest quartile for continuous variables or in the category with the highest observed frequency for categorical variables. The individual effect of clinical data, resting ejection fraction and exercise testing results on survival was evaluated by Cox's proportional-hazards regression analysis. Proportional hazard assumption was checked by plotting Schoenfeld results against fitted time and varying coefficients and with the Grambsh and Therneau test [19]. In order to assess whether SRI added prognostic information to routinely obtained information, clinical and exercise testing data were entered first (model 1) and Stress-Recovery Index last (model 2). All variables were entered into the model without any transformation or cutting-off. Nonlinearity was assessed by Wald test comparing higher-order models with that including only linear terms. In case of nonlinearity, a restrictive cubic spline [20] was used to model a nonlinear effect of the covariate. Selection criteria was the Akaike Information Criterion [21] applied backward for each model. Models were cross-validated by bootstrap technique [22]. Somer's concordance Index Dxy (the closer to one in absolute value the better), representing the concordance between predicted and observed outcome adjusted for data censoring, was obtained.

Table 1
Clinical characteristics and exercise testing results

	No event (n=146)	Event (n=19)	Combined (n=165)	Hazard ratio
Age (years)	62 [58, 67]	67 [65, 71]	64 [59, 68]	2.76 [1.57, 4.86]
Diabetes	11 (8%)	0 (0%)	11 (7%)	–
Presently smokers	43 (30%)	4 (21%)	47 (29%)	0.38 [0.09, 1.63]
Hypertension	68 (48%)	16 (84%)	84 (52%)	6.48 [1.88, 22.3]
Hypercholesterolemia	44 (31%)	4 (21%)	48 (30%)	0.70 [0.22, 2.04]
Ejection fraction (%)	55 [50, 60]	55 [50, 60]	50 [55, 60]	1.00 [0.82, 1.23]
Beta-blockers [a]	25 (17%)	5 (26%)	30 (18%)	1.69 [0.64, 4.32]
Ca-antagonists [a]	8 (5%)	1 (5%)	9 (5%)	1.11 [0.74, 2.16]
ACE-inhibitors	46 (32%)	7 (43%)	53 (32%)	1.73 [0.64, 4.79]
AT_1 receptor blockers	2 (1%)	–	13 (8%)	–
Statins	31 (21%)	4 (21%)	35 (21%)	1.02 [0.59, 2.09]
Resting heart rate (beats/min)	73 [62, 84]	76 [66, 85]	74 [62, 84]	1.32 [0.76, 2.29]
Resting systolic blood pressure (mm Hg)	130 [120, 150]	140 [125, 150]	130 [120, 150]	1.36 [0.69, 2.67]
Resting diastolic blood pressure (mm Hg)	80 [80, 90]	80 [80, 90]	80 [80, 90]	1.07 [0.67, 1.70]
Peak heart rate (beats/min)	130 [115, 147]	137 [116, 150]	133 [115, 149]	1.06 [0.53, 2.12]
85% of maximal heart rate achieved	75 (51%)	8 (42%)	83 (50%)	0.53 [0.12, 1.56]
Peak systolic blood pressure (mm Hg)	180 [170, 200]	180 [165, 190]	180 [170, 200]	0.84 [0.51, 1.40]
Peak diastolic blood pressure (mm Hg)	100 [90,105]	100 [95, 107]	100 [90,105]	0.98 [0.56, 1.74]
Exercise capacity (kpm)	1800 [1350, 2456]	1350 [1125, 1912]	1800 [1350, 2400]	0.72 [0.41, 1.26]
Maximal ST-segment depression (mV)	0 [0, 1.4]	1.1 [0, 1.8]	0 [0, 1.5]	1.22 [0.71, 1.63]
Exercise-induced chest pain	42 (30%)	7 (37%)	49 (30%)	1.67 [0.66, 4.26]
ST/HR Index (μV/bpm)	0.0 [0.0, 2.2]	1.5 [0.0, 3.2]	0.0 [0.0, 2.4]	1.79 [1.15, 1.92]
SRI (mV bpm)	−12 [−25, −0.67]	−18 [−64, −5.2]	−12 [−27, −1.0]	0.59 [0.42, 0.83]

Continuous variables are presented as median (first and third quartile in squared brackets). Categorical variables are presented as absolute number (% in brackets). Univariate Hazard Ratios (95% CI in squared brackets) refer to the effect of an interquartile difference for continuous variables and to the category with the highest observed frequency for categorical variables.

