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Identification of very low risk chest pain using clinical data in the emergency department

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ABSTRACT

Background: Evaluation of chest pain of uncertain origin in the emergency department is a challenge. Chest pain units, involving non-invasive stress testing, have logistic constraints. Our aim was to identify very low risk patients for early discharge using clinical data.

Methods: A total of 772 patients were studied. Ischemia in the electrocardiogram, troponin elevation or history of ischemic heart disease, were exclusion criteria. The primary end point was 30 day cardiac events (death, myocardial infarction or revascularization). The secondary end point was 1 year major events (death or myocardial infarction).

Results: The primary and secondary end point rates were 123 (18%) and 31 (4%). Predictive variables for the primary end point were typical chest pain (OR = 1.8, $p = 0.007$), ≥2 pain episodes in last 24 h (OR = 3.4, $p = 0.0001$), age ≥ 55 years (OR = 1.8, $p = 0.03$), male (OR = 2.2, $p = 0.001$), diabetes (OR = 1.8, $p = 0.01$) and family history of ischemic heart disease (OR = 2.0, $p = 0.02$). A very low risk category could be distinguished (<2 predictors, $n = 114$) that showed only 3 (2.6%) events at 30 days (all 3 revascularizations), compared with 120 (18%) in the remaining patients ($p = 0.0001$). The very low risk criteria had 97% negative predictive for 30 day cardiac events. No very low risk patient presented major events at 1 year compared with 31 (4.7%) in the remaining patients ($p = 0.009$).

Conclusion: In patients presenting to the emergency department with chest pain of uncertain origin and without prior ischemic heart disease, very low risk patients can be identified using clinical data. These patients could be quickly discharged without further non-invasive stress testing.

1. Introduction

Evaluation of acute chest pain without evidence of acute coronary syndrome, as ischemic changes in the electrocardiogram or troponin elevation, remains a challenge in the emergency departments. Although many of these patients have an excellent prognosis, there are some high risk patients whose identification is mandatory [1]. Non-invasive stress tests via a chest pain unit protocol are the main tools for decision making. Among them, the exercise test is the most widely available [2–5], although stress echocardiography and multi-slice coronary computed tomography constitute promising alternatives [6,7].

The use of non-invasive tests, however, consumes time and increases costs. Therefore, they should not be offered to all patients with chest pain of uncertain origin in the emergency departments. In this scenario, a clinical model capable of identifying low risk patients for early discharge without chest pain unit evaluation would be of great value. In previous studies, clinical models demonstrated to be useful for distinguishing patients at high risk of long term hard events [1,8]. However, those patients with lower risk unstable angina who might need hospitalization for stabilization or revascularisation were not properly identified [9]. Therefore, some concern persists about decision making based on simple clinical data in patients with chest pain of uncertain origin.

The present study involves a consecutive series of patients presenting to the emergency department with chest pain and evaluated using a chest pain unit protocol with exercise testing. The analysis focuses on the identification of very low risk patients. Therefore, those without a prior documented history of ischemic heart disease were selected. The purpose was to investigate whether very low risk patients can be identified in this specific population, using clinical data. If this was the case, these patients might avoid the complexity of a chest pain unit evaluation.

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2. Methods

2.1. Population

The study group consisted of 772 patients presenting to the emergency department with chest pain considered by the cardiologist on duty to be of possible coronary origin, from 15 January 2001 to 15 September 2007. This is a prospective single hospital study that was reviewed and approved by the Ethic Board of the University Clinic Hospital of Valencia. To be included in the study, the following conditions were required: (1) absence of prior documented ischemic heart disease (either significant coronary stenosis or prior acute coronary syndrome); (2) absence of ischemia in the ECG (ST-segment deviation ≥1 mm or T wave inversion ≥1 mm) or left bundle branch block in the initial electrocardiogram; and (3) normal troponin I levels after serial determination at arrival and at 8–12 h from pain onset. Baseline and any other ECG performed in the emergency department before the exercise test were considered for the definition of ischemia. Two different troponin I assays were used: the Immulite assay (Diagnostic Products Corporation, Los Angeles, CA, USA) until October the 1st 2003, and the Dimension assay (Dade Behring, Newark, DE, USA) since October the 1st 2003. Positive and negative values for myocardial infarction were assigned according to the minimal troponin threshold measured with a coefficient of variation <10% in each assay, as indicated by the manufacturer; the precision of the troponin thresholds was confirmed by our laboratory.

