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Original Article

Incremental value of exercise echocardiography over exercise electrocardiography in a chest pain unit

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ABSTRACT

Background: Limited data are available on the added value of exercise echocardiography (ExEcho) over exercise electrocardiography (ExECG) in patients with suspected acute coronary syndromes (ACS) referred to a chest pain unit. We aimed to assess the incremental value of ExEcho over ExECG in this setting.
Methods: ExECG and ExEcho were performed in parallel in 1052 patients with suspected ACS, nondiagnostic but interpretable electrocardiograms, and negative serial troponin results. The primary outcome was a composite of coronary death, nonfatal myocardial infarction or unstable angina with angiographic documentation of significant coronary artery disease within 6 months.
Results: The primary outcome occurred in 2/614 patients (0.3%) with both negative ExECG and ExEcho, 3/60 (5%) with positive ExECG and negative ExEcho, 73/135 (54.1%) with negative ExECG and positive ExEcho, 106/136 (77.9%) with both positive ExECG and ExEcho, and 8/107 (7.5%) with inconclusive results. The addition of ExEcho data to a model based on clinical and ExECG data significantly increased the *c* statistic from 0.898 to 0.968 (change +0.070, 95% confidence interval 0.052–0.092), with a continuous net reclassification improvement of 1.56 and an integrated discrimination improvement of 22% ($p < 0.001$). Decision curve analysis showed that a strategy of referral to coronary angiography based on ExEcho was associated with the highest net benefit and with the largest reduction in unnecessary coronary angiographies.
Conclusion: ExEcho provides significant incremental prognostic information and higher net clinical benefit than a strategy based on ExECG in patients referred to a chest pain unit for suspected ACS and negative troponin levels.

1. Introduction

Chest pain is one of the most common causes of presentation to the emergency department [1]. Many of these patients are hospitalized for a possible acute coronary syndrome at a significant cost [2]. However, a cardiac etiology is eventually found in less than one third of these patients [3]. Although it is important to reduce unnecessary admissions, patients inappropriately discharged with an unnoticed acute coronary syndrome have a significantly worse prognosis; the mortality rates for patients with missed unstable angina (UA) have been reported to be more than twice as high as for those who are admitted and treated [4], and this constitutes a major potential source of malpractice liability in the emergency department [5].

Exercise testing soon after admission can help establish the safety of discharge. Exercise electrocardiography (ExECG) has been the preferred initial noninvasive test in this setting [6], but its lower accuracy, as compared with noninvasive imaging techniques, may have prognostic implications [7]. Exercise echocardiography (ExEcho) is an add-on to ExECG that provides several advantages. Its diagnostic accuracy is similar to myocardial perfusion imaging [8], but ExEcho is more versatile, faster and safer; it does not involve the use of radiation, and has a significantly lower cost. However, there is scarce data on the added value of ExEcho over ExECG in the setting of a chest pain unit. Furthermore, an improvement in predictive accuracy is not sufficient to establish whether ExEcho would actually benefit patients, since the consequences of clinical decisions, such as unnecessary coronary angiographies or inappropriate discharges of patients with missed UA, have to be taken into account.

Thus, our aim was to evaluate the incremental value of ExEcho over ExECG and its ability to improve clinical decision-making in patients

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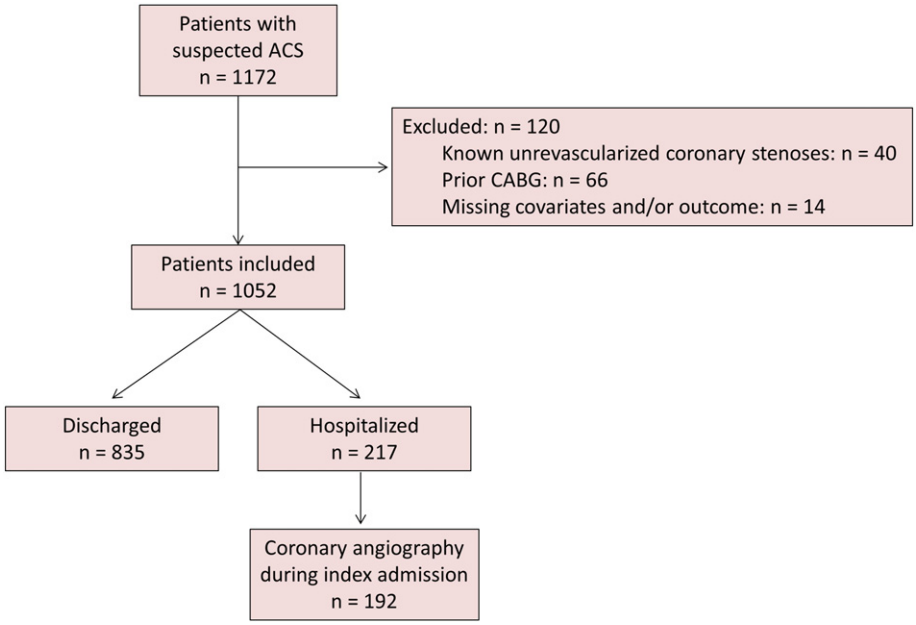

