Original articles

Management of patients with low-risk chest pain at the time of admission: a prospective study on a non-selected population from the Emergency Department

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Chest pain; Troponins.

Background. **The management of patients with acute chest pain is a common and difficult challenge from the epidemiological, clinical, organizational and malpractice points of view. Our purpose was to test and implement a simple clinical protocol for the management of patients with acute chest pain and at low-risk for an acute coronary syndrome (ACS) at the time of admission to the Emergency Department (ED).**

Methods. **During a 5-month study period, 570 consecutive patients were admitted to the ED with acute chest pain: 224 patients were excluded owing to the presence of a clear diagnosis of an ACS or of high-risk factors. The remaining 346 were considered, at the time of admission, as being at low risk for an ACS and constituted the study group (208 males, 138 females, mean age 65 years). These 346 patients were evaluated in the ED area by means of multiple ECGs and multiple blood sampling for the creatine kinase-MB mass and troponin I serum levels at the time of admission and 6 and 12 hours later. In selected cases a treadmill stress test was requested in order to further clarify the diagnosis.**

Results. **The ECG at the time of admission was normal or nearly normal in 79% of the patients. Stress testing was performed in 79 patients (25%). Sixty-six/346 low-risk patients (19%) were admitted to the coronary care unit during ED observation: 38 patients because of positive markers, 10 because of a positive ECG, 13 because of positive markers and ECG, and 5 because of a positive stress test. Two hundred and eighty low-risk patients without evidence of acute ischemia were definitively discharged and classified as having non-ischemic chest pain. At 1 month of follow-up, 1 patient underwent coronary artery bypass grafting, 1 patient was again admitted to the ED for acute pulmonary edema, and 2 patients had acute extracardiac events. Within 1 year of follow-up 4 deaths occurred: 2 were cancer-related and 2 were sudden deaths.**

Conclusions. **The tested strategy, based on integrated clinical, ECG and multimarker data, and on a short "test of time" period of low-risk patient observation, can allow the identification of patients having an ACS on the one hand and of those for whom a safe, rapid and early discharge is possible on the other, in a low-cost environment.**

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Introduction

The management of patients with acute chest pain is a common and difficult challenge from an epidemiological, clinical, organizational and malpractice point of view[1-5].

Each year, in the United States about 5 million patients come to the Emergency Department (ED) with chest pain for an estimated cost of 6 billion dollars[6,7]. Some do have an acute life-threatening illness, but many have nothing seriously wrong. Traditionally, many patients are admitted to the hospital on the basis of their clinical history, physical examination and ECG data, even though most of them are thereafter diagnosed as non-ischemic patients. Despite this low threshold for admission, up to 8% of patients with acute myocardial infarction (AMI) are discharged home, with an associated significant high mortality rate, accounting for approximately 20% of the ED malpractice expenses in the United States[8-11].

The task of physicians in the ED is to sort out, in a rapid, accurate and efficient manner, the confusing array of patients with chest pain.

In recent years a considerable investigative interest has been focused on new markers of myocardial injury, especially troponins. Although many data suggest that troponins are more sensitive and specific than creatine kinase (CK)-MB for the detection of myocardial damage, most clinical studies have been restricted to high-risk patients with unstable angina[12,13]. The diagnostic performance of these assays in unselected patients with acute chest pain but at lower risk for acute coronary syndromes (ACS) and cardiac events is not completely clear[14-19].

Other tests, such as the treadmill stress test, echocardiography and radionuclide imaging, are not always easily available and not always cost-effective[20-24]. Furthermore, many studies are performed on hospitalized patients, who are not representative of the population with a low prevalence of ACS typically seen in the ED. Indeed, in many studies patients classified as potential candidates for rapid early discharge were evaluated during the follow-up while still staying in hospital. In the present study, a more realistic evaluation of the true risk of the entire population has been obtained by including all patients requiring hospital admission as well as individuals actually discharged from the ED.

The purpose of the present study was to test and implement, in the ED, a simple clinical prospective protocol for the management of patients with acute chest pain and at low risk for ACS by reaching a consensus for the identification and definite rapid early discharge of patients with negative tests. These patients were classified as having non-ischemic chest pain and were sent home.