[a] Withdrawn before testing.

Multivariate Hazard Ratios are presented with their 95% confidence intervals. Area under receiver-operating-characteristic (ROC) curve [23] of the estimated cumulative hazard functions were compared to provide evidence of significant increase in predictive accuracy of the model after the addition of SRI. Multivariate Hazard Ratios (HR) has been presented along with their 95% confidence intervals (CI).

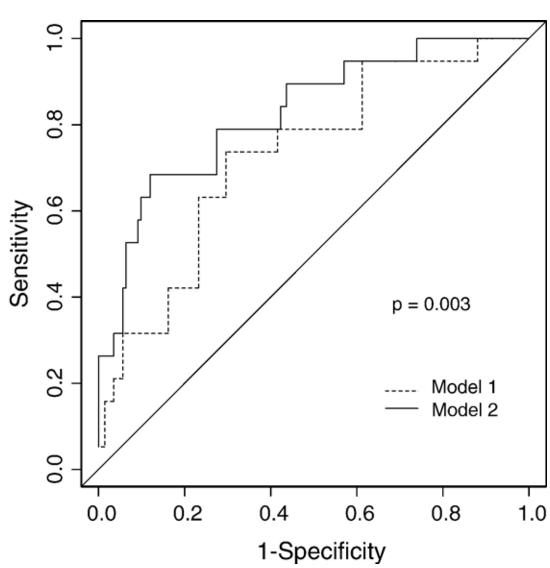

Fig. 1. Comparison of the areas under the ROC curve of model 1 and 2.

Effect of SRI on survival was analyzed using the product-limit Kaplan Meier method.

The statistical significance was settled at a p value < 0.05. S-plus release 6.0 statistical package (Insightful Corporation, Seattle WA, USA), Harrell's Design and Hmisc libraries (http://hesweb1.med.virginia.edu/biostat/s) and GraphPad Prism version 4.00 for Windows (GraphPad Software, San Diego California USA, www.graphpad.com) were used for analysis.

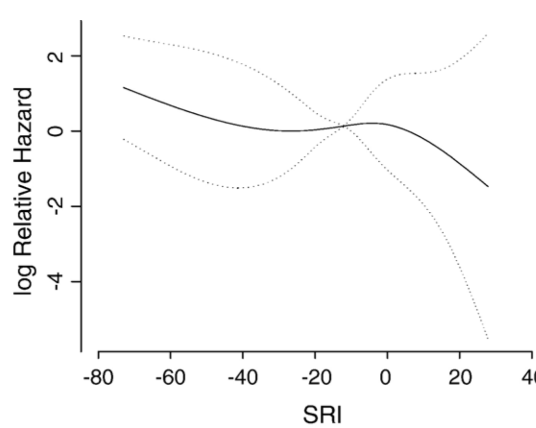

Fig. 2. Effect of SRI on outcome estimated by restricted cubic spline. Dotted lines mark the 95% CI.

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3. Results

3.1. Clinical characteristics and exercise testing results

Clinical characteristics of the study population and exercise testing results are summarized in Table 1. Exercise test was stopped because of muscular fatigue in 132 (79%), orthopedic limitation in 2 (1%), intolerable chest pain in 16 (10%), ST-segment depression >0.3 mV in 9 (6%), excessive increase in blood pressure in 3 (2%), and significant arrhythmias in 3 (2%). No complication was observed. Age-predicted maximal heart rate was achieved in 104 (63%) patients. According to the standard electrocardiographic criteria, 54 (32%) patients had a positive and 111 (68%) a negative test result.

3.2. Follow-up results and outcome prediction

Follow-up information was available in all patients. During a median follow-up time of 42 (1st quartile 29, 3rd quartile 54) months, 19 (12%) target events (14 cardiac deaths and 5 nonfatal myocardial infarction) were observed. A cardiac origin of death was proven in 9 patients (6 fatal infarctions and 3 refractory heart failure), whilst 5 patients died suddenly. Revascularization procedures were performed in 20 (12%) patients.

