Use of a Coronary Risk Score (the TIMI Risk Score) in a Non-Selected Patient Population Assessed for Chest Pain at an Emergency Department

Francisco J. García Almagro, Juan R. Gimeno, Manuel Villegas, Luis Muñoz, Eugenia Sánchez, Francisca Teruel, José Hurtado, Josefa González, María J. Antolinos, Domingo Pascual, and Mariano Valdés

Servicio de Urgencias, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain.
Servicio de Cardiología, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain.
Servicio de Cardiología, Hospital General Universitario Morales Meseguer, Murcia, Spain.

Introduction and objectives. Stratification algorithms for acute coronary syndrome enable the identification of high-risk patients who will benefit from more aggressive treatment. The TIMI Risk Score (TRS) has been shown to be useful in intermediate- and high-risk patients. However, little is known about its value in non-selected patients. Our aim was to assess the efficacy of the TRS for risk stratification in a non-selected population with chest pain.

Patients and method. We evaluated 1254 consecutive patients (age, 54 ± 19 years; 57% male) attending an emergency department for chest pain. Overall, 343 (27%) were admitted and 911 (73%) were discharged. All cardiac events during 6-month follow-up were recorded.

Results. Of the 911 discharged patients, 45 (5.3%) were admitted during follow-up: 9 (1.1%) underwent revascularization, 5 (0.6%) had a myocardial infarction (MI), and 2 (0.2%) died from cardiovascular disease. Patients with a high TRS had a significantly higher risk of reaching the composite endpoint of death, MI, or revascularization (relative risk per unit of TRS increase, 3.63; 95% CI, 2.20-6.00; P<0.001). Of the patients who were initially admitted, 22 (6.4%) underwent revascularization, 4 (1.2%) had an MI, and 14 died (4.1%) from cardiovascular disease during follow-up. The relative risk of the composite endpoint per unit of TRS increase was 1.72 (95% CI, 1.32-2.24; P<0.001).

Conclusions. The TIMI risk score is useful for stratifying cardiovascular event risk in non-selected patients with chest pain. The score can identify high-risk patients who will benefit from hospital admission and early aggressive treatment.

Key words: Chest pain. Prognostic stratification. TIMI Risk Score. Chest pain unit.

Aplicación de una puntuación de riesgo coronary (TIMI Risk Score) en una población no seleccionada de pacientes que consultan por dolor torácico en un servicio de urgencias

Introducción y objetivos. Diferentes algoritmos de estratificación del síndrome coronario agudo (SCA) permiten identificar a los individuos con un mayor riesgo que pueden beneficiarse de tratamientos más agresivos. Se ha demostrado que el TIMI Risk Score (TRS) es útil en pacientes con un riesgo intermedio y alto, pero faltan evidencias acerca de su aplicabilidad clínica en pacientes no seleccionados. El objetivo es comprobar la eficacia del TRS en la estratificación del riesgo en una población con dolor torácico no seleccionada.

Pacientes y método. Se incluyó a 1.254 pacientes consecutivos que acudieron a urgencias por dolor torácico no traumático sin ascenso del segmento ST (edad 54 ± 19 años, 57% varones). Se ingresó a 343 (27%) y se dio de alta a 911 (73%). Se registró la aparición de eventos cardíacos a los 6 meses.

Resultados. En el grupo dado de alta desde urgencias, 45 (5.3%) pacientes fueron ingresados durante el seguimiento, 9 (1.1%) recibieron tratamiento de revascularización, 5 (0.6%) presentaron un infarto agudo miocárdico (IAM) y 2 (0.2%) fallecieron por causa cardiovascular. Los que obtuvieron una mayor puntuación en el TRS presentaron más riesgo de presentar el evento combinado de muerte, infarto o revascularización (riesgo relativo por incremento de unidad = 3.63; intervalo de confianza [IC] del 95%, 2.20-6.00; p < 0.001). En el grupo de ingresados hubo 22 revascularizaciones (6.4%), 4 IAM (1.2%) y 14 muertes de causa cardiovascular (4.1%) durante el seguimiento. El riesgo relativo de evento combinado por cada incremento del TRS fue 1.72 (IC del 95%, 1.32-2.24; p < 0.001).
INTRODUCCIÓN

Chest pain is one of the most frequent causes for attending clinics in Spain. Results of initial studies conducted in different countries showed that a high percentage of high-risk patients were incorrectly diagnosed; notably, 5%-10% of patients with an acute myocardial infarction (AMI) were discharged from emergency departments. In recent years we have witnessed the setting up of chest pain units which use algorithms to generate management protocols for patients attending emergency departments.

Numerous risk evaluation scales (scores), based on clinical characteristics and laboratory markers, have been proposed for this type of patient. One of the most widely used is the TIMI Risk Score (TRS). Despite the proven usefulness of the TRS in high-risk non-ST segment elevation ACS, its value in the general context of non-selected patients with chest pain is not fully defined.

Thus, the objective of the present study is to test the efficacy of the TRS as an index of risk stratification in a non-selected population attending emergency departments for chest pain.

PACIENTES Y MÉTODO

From May thru October 2001, 1334 (3.2%) of a total of 41,409 patients attending our emergency department had non-traumatic chest pain. We excluded 80 patients with ST-segment elevation ACS, which left a final study population of 1254 consecutive patients.

Initially, patients were evaluated by the emergency department physician and the opinion of a cardiologist was requested if a cardiac cause was suspected. Patients with non-cardiac chest pain were discharged or treated according to the diagnosis which was reached.