Fig. 1. Flow chart of patients enrolled in the study. ACS denotes acute coronary syndrome.

referred to a chest pain unit for acute chest pain, nondiagnostic electrocardiograms and negative troponin levels.

2. Methods

2.1. Patients

Patients who were referred to our chest pain unit from July 2007 to December 2012 and underwent treadmill ExEcho were initially considered for inclusion in the study. Eligibility criteria were as follows: nontraumatic acute chest pain suspected of having an ischemic origin (in the absence of any obvious alternative cause), non-diagnostic but interpretable electrocardiograms, normal serial troponin levels, and ability to exercise on a treadmill. Patients with repolarization abnormalities precluding a proper interpretation of ExECG (i.e., left bundle branch block, preexcitation, paced rhythm, left ventricular hypertrophy with strain, other repolarization abnormalities or treatment with digoxin) and those with at least one cardiac troponin I value above the diagnostic threshold for myocardial necrosis were not included. Patients with a history of coronary artery bypass grafting and those with known, significant, unrevascularized coronary stenoses were excluded (Fig. 1). Patients with any missing covariate or outcome data were also excluded (Fig. 1); the baseline characteristics of the latter did not differ significantly from those of the remaining subjects. The final study population consisted of 1052 patients. The research protocol was approved by the Comité Autonómico de Ética da Investigación de Galicia, our regional Ethics Committee.

2.2. Clinical and laboratory data

The work-up in the emergency department consisted of clinical history, 12-lead electrocardiogram, chest X-ray, and at least 2 cardiac

Table 1
Baseline characteristics of 1052 patients with acute chest pain in the whole cohort and according to the subsequent development of coronary events.

	All patients ($n = 1052$)	Without primary outcome ($n = 860$)	With primary outcome ($n = 192$)	p
Male, *n* (%)	675 (64.2)	518 (60.2)	157 (81.8)	<0.001
Age (years)	61.7 ± 12.5	61.1 ± 12.6	64.4 ± 11.9	0.001
Smokers, *n* (%)	251 (23.9)	195 (22.7)	56 (29.2)	0.06
Diabetics, *n* (%)	196 (18.7)	140 (16.3)	56 (29.2)	<0.001
Hypertension, *n* (%)	558 (53.0)	444 (51.6)	114 (59.4)	0.05
Hypercholesterolemia, *n* (%)	542 (51.5)	425 (49.4)	117 (60.9)	0.004
Family history of CAD, *n* (%)	72 (6.8)	54 (6.3)	18 (9.4)	0.20
Prior MI, *n* (%)	204 (19.4)	155 (18.0)	49 (25.5)	0.02
Prior coronary revascularization, *n* (%)	241 (22.9)	176 (20.5)	65 (33.9)	<0.001
Type of chest pain				
Typical angina, *n* (%)	109 (10.4)	51 (5.9)	58 (30.2)	<0.001
Atypical angina, *n* (%)	441 (41.9)	348 (40.5)	93 (48.4)	0.04
Nonischemic chest pain, *n* (%)	493 (46.8)	455 (52.9)	38 (19.8)	<0.001
Medications				
β-Blockers, *n* (%)	259 (24.6)	194 (22.6)	65 (33.9)	0.001
Calcium channel blockers, *n* (%)	78 (7.4)	64 (7.4)	14 (7.3)	0.78
Nitrites, *n* (%)	56 (5.3)	33 (3.8)	23 (12.0)	<0.001
RAAS blockers, *n* (%)	381 (36.3)	302 (35.1)	79 (41.1)	0.12
SBP, mm Hg	128 ± 27	127 ± 28	131 ± 20	0.12
Heart rate, bpm	79 ± 16	80 ± 16	76 ± 13	0.001
Left ventricular ejection fraction, %	60.9 ± 5.7	61.2 ± 5.5	59.5 ± 6.4	<0.001

bpm, beats per minute; CABG, coronary artery bypass grafting; CAD, coronary artery disease; MI, myocardial infarction; PCI, percutaneous coronary intervention; RAAS, renin–angiotensin–aldosterone system; SBP, systolic blood pressure.