The univariate effect of clinical and exercise testing data on outcome is reported in Table 1. Multivariate analysis showed that, after adjusting for the significant clinical and exercise testing covariates (model 1), age (hazard ratio 3.58, 95% CI 0.87–15) and SRI (hazard ratio 0.62, 95% CI 0.42–0.92) remained the only variables independently correlated to the outcome (model 2). The addition of the SRI improved the accuracy of the model as demonstrated by the significant ($p=0.003$) increase (from 0.71, 95% CI 0.58–0.83 to 0.82, 95% CI 0.72–0.92) of the corresponding area under the ROC curve (Fig. 1). Similarly, the addition of the SRI increased the discriminating capacity of the model as demonstrated by the change in Dxy Index, that increased by 50% (from 40 to 61).

The effect of SRI on outcome, estimated by restricted cubic spline, is reported in Fig. 2. Negative values are associated with increasing risk of adverse events, whilst positive values predict a favourable long-term outcome. In keeping with previous findings in different populations [9], the flex point of the curve corresponds to a SRI of −15 mV·bpm.

Finally, ascending quartiles of the SRI provided a significant discrimination of the event-free survival (Fig. 3).

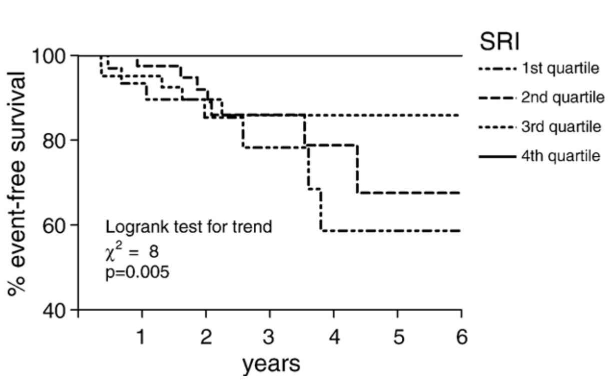

Fig. 3. Kaplan–Meier plots associating SRI by quartiles with event-free survival.

4. Discussion

Despite the efforts of investigators, public health and policymakers, heart disease continues to be the leading cause of death in women throughout most of the world [1]. CAD also is a substantial cause of morbidity and disability for women [24]. An effective diagnostic strategy seems to be critical in women at risk because up to 40% of initial cardiac events are fatal [2]. Noninvasive testing offers the potential to identify women at increased CAD risk and establishes the basis for instituting preventive and therapeutic interventions. As the actual use of myocardial revascularization procedures tends to be sex-neutral and based on the severity of coronary arterial obstruction at angiography [25], the appropriate application of noninvasive testing is pivotal. However, concern still exists about validated gender-neutral testing procedures with equivalent diagnostic accuracies in men and women [5]. American College of Cardiology/American Heart Association (ACC/AHA) exercise testing guidelines suggest that women should undergo exercise testing if they are at an intermediate pretest risk of CAD on the basis of symptoms and risk factors, have a normal resting ECG, and are capable of maximal exercise [26]. Nevertheless, ECG changes during exercise have been reported to be of diminished accuracy in women as a result of complex epidemiological (lower prevalence of CAD and more frequent conditions potentially associated with false positive results, such as syndrome X, mitral valve prolapse, and coronary vasospasm) and physiological (ECG voltage, hormonal fluctuations, and lower exercise ability) factors [5]. In particular, the sensitivity and specificity of ST-segment depression were 61 and 70%, respectively, in a meta-analysis of 19 studies including 3721 women [27].

In the last few years, the SRI has been emerging as a prognostically useful modality for risk stratification in unselected [11] populations as well as in specific subgroups of patients [8–10]. The results of the present study extend these findings to the setting of women with typical chest pain at intermediate risk of CAD, who represent a major target of the use of exercise ECG as primary screening tool in clinical practice. Noteworthy, the SRI was the only parameter, available from exercise testing, independently associated to the outcome. This confirms its potential ability to overcome established limitations of the standard interpretation of exercise ECG, that is expected to be of major help in populations at intermediate level of risk. The pathophysiological rationale of the comparative stress-recovery adjustment of ST-segment depression and the ability of SRI to identify the exercise-induced ischemia with the greatest prognostic potential has been previously discussed [11].

