Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 46, No. 3, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2005.04.037

New Risk Score for Patients With Acute Chest Pain, Non–ST-Segment Deviation, and Normal Troponin Concentrations

A Comparison With the TIMI Risk Score

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OBJECTIVES The purpose of this research was to develop a risk score for patients with chest pain, non–ST-segment deviation electrocardiogram (ECG), and normal troponin levels.

BACKGROUND Prognosis assessment in this population remains a challenge.

METHODS A total of 646 consecutive patients were evaluated by clinical history (risk factors and chest pain score according to pain characteristics), ECG, and early exercise testing. ST-segment deviation and troponin elevation were exclusion criteria. The primary end point was mortality or myocardial infarction at one year. The secondary end point was mortality, myocardial infarction, or urgent revascularization at 14 days (similar to the Thrombolysis In Myocardial Infarction [TIMI] risk score).

RESULTS Primary and secondary end point rates were 6.7% and 5.4%. A risk score was constructed using the variables related to the primary end point: chest pain score ≥10 points (hazard ratio [HR] = 2.5; 1 point), ≥2 pain episodes in last 24 h (HR = 2.2; 1 point), age ≥67 years (HR = 2.3; 1 point), insulin-dependent diabetes mellitus (HR = 4.2; 2 points), and prior percutaneous transluminal coronary angioplasty (HR = 2.2; 1 point). Patients were classified into five categories of risk ($p = 0.0001$): 0 points, 0% event rate; 1 point, 3.1%; 2 points, 5.4%; 3 points, 17.6%; ≥4 points, 29.6%. The accuracy of the score was greater than that of the TIMI risk score for the primary (C index of 0.78 vs. 0.66, $p = 0.0002$) and secondary (C index of 0.70 vs. 0.66, $p = 0.1$) end points.

CONCLUSIONS Patients presenting with chest pain despite no ST-segment deviation or troponin elevation show a non-negligible rate of events at one year. A risk score derived from this specific population allows more accurate stratification than when using the TIMI risk score. (J Am Coll Cardiol 2005;46:443–9) © 2005 by the American College of Cardiology Foundation

The availability of troponin assay in emergency departments has afforded substantial improvement in the diagnosis and management of patients with non–ST-segment elevation acute coronary syndrome (ACS). Troponin is a very sensitive and specific marker of myocardial necrosis (1) and is helpful as a guide to best management, including early revascularization (2,3). The ST-segment depression in the initial electrocardiogram (ECG) is also helpful for identifying patients with ACS at medium to high risk of events, and for guiding their management (4,5). In contrast to these high-risk markers, diagnosis and prognosis assessment in patients with chest pain without ST-segment deviation or troponin elevation remains a challenge. Though some data suggested that a normal troponin result implies excellent prognosis (6), other studies report a non-negligible 3% rate of myocardial infarction or death at 30 days (7), which increased to 4.8% at six months of follow-up (8). Therefore, careful risk stratification seems mandatory.

Several risk scores have been described for non–ST-segment elevation ACS (9–13). The Thrombolysis In Myocardial Infarction (TIMI) risk score is the most widely used. Such scores derive from populations that include high-risk subsets (including ST-segment deviation and/or positive cardiac markers). Consequently, the applicability of these scores to lower-risk patients may not be adequate. Furthermore, troponin was not routinely used as marker of necrosis in most of these studies, and patients were not managed by a chest pain unit protocol, which seems to be the most appropriate management for these lower-risk patients (14).

The present study examined a series of patients with acute chest pain without ST-segment deviation and presenting normal troponin concentrations. They were managed by a chest pain unit protocol and were followed-up for one year. A risk score was elaborated using the predictors of poor outcome, and its performance was compared to the TIMI risk score.

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Manuscript received March 4, 2005; revised manuscript received March 29, 2005, accepted April 13, 2005.

Abbreviations and Acronyms

ACS = acute coronary syndrome
CABG = coronary artery bypass graft
CI = confidence interval
HR = hazard ratio
IDDM = insulin-dependent diabetes mellitus
PTCA = percutaneous transluminal coronary angioplasty
ROC = receiver-operating characteristic
TIMI = Thrombolysis In Myocardial Infarction

METHODS

The study group consisted of 646 consecutive patients (from January 15, 2001 to November 30, 2003) coming to the emergency room with acute chest pain of possible coronary origin. ST-segment deviation (≥1-mm elevation or depression) in the initial ECG or troponin I elevation were exclusion criteria. Troponin I was determined in our institution on arrival and at 6 h (in patients arriving within the first 2 h from pain onset), 8, and 12 h after pain onset (8,15,16). All patients had normal troponin concentrations at all determinations.