Methods

In our hospital a "chest pain project" was started in 1999 in order to improve the management of patients admitted to the ED with acute chest pain.

To minimize the number of cases of inappropriate discharge and hospital admission, a consensus protocol was adopted and prospectively tested after several meetings including all the physicians of the staff in the Cardiology and ED Units, with the clinical and technical support of the Clinical Laboratory.

The project was run on the basis of 5-month study periods and included consecutive patients admitted for acute chest pain.

The inclusion criteria were: age > 18 years, chest pain onset ≤ 24 hours, a reasonable probability of an adequate subsequent follow-up. The exclusion criteria were: a history of trauma or any other evident medical cause of chest pain and a patient history including significant risk factors. Table I shows the criteria for the identification of high-risk patients.

The data were collected by physicians at the time of arrival of the patients and reported on a specific form which included: the time of onset, duration and characteristics of the chest pain, the family history, major risk factors for coronary heart disease, a previous history of cardiac-related diseases, a previous history of coronary revascularization, physical examination and ECG findings.

Table I. Definition of high-risk patients.

1. Typical chest pain lasting > 20 min
2. Electrocardiographic evidence of myocardial ischemia
3. Ongoing typical chest pain
4. Typical chest pain lasting < 20 min in the presence of:
   - known coronary artery disease
   - diabetes mellitus
   - at least two coronary disease risk factors
5. Congestive heart failure at the initial clinical examination
6. Other potential life-threatening conditions at the initial clinical examination

Chest pain characteristics. Typical angina was defined as a deep, poorly localized chest (or jaw, neck, ear, arm and epigastric) discomfort that was reproducibly associated with physical exertion or emotional stress and which promptly resolved following rest and/or sublingual nitroglycerin. Angina was defined as unstable if the episodes were more severe and prolonged or if they occurred at rest, or if they were precipitated by less exertion than previously. Patients presenting with symptoms that were not characteristic of typical angina were considered as having atypical chest pain.

Electrocardiographic findings. ST-segment changes were considered ischemic if ≥ 0.05 mV in one or more leads. Inverted T waves were considered ischemic if symmetric and ≥ 0.2 mV in one or more leads[25]. The remaining changes were considered as non-specific.

Patients included in the study were evaluated by determining the CK-MB and troponin I serum levels at the time of admission and 6 and 12 hours later. During this time the patients remained in the ED. A 12-lead ECG was also obtained at 6 and 12 hours after admission (Fig. 1). Additional ECGs were obtained for episodes of chest pain or suspected ischemia. The ECGs were interpreted by the attending cardiologist.

After 12 hours, a consensus was again achieved by integrating the clinical and laboratory data and a decision was made on the basis of the following:

• patients with a negative clinical course for an ACS (without biochemical or ECG evidence of myocardial damage and without recurrent symptoms while under observation) were discharged early and sent home (classified as non-ischemic chest pain) with or without a treadmill stress, according to the ANMCO-SIC guidelines[26]. Patients with typical chest pain and patients with atypical chest pain but multiple (> 2) coronary risk factors or diabetes mellitus were submitted to the exercise test, if they were in the condition to perform exercise;

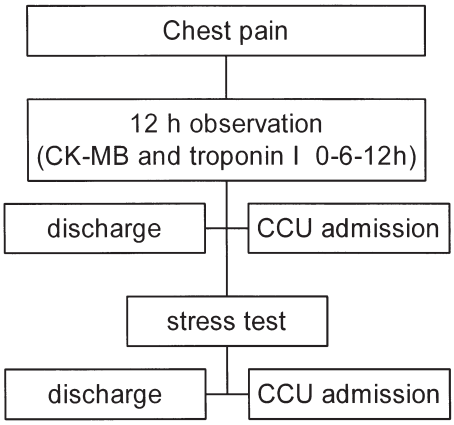

Figure 1. *Proposed algorithm for the management of patients with acute chest pain. In the Emergency Department, patients with chest pain were evaluated by means of multiple ECGs and blood sampling for the determination of the creatine kinase (CK)-MB mass and of the serum levels of troponin I at the time of admission and 6 and 12 hours later. A treadmill stress test was requested in selected cases. CCU = coronary care unit.*

• patients with a positive clinical course or positive ECG/biochemical test results for an ACS were hospitalized.