2.2. Study protocol

A number of clinical variables were recorded at admission including symptoms at presentation, coronary risk factors, prior vascular disease (peripheral artery disease or stroke) and renal failure defined by creatinine ≥1.4 mg/dl at admission. The characteristics of chest pain at presentation were collected using a predefined questionnaire introduced by Geleijnse et al., evaluating pain location, radiation, character, severity, influences, associated symptoms and previous history of exertional angina [10]. A number of points were assigned according to the presence or absence of these characteristics. Based on previous studies, typical chest pain was defined by ≥10 points [1]. The number of pain episodes in the last 24 h was also considered. Finally, the TIMI risk score was calculated [11].

All patients were managed by chest pain unit protocol, with early (<24 h) exercise test capability, described elsewhere [1,12]. In brief, patients with a positive result in the exercise test were hospitalised while those with a negative result were discharged. In the case of an inconclusive result, the final decision was at the criterion of the attending physician. On the other hand, those patients with inability to exercise were hospitalised for further evaluation. In-hospital management was at discretion of the attending physician by using either cardiac magnetic resonance with dypiridamole, coronary angiogram or medical treatment without further study.

2.3. Measurements

The main outcome was 30 day cardiac events (death, myocardial infarction or revascularization). The secondary end point was major events (death or myocardial infarction) at 1 year. An acute myocardial infarction was defined as a new episode of chest pain with increased troponin I. Acute myocardial infarction was also defined if creatine kinase MB mass increased to ≥3 times the upper limit of normal after coronary angioplasty or to ≥5 times the upper limit of normal after coronary bypass surgery.

2.4. Data analysis

Relationship between clinical variables and outcomes was analysed by the univariate chi-square test. Age was transformed into a qualitative variable after calculating its quartile distribution and choosing the first quartile as the best cut off value for the primary end point. Those variables associated with the main outcome ($p<0.20$) were introduced in a logistic regression model (backward method) to analyse the independent predictors. The odds ratio (OR) and 95% confidence intervals (CIs) were calculated. A final model was obtained, allowing the identification of a low risk subgroup. The relative risk (RR) and 95% CI were estimated.

3. Results

3.1. Characteristics of study subjects

Table 1 shows the characteristics of the patient population. In more than a half of the patients the chest pain was considered typical according to the predefined questionnaire, and one third presented recurrent chest pain in the last 24 h. The distribution of the main outcome among age quartiles was as follows: 11%, <55 years; 16%, 55–63 years; 19%, 64–70 years; 19%, >70 years. Based on this distribution, the first quartile was chosen as a cut off value (55 years). The area under the ROC curve was 0,60, showing the first quartile cut point 82% sensitivity and 31% specificity. The mean TIMI risk score of the population was 1,3 points (range 0 to 4). Exercise testing was performed in 550 patients. The result was positive in 101, negative in 346 and inconclusive in 103.

At 30 days, 123 (16%) patients presented cardiac events: 4 (0.5%) died, 12 (1.6%) had an acute myocardial infarction and 118 (15%) were revascularized. At 1 year, 13 patients (1.7%) died and 19 (2.5%) suffered an acute myocardial infarction. Four of the myocardial infarctions were related to revascularization procedures.

Table 1
Characteristics of the patient population ($n=772$).

Typical chest pain[a]	399	(52%)
≥2 chest pain episodes in last 24 h	265	(34%)
Age (years)	63 ± 11	
Age >55 years	572	(74%)
Men	494	(64%)
Current smokers	200	(26%)
Hypertension	432	(56%)
Hypercholesterolemia	383	(50%)
Diabetes mellitus	198	(26%)
Family history	90	(12%)
Peripheral artery disease	31	(4%)
Stroke	52	(7%)
Creatinine ≥1.4 mg/dl	46	(6%)

[a] Chest pain score ≥10 points.