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Besides SRI, age was the only multivariate predictor of outcome in the present study. This is in keeping with the known evidence that, at the time of presentation with heart disease women tend to be 10 years older than men, and at the time of their first myocardial infarction they are usually 20 years older [28]. As CAD is usually considered a disease of the older woman, it is generally believed that women can postpone attempts to reduce their risk. In addition, the diminished diagnostic accuracy with various noninvasive testing modalities when administered to women may lead to a lack of physician confidence and, in turn, to an underuse of available diagnostic procedures.

4.1. Clinical implications

Management of CAD in women has major economical implications. The estimated lifetime cost for women with unknown CAD, who present with symptoms suggestive of myocardial ischaemia, approaches $750,000 in the United States [29]. A substantial proportion of this expenditure is due to recurrent diagnostic procedures either noninvasive or invasive. Though a wide range of diagnostic modalities has become available over the last decades, the accuracy and limitations of stress testing in women patients remains an area of significant confusion. A consistent body of evidence documents that women are less likely than age-matched men to have obstructive CAD; in particular, triple-vessel or left main CAD is more common in men, even though more women than men die from CAD [1,30,31]. Therefore, an anatomy-based treatment strategy is more likely to give inconsistent results in women than in men. Changing from an anatomy-based to a risk-based treatment strategy tailored on the result of noninvasive testing is expected to be more valuable in symptomatic women in whom nonobstructive coronary disease is prevalent as compared to men. The results of the present study suggest that the SRI may have a role in the identification of subsets of women who are at increased risk of major cardiac events and should be referred for an intensive diagnostic and therapeutic program. On the other hand, SRI may allow to identify women at low risk who can be conservatively managed with medical therapy and risk-factor modification, thus avoiding expensive diagnostic procedures and saving economic and organizational resources.

4.2. Study limitations

Some limitations of the present study have to be acknowledged.

The patient population included in the present study presents was specifically selected based on the presence of a typical, angina-like chest pain and presents with somewhat increased risk profile compared to the female population generally undergoing evaluation for the assessment of chest pain. Therefore, our results cannot be extrapolated tout-court to subgroups of patients with different risk profiles.

Information on over time changes of medical treatment was not available in all patients and, consequently, was not evaluated in the statistical model. However, this study was not aimed at broadly assessing the prognostic determinants of women complaining of chest pain, but rather at verifying whether the Stress-Recovery Index could be able to improve the prognostic value of standard exercise ECG analysis in this clinical setting.

References

[1] American Heart Association. Heart and stroke facts. Dallas, Tex: American Heart Association; 2005.

[2] Mosca L, Manson JE, Sutherland SE, Langer RD, Manolio T, Barrett-Connor E. Cardiovascular disease in women. A statement for healthcare professionals from the American Heart Association. Circulation 1997;96:2468–82.

[3] Hlatky MA, Pryor DB, Harrell Jr FE, Califf RM, Mark DB, Rosati RA. Factors affecting sensitivity and specificity of exercise electrocardiography: multivariable analysis. Am J Med 1984;77:64–71.

[4] Kwok YS, Kim C, Grady D, et al. Meta-analysis of exercise testing to detect coronary artery disease in women. Am J Cardiol 1999;83:660–6.

[5] Bigi R, Cortigiani L. Stress testing in women: sexual discrimination or equal opportunity? Eur Heart J 2005;26:423–5.

[6] Mieres JH, Shaw LJ, Arai A, et al. Role of noninvasive testing in the clinical evaluation of women with suspected coronary artery disease: consensus statement from the Cardiac Imaging Committee, Council on Clinical Cardiology, and the Cardiovascular Imaging and Intervention Committee, Council on Cardiovascular Radiology and Intervention, American Heart Association. Circulation 2005;111:682–96.

[7] Bigi R, Maffi M, Occhi G, Bolognese L, Pozzoni L. Improvement in identification of multivessel disease after acute myocardial infarction following stress-recovery analysis of ST depression in the heart rate domain during exercise. Eur Heart J 1994;15:1240–6.