To evaluate the appropriateness of the decisions, a clinical 1-month and 1-year follow-up, including a medical visit (214 patients) or a telephone interview (52 patients) made by physicians of the cardiology staff, was obtained in 95% (266/280) of the patients who were discharged. The following events were considered: death, AMI, angina requiring hospitalization, acute pulmonary edema, coronary revascularization.

Laboratory data. The CK-MB mass and troponin I assays were determined using the same immunometric method (Bekman Acces, Fullerton, CA, USA). A CK-MB mass ≥ 5 ng/ml and a troponin I level ≥ 0.03 ng/ml were considered positive. The lower limit for the detection of troponin I with this method was 0.03 ng/ml.

AMI was confirmed if symptoms were consistent with myocardial ischemia with a characteristic time-related increase in the CK-MB mass (CK-MB value higher than the upper limit of the reference range).

Descriptive statistics (means ± SD were specified for continuous variables and proportioned for categorical variables) were generated for the baseline characteristics. A survival analysis was planned but, due to the small number of events at follow-up, not performed.

Means were compared using the unpaired Student's t-test and the χ^2 test. The significance level was set at 5%.

Results

Patient demographics. During the 5-month study period, a total of 10 103 patients were evaluated in the ED with 1192 consultancies by cardiologists (12%); 570 of these patients were admitted to the ED for acute chest pain (48% of the total cardiology consultancies in the ED and 5.6% of the total number of admissions to the ED). Among these 570 patients, 204 were immediately excluded owing to the presence, in their medical history, of relevant risk factors for an ACS (according to the "high-risk" criteria, points 1-4, Table I). Another 20 patients were not enrolled because they presented with other exclusion criteria (according to the "high-risk" criteria, points 5 and 6, Table I). The 346 (61%) remaining patients were considered the low-risk patient study group for an ACS. Among these 346 patients, 208 were male (60%). The mean age was 65 years (range 23-94 years). The coronary risk factors in the study group included: hypertension in 176 patients (51%), hyperlipidemia in 90 patients (26%), diabetes mellitus in 59 patients (17%), current smoking in 63 patients (18%), and a family history of coronary artery disease in 52 patients (15%). A past history of an ACS was present in 48 patients (14%) and previous coronary interventions had been performed in 27 patients (8%). These data are shown in table II.

When compared to the 204 patients immediately admitted for an ACS, the low-risk group of patients had a significantly lower prevalence of hyperlipidemia ($p < 0.05$), diabetes mellitus ($p < 0.001$) and a previous documented ACS ($p < 0.001$).

Electrocardiographic findings. The ECG at the time of admission to the ED was normal or with non-specific ST-T wave abnormalities in 273 patients (79%), it was suggestive of left ventricular hypertrophy or right bundle branch block in 60 patients (17%) and of left bundle branch block in 13 patients (4%). The ECG findings are shown in table II.

Exercise electrocardiographic test. A treadmill stress test was performed in 79 patients (25%). A positive exercise test was observed in 5 patients who were consequently hospitalized.

Table II. Baseline characteristics of the 346 patients with acute chest pain at low risk for acute coronary syndrome.

Demographic data	
Age (years)	65 (range 23-94)
Males	208 (60%)
ECG findings	
Normal ECG	273 (79%)
Left bundle branch block	13 (4%)
Left ventricular hypertrophy/RBBB	60 (17%)
Coronary risk factors and history of CAD	
Hypertension	176 (51%)
Hyperlipidemia	90 (26%)
Current smokers	63 (18%)
Diabetes mellitus	59 (17%)
Family history of CAD	52 (15%)
Previous AMI/UA	48 (14%)
Previous revascularization	27 (8%)

AMI = acute myocardial infarction; CAD = coronary artery disease; RBBB = right bundle branch block; UA = unstable angina.