3.2. Predictors of risk

Table 2 shows the results of the univariate analysis. Typical chest pain, ≥2 pain episodes in last 24 h, age ≥55 years, male sex, diabetes, family history of ischemic heart disease and peripheral artery disease, were related with the outcome. In contrast, smoking, hypertension, hypercholesterolemia, prior stroke and renal failure, lacked of predictive value.

In the multivariable analysis, the following variables were found to be independently related with 30 day cardiac events: typical chest pain (OR = 1.8, 95% CI 1.2 to 2.7, $p=0.007$), ≥2 pain episodes in last 24 h (OR = 3.4, 95% CI 2.3 to 5.1, $p=0.0001$), age ≥55 years (OR = 1.8, 95% CI 1.1 to 3.1, $p=0.03$), male sex (OR = 2.2, 95% CI 1.4 to 3.5, $p=0.001$), diabetes mellitus (OR = 1.8, 95% CI 1.2 to 2.8, $p=0.01$) and family history (OR = 2.0, 95% CI 1.1 to 3.6, $p=0.02$).

The Fig. 1 depicts the rate of 30 day cardiac events according to the number of predictive variables. A very low risk category could be distinguished ($n=114$), defined by the presence of 0 or only 1 of these predictors, that showed only 3 (2.6%) events at 30 days (all 3 revascularizations procedures), compared with 120 (18%) in the remaining patients with ≥2 predictors (RR = 8.3, 95% CI 2.6 to 26.4, $p=0.0001$). The risk criteria had 97% negative predictive value and 97% sensitivity for 30 day cardiac events, being the positive predictive value and specificity 18% and 17% respectively.

The result of the exercise test was positive in only 5 patients from the low risk subgroup; in 3 of them it was a false positive result since they showed a normal coronary angiogram. Of the other 2 patients, 1 was revascularized and another received medical treatment.

No very low risk patient died or suffered myocardial infarction at 1 year while 31 (4.7%) of the remaining patients presented major events ($p=0.009$) (Fig. 2); without taking into account periprocedural myocardial infarctions, the rate of major events was 27 (4.1%, $p=0.02$).

The TIMI risk score was not as precise for identifying a very low risk subgroup, since the rate of 30 day cardiac events was as follows: 0 points, 10 events (5,3%); 1 point, 38 events (13%); 2 points, 48 events (24%); and ≥3 points, 27 events (32%).

4. Discussion

4.1. Main results

The present study provides a clinical model for the initial screening of patients presenting to emergency department with chest pain of

Table 2
Variables related with 30 day cardiac events in the univariate analysis.

	RR	95% CI	p
Typical chest pain	1.9	1.3–2.9	0.002
≥2 chest pain episodes in last 24 h	3.2	2.2–5.0	0.0001
Age ≥55 years	1.7	1.1–2.8	0.03
Men	1.7	1.1–2.7	0.01
Current smokers	0.9	0.6–1.4	0.73
Hypertension	1.2	0.8–1.8	0.32
Hypercholesterolemia	1.1	0.7–1.6	0.77
Diabetes mellitus	1.7	1.1–2.6	0.01
Family history[a]	1.6	0.9–2.7	0.09
Peripheral artery disease	3.0	1.4–6.6	0.005
Stroke	1.3	0.6–2.6	0.55
Creatinine ≥1.4 mg/dl	0.8	0.3–1.9	0.68

[a] Ischemic heart disease in a male relative with onset at age 55 years or younger or a female relative with onset at age 65 years or younger.

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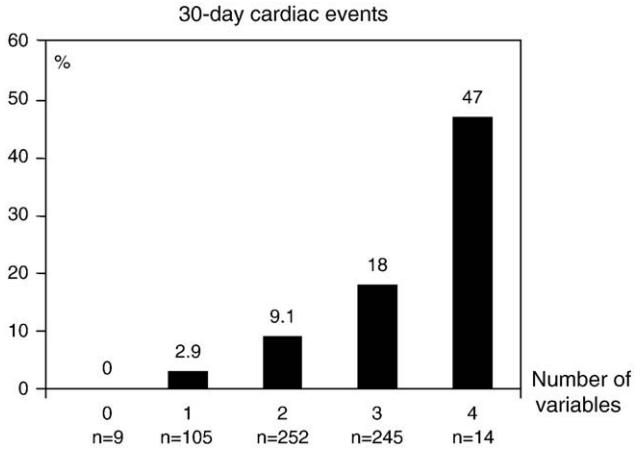