Troponin I was determined immunologically using an Immulite assay (Diagnostic Products Corp., Los Angeles, California). According to the instructions of the manufacturer, the Immulite troponin kit was used to test 255 serum samples from healthy laboratory volunteers and from hospitalized patients who had been shown to be negative for troponin I by another immunometric method. The median values for these samples was non-detectable; 98% of the values were below 1.0 ng/ml. Troponin I increase was defined as ≥1 ng/ml (upper limit of normality). The troponin I assay was tested in our laboratory, the coefficient of variation being <10%. Coefficients of variation were obtained at two levels: one within the normal range and the other above the normal range.

Patients were evaluated by a chest pain unit protocol that included evaluation of the clinical history and ECG, and early exercise testing in patients without contraindication to exercise (physical incapacity or abnormalities in the baseline ECG) (8,12,13).

Clinical evaluation. The clinical characteristics of chest pain presentation were assessed. On the basis of these characteristics, the semiquantitative score previously reported by Geleijnse et al. (17) was calculated (Appendix). In addition, the following variables were recorded, including those variables collected in the TIMI risk score study (9): gender, age, smoking, arterial hypertension, diabetes mellitus, insulin-dependent diabetes mellitus (IDDM), hypercholesterolemia, family history of ischemic heart disease, at least three risk factors for coronary artery disease, ≥2 chest pain episodes in last 24 h, Killip class >1 at presentation, evidence of prior coronary stenosis ≥50%, use of aspirin in the last seven days, prior myocardial infarction, prior percutaneous transluminal coronary angioplasty (PTCA), prior coronary artery bypass graft (CABG), and a history of heart failure. The TIMI risk score was calculated in all patients.

An ECG was recorded in the emergency room and evaluated for T-wave inversion (≥1 mm) or confounding ECG (left bundle branch block of paced rhythm).

Early exercise testing. A total of 322 patients (50%) were eligible for early exercise testing (within the first 24 h after arrival). A symptom-limited Bruce protocol was used. The result was considered positive in the case of ischemia induction (indicated by a 1-mm horizontal or downsloping depression of the ST-segment at 80 ms from the J point, or a 1-mm ST-segment elevation). A negative test was considered when at least a submaximal test was performed without ST-segment changes. An inconclusive test was considered if the patient was unable to reach submaximal heart rate (85% of the theoretical-age-predicted heart rate) without ischemia. All 190 patients with a negative result were discharged after the exercise test, while all 52 with a positive test were hospitalized. In the case of an inconclusive test, the final decision was left to the criterion of the supervising physician.

In-hospital management. Overall, 216 patients were early discharged and 430 hospitalized. All hospitalized patients were treated with aspirin, low-molecular-weight heparin, and beta-blockers (unless contraindicated). Patients underwent invasive management in case of recurrent chest pain or evidence of ischemia in noninvasive tests. Cardiac catheterization was performed in 227 patients (35% of the global population and 53% of the hospitalized patients). During hospitalization 68 patients underwent PTCA and 31 CABG. Creatine kinase-MB mass (5 ng/ml upper limit of normal) was routinely determined 12 and 24 h after a revascularization procedure. Fifty-seven patients had normal coronary arteries.

End points. Patients were followed-up for one year. Complete follow-up was obtained in 98% of the patients (a total of 11 cases were missed). The end points considered in the TIMI risk score study were used in the present study (9). Therefore all-cause mortality, acute myocardial infarction, and urgent revascularization were recorded. An acute myocardial infarction was defined as a new episode of chest pain with increased troponin I. Acute myocardial infarction was also considered if creatine kinase-MB mass increased to ≥3 times the upper limit of normal after PTCA or to ≥5 times the upper limit of normal after coronary bypass surgery. Severe recurrent ischemia requiring urgent revascularization was defined as an episode of recurrent angina prompting the performance of coronary revascularization on the index hospitalization or an episode of recurrent angina after discharge that resulted in re-hospitalization during which coronary revascularization was performed.

The primary end point was a composite of all-cause mortality or non-fatal myocardial infarction at one year. The secondary end point was a composite of all-cause mortality, non-fatal myocardial infarction, or urgent revas-