Patients admitted to the coronary care unit. Sixty-six patients (19%) were admitted during ED observation (38 patients for positive markers, 10 patients for a positive ECG, 13 patients for positive markers and ECG, 5 patients for a positive stress test). Among the 51 patients with positive markers, all had increased troponin I values and 13 also had an increased CK-MB mass. These data are shown in figure 2.

Follow-up. Two hundred and eighty patients with a diagnosis of non-ischemic chest pain were discharged and sent home. The 1-month and 1-year follow-up was available for 266 patients (95%). Within 1 month of follow-up, 1 patient required coronary bypass surgery, 1 patient was again admitted to ED for acute pulmonary edema, and 2 patients had acute extracardiac problems (pneumothorax and an acute abdomen necessitating surgical intervention). Within 1 year of follow-up, 4 patients died: 2 of cancer and 2 of sudden death (a 27-year-old female with severe mitral regurgitation, and an 84-year-old female with hypertensive heart disease). The follow-up data are shown in table III.

Discussion

The most important early clinical markers of myocardial ischemic events are chest pain and ECG repolarization abnormalities. Their significance has been extensively validated[27-29].

In the ED the physician's first goal is to identify patients with ST-segment elevation and to promptly initiate an adequate reperfusion therapy[30]. Cell necrosis is revealed by the release of cytoplasmic enzymes, such as CK-MB, and of structural components, such as troponin I or T.

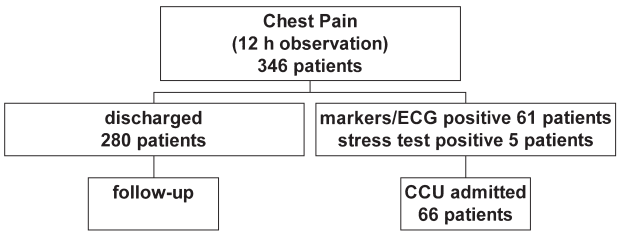

Figure 2. *Distribution of the 346 patients according to our chest pain protocol. CCU = coronary care unit.*

Table III. Follow-up of the 280 patients discharged from the Emergency Department.

Events	1 month	1 year
Death	0	4
Myocardial infarction	0	0
Revascularization	1	1
Acute pulmonary edema	1	1
Non-cardiac events	2	2

When patients with the classical clinical markers of myocardial damage are admitted to the ED, clinicians have little difficulty in making the diagnosis. However, such patients constitute the minority (15-20%) of those who come to the ED because of acute chest pain. The real problem is to distinguish between the 30-35% of patients with unstable ischemic heart disease and the 50% or more whose pain is not of ischemic origin[8].

The physician must decide whether to admit the patients to hospital, to request further tests in the ED, or to send the patient home with a plan for outpatient evaluation and management. The critical factor in this choice is the patient's short-term risk of death or of AMI.

Considerable information about the diagnosis and short-term risk is deducible from the medical history, the physical examination and the electrocardiogram[31,32]. Further tests can be helpful if the findings deriving from these steps are not diagnostic.

Several different types of tests are available, including those that permit the identification of minimal evidence of myocardial damage through sensitive assays of intracellular proteins such as CK-MB, myoglobin, and troponin I or T[14-17,33-38]. Other tests can help to make a correct diagnosis and prognosis: those that reveal abnormalities in the left ventricular wall motion (i.e. the echocardiogram) or myocardial ischemia by detecting a defect in myocardial perfusion (i.e. the technetium-99m sestamibi scan)[22-24]. Again, previous studies have shown that the stress test can be safely performed in low-risk patients with acute chest pain, and the test results are routinely used at many institutions to identify patients for early discharge. This, even though early discharge is not a constant and the patient is not usually sent home[20,21,39,40].

Furthermore, not all these tests are useful for the entire population of chest pain patients and besides, not all the tests are easily available in all EDs 24 hours a day and 7 days a week.