Fig. 1. Distribution of 30 day cardiac events according to the number of predictive variables. These variables are: typical chest pain, ≥2 pain episodes in the last 24 h, male sex, age older than 55 years, diabetes mellitus and family history of ischemic heart disease.

uncertain origin and without prior ischemic heart disease. The proposed clinical criteria have a high negative predictive value for 30 day cardiac events. Therefore, these patients might be quickly discharged without further non-invasive stress testing. Moreover, low risk patients did not show hard events after 1 year follow-up. The low positive predictive value of the clinical data, however, warrants the implementation of non-invasive stress tests for completing screening in non-low risk patients.

4.2. Patient characteristics

The policy in our institution required that a cardiologist defines the chest pain as of possible coronary origin. Consequently, patients included in the study had at least an intermediate probability of unstable angina, and few atypical chest pains were considered. Indeed, in more than a half of the patients the pain characteristics were qualified as typical according to a predefined questionnaire [1,10]. Evaluation of these patients constitutes the main goal of chest pain units, since atypical chest pain does not need the complexity of a chest pain unit protocol.

Patients with prior documented ischemic heart disease were excluded. The history of ischemic heart disease is a high risk factor by itself. In this sense, guidelines of the European Society of Cardiology advise invasive management in these patients [13]. Consequently, we focused on patients without prior ischemic heart disease in looking for the low risk subgroup.

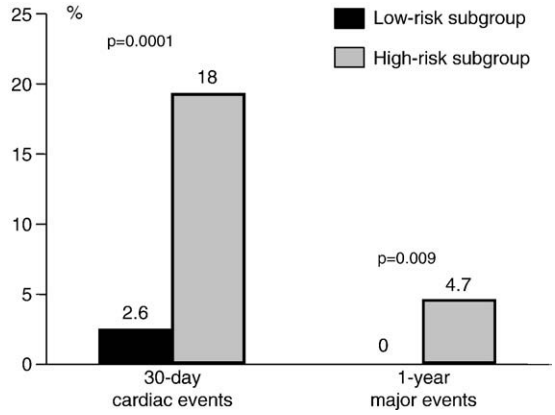

Fig. 2. Frequency of 30 day cardiac events (death, acute myocardial infarction or revascularization) and 1 year major events (death or myocardial infarction) in the low (0–1 variables of risk) and high (≥2 variables) risk categories.

4.3. Predictors of risk

Six predictors of risk were found, such as typical pain, ≥2 pain episodes in the last 24 h, male sex, age older than 55 years, diabetes mellitus and family history of ischemic heart disease. All are well known risk factors [11,14–20], some of them included in the Framingham score. However, they have not been evaluated for identification of very low risk in patients presenting to the emergency department with chest pain of uncertain origin.

Low risk patients underwent only 2.6% revascularization procedures at 30 days and none died or suffered myocardial infarction at 1 year. Revascularization could influence on the outcome. A previous study on chest pain unit patients, however, failed to demonstrate the protective effects of revascularisation for long term death or myocardial infarction [21]. Furthermore, in non-ST-segment elevation acute coronary syndrome trials revascularisation lacked of benefit in normal troponin patients [22,23]. Conceivably, these patients could be managed in the ambulatory setting in order to complete chest pain study and plan potential revascularization procedure.

5. Conclusions

In patients presenting to the emergency department with chest pain, without ischemia in the electrocardiogram or troponin elevation, and without prior ischemic heart disease, the main predictors of short-term events are: typical chest pain, ≥2 pain episodes in the last 24 h, male sex, age older than 55 years, diabetes mellitus and family history of ischemic heart disease. Patients with 0 or only 1 predictor have a very low rate of events and might be quickly discharged to the ambulatory setting, avoiding the complexity of further non-invasive stress tests for decision making. This policy can simplify the process of chest pain assessment.

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The authors of this manuscript have certified that they comply with the Principles of Ethical Publishing in the International Journal of Cardiology [24].

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