[8] Bigi R, Cortigiani L, Gregori D, De Chiara B, Fiorentini C. Exercise versus recovery electrocardiography in predicting mortality in patients with uncomplicated myocardial infarction. Eur Heart J 2004;25:558–64.

[9] Bigi R, Cortigiani L, Gregori D, De Chiara B, Parodi O, Fiorentini C. Exercise versus recovery electrocardiography for predicting outcome in hypertensive patients with chest pain. J Hypertens 2004;22:2193–9.

[10] Bigi R, Cortigiani L, Gregori D, Colombo P, Fiorentini C. Stress-Recovery Index for risk stratification of asymptomatic patients following coronary bypass surgery. Chest 2005;128:42–7.

[11] Bigi R, Cortigiani L, Gregori D, Bax JJ, Fiorentini C. Prognostic value of combined exercise and recovery electrocardiographic analysis. Arch Intern Med 2005;165:1253–8.

[12] Braunwald E, Zipes DP, Libby P, editors. Heart disease. A textbook of cardiovascular medicine. 6th ed. Philadelphia: Saunders; 2001. p. 1273.

[13] The fifth report on the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1993;153:154–83.

[14] World Health Organization: Diabetes Mellitus: Report of a WHO Study Group. Geneva, World Health Org., 1985 (Tech. Rep. Ser. no. 727).

[15] Sacks FM, Pfeffer MA, Moye LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. N Engl J Med 1996;335:1001–9.

[16] Rogers EW, Feigenbaum H, Weyman AE. Echocardiography for quantitation of cardiac chambers. In: Yu PN, Goodwin JF, editors. Progress in cardiology, vol. 8. Philadelphia: Lea & Febiger; 1979. p. 807.

[17] The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined—a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. J Am Coll Cardiol 2000;36:959–69.

[18] Detrano R, Salcedo E, Passalacqua M, Friis R. Exercise electrocardiographic variables: a critical appraisal. J Am Coll Cardiol 1986;8:836–47.

Please cite this article as: Bigi R et al. The Stress-Recovery Index for the risk stratification of women with typical chest pain. Int J Cardiol (2007), doi:10.1016/j.ijcard.2007.06.001

[19] Grambsh P, Therneau T. Proportional hazard tests and diagnostics based on weighted residuals. Biometrika 1994;81:515–26.
[20] Hastie T, Tibshirani R. Generalized additive models. London: Chapman & Hall; 1990.
[21] Kitagawa G, Sakamoto Y, Ishiguro M. Akaike information criterion statistics. Stuttgart: Kluwer Academic Pub; 1987.
[22] Efron B, Tibshirani R, Robert J. An introduction to the bootstrap. London: Chapman & Hall; 1993.
[23] Hanley JA, MCNeil BJ. The meaning and the use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143:29–36.
[24] Pinsky JL, Jette AM, Branch LG, Kannel WB, Feinleib M. The Framingham Disability Study: relationship of various coronary heart disease manifestations to disability in older persons living in the community. Am J Public Health 1990;80:1363–7.
[25] Weintraub WS, Kosinski AS, Wenger NK. Is there a bias against performing coronary revascularization in women? Am J Cardiol 1996;78:1154–60.
[26] Gibbons RJ, Balady GJ, Bricker JT, et al. American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). Circulation 2002;106:1883–92.
[27] Kwok Y, Kim C, Grady D, Segal M, Redberg R. A meta-analysis of exercise testing to detect coronary artery disease in women. Am J Cardiol 1999;83:660–6.
[28] Wenger NK. Coronary heart disease: the female heart is vulnerable. Prog Cardiovasc Dis 2003;46:199–229.
[29] National health expenditures amounts, and average annual percent change, by type of expenditure: selected calendar years 1980–2012 (cms.hhs.gov).
[30] Benjamin EJ, Smith Jr SC, Cooper RS, Hill MN, Luepker RV. Task force #1-magnitude of the prevention problem: opportunities and challenges. 33rd Bethesda Conference. J Am Coll Cardiol 2002;40:588–603.
[31] Vaccarino V, Parsons L, Every NR, Barron HV, Krumholz HM. Sex-based differences in early mortality after myocardial infarction. National Registry of Myocardial Infarction 2 Participants. N Engl J Med 1999;341:217–25.

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