In our prospective study we used a protocol focusing on three points. The first was to use simple and readily available tests: complete medical history, physical examination, ECG, sensitive and specific markers of myocardial damage (CK-MB mass and troponin I) with the final decision to actually discharge and send home the patients diagnosed as having non-ischemic chest pain or to hospitalize patients with positive tests through consensus between physicians of the Cardiology and ED staffs. The second was the test of time, that is, the use of a brief observation period (12 hours) in the ED (low-cost setting). If necessary, other tests, such as the treadmill stress test, were requested before discharge. Finally, the short- and long-term follow-up were obtained and we were hence able to put this strategy to the test of time.

In the present study, during a period of 5 months, 10 103 patients came to our ED and 570 (5.6%) complained of chest pain, a percentage similar to that reported in the CHEPER Registry (5.3%)[41]. Of these, 346

met our low-risk for an ACS inclusion criteria and were asked to remain at the ED for a period of 12 hours during which an ECG recording was taken and cardiac markers assayed.

Similar to what reported in other studies, at the time of admission to the ED the majority of the patients had a non-diagnostic ECG[4,5].

Cardiac troponins are reported to be sensitive predictors of myocardial infarction and the predictive value increases up to 100% for repeated tests[42]. Moreover, they are now considered as major criteria for the diagnosis of AMI[43,44].

Hamm et al.[15] suggested that negative serial troponin assaying results are associated with such a low risk as to allow rapid and safe discharge of ED patients. But false negative results may occur in patients who subsequently develop life-threatening complications due to plaque rupture or arrhythmia[16]. For this reason, our approach included repeated blood sampling for cardiac markers and an integrated evaluation of the clinical, biochemical and ECG findings.

In our study cardiac markers became positive during the observation period in 51 patients. This finding strengthens the "test of time" concept in the evaluation of patients with acute chest pain.

The failure to hospitalize patients with an ACS is a serious public health issue. In a recent multicenter prospective study including 10 698 patients admitted to the ED for chest pain, 2.1% of patients with an AMI and 2.3% of patients with unstable angina were mistakenly discharged from the ED[11]. Multivariate analysis showed that patients who presented to the ED with acute cardiac ischemia were more likely not to be hospitalized if they were women, < 55 years old, if they were non-white, reported atypical symptoms or had a normal or non-diagnostic electrocardiogram. The risk-adjusted mortality ratio for those who were not hospitalized, as compared with those who were, was 1.9 for AMI patients and 1.7 for unstable angina patients[11].

The best validation of any strategy for the diagnosis and management of patients defined as having non-ischemic chest pain should be the follow-up of the patients actually discharged and sent home. In our study, no deaths or myocardial infarctions occurred within 1 month of follow-up, while 1 patient was revascularized and another had an acute pulmonary edema. At 1 year of follow-up, 2 sudden deaths were recorded. These were probably not related to the first ED examination and were possibly arrhythmic deaths.

Limitations of the study. This prospective study includes patients presenting to the ED of a single hospital and therefore our conclusions cannot be extended as such to other institutions. The precise time of onset of symptoms has not been universally recorded in this series. The time of arrival to the ED was considered as the reference time and subsequent evaluations were obtained at 6 and 12 hours after ED admission.

Despite these limitations this is a prospective study, where the patients classified as having non-ischemic chest pain and as being at low risk for ACS were actually discharged and sent home at the end of the observation period. This is different from other studies which reported the predictive values of the risk of early discharge calculated on the basis of a *post-hoc* analysis of clinical and laboratory data in patients who were usually still in the hospital. In this study we prospectively included all consecutive patients presenting to the ED for chest pain; this allowed us to completely evaluate the actual risk of this entire population at the time of admission and then to verify, through a 1-month and 1-year follow-up (complete for 95% of the patients), the actual risk of the patients who were discharged.

Finally, in our study a "chest pain project" more than a "chest pain unit" was considered as the final goal inside the ED. For this purpose, specific chest pain care protocols, shared by cardiologists and ED staff physicians, were utilized.

In conclusion, the reported strategy, based on integrated clinical, ECG and multimarker data and on a short "test of time" period of patient observation in a low-cost setting, can allow the identification of ischemic patients and the management of low-risk patients at the time of admission through a careful evaluation which permits the safe, rapid and early discharge of patients with negative tests and non-ischemic chest pain and the referral of patients with positive tests to the coronary care unit.

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