After patient evaluation, the cardiologist decided to admit or discharge on the basis of clinical, electrocardiographic and laboratory data (creatinkinase [CK], MB isoenzyme of creatinkinase [CK-MB], and troponins) over the first 24 hours.

For each patient, characteristics of the pain, relevant personal antecedents, cardiovascular risk factors, previous treatment, and TRS based on 7 clinical variables were recorded. We prospectively calculated TRS for each patient, with scores in the 0 to 7 point range based on the simple arithmetic sum of each of the following characteristics: age ≥65 years; presence of 3 or more traditional risk factors (arterial hypertension, hypercholesterolemia, diabetes mellitus, smoking, and family history of early ischemic heart disease); previous history of significant coronary disease (stenosis ≥50%); administration of aspirin in the last 7 days; at least 2 episodes of angina in the last 24 hours; elevation of cardiac necrosis markers and ≥0.5 mm ST-segment alteration.

We defined 2 groups of patients:

– Group A: patients discharged from the emergency department.
– Group B: patients admitted to the cardiology department.

Patients hospitalized received antiplatelet treatment (aspirin, 100-300 mg/day; clopidogrel, 75 mg/day, with a 300 mg loading dose) and subcutaneous enoxaparin (1 mg/kg every 12 hours) unless contraindicated. Other drugs, such as beta-blockers, calcium antagonists or nitrates were administered in different combinations to control symptoms.

Síntomas

The 6-month follow-up included 1190 patients (94.9%) and we collected data on control of risk factors, compliance to treatment regimen, presence of symptoms, functional class, need for readmission, revascularization, occurrence of events such as AMI or death, and major or minor bleeding. The composite endpoint was defined as occurrence of any of the following: coronary revascularization, AMI, or cardiovascular death.

ANÁLISIS ESTADÍSTICO

Statistical analysis was performed with SPSS 11.0 (SPSS Inc. Chicago, Illinois, USA). Data were given as mean ± standard deviation (SD), range or frequency (percentage). We used the Kolmogorov-Smirnov test to evaluate the normality of the distribution of continuous quantitative variables in ≤30 patients. We used the Student t test to compare continuous quantitative variables in 2 groups when these were normal or there

ABREVIACIONES

CK-MB: MB isoenzyme of creatinkinase.
AMI: acute myocardial infarction.
ACS: acute coronary syndrome.
TRS: TIMI Risk Score.
were >30 cases; otherwise we used a nonparametric test (Mann-Whitney U). We used the Pearson $\chi^2$ test to compare 2 dichotomous variables if the number of expected observations in all cells was >5, and the Fisher exact test for 2 to 5 expected observations. The logistical regression test was used to evaluate the relationship between significant variables and events. Statistical significance was set at $P<.05$.

RESULTS

The prevalence of chest pain as a motive for attending the clinic was 3.2%. Baseline patient characteristics, both overall and for each of the 2 groups are summarized in Table 1. Hospitalized patients were significantly older and mostly male. They presented a greater number of risk factors, higher incidence of infarction or previous revascularization and cardiovascular treatment. Typical chest pain suggestive of angina was present in 64% of patients hospitalized versus 2.4% of patients discharged from the emergency department. Pain was considered non-specific in 61% of these patients. Chest pain was accompanied by dynamic electrocardiographic changes in 17% of hospitalized patients and 32% had troponin I elevation. Electri-
cal changes (n=3) or elevated troponin I levels (n=4) were present in less than 0.5% of patients discharged; both abnormalities were attributed to non-ischemic alterations or occurred in patients not considered for admission.

The TRS distribution of the patient population is described in Table 2: 4.9% (n=45) with TRS >3 were discharged and 24.5% (n=84) with TRS=0-1 were hospitalized.

Dual antplatelet treatment with aspirin and clopidogrel was administered to 180 patients (52.5%), this was associated with tirofiban in 43 (12.5%). We tested 45% of hospitalized patients for ischemia (37% were positive) and 47% underwent coronary angiography; single vessel disease was found in 49 patients (30%); multivessel disease in 78 (48%) and absence of significant lesions in 34 (21%).

Table 3 shows in-hospital events at 6 months for the study population. Among hospitalized patients, only 17 (5%) of those who received in-hospital revascularization underwent surgery. Of the 7 cardiovascular deaths, 3 were sudden, 2 due to heart failure and 2 followed cardiovascular surgery (1 intestinal ischemia and 1 septic shock). Other 2 patients died of non-cardiac cause. Final diagnoses of the 343 hospitalized pa-

---

**TABLE 1. Clinical Characteristics of the Study Population**

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Discharged From Emergency Department</th>
<th>Hospitalized</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>1254</td>
<td>911 (72.6%)</td>
<td>343 (27.6%)</td>
<td></td>
</tr>
<tr>
<td>Age, years, mean±SD</td>
<td>54±19</td>
<td>49±19</td>
<td>66±12</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Men</td>
<td>720</td>
<td>501 (55.0%)</td>
<td>221 (64.4%)</td>
<td>.003</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>523</td>
<td>299 (32.8%)</td>
<td>226 (65.9%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>209</td>
<td>107 (11.7%)</td>
<td>103 (30.1%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Oral anti diabetic drugs</td>
<td>164</td>
<td>91 (10.0%)</td>
<td>74 (21.6%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Insulin</td>
<td>45</td>
<td>16 (1.8%)</td>
<td>29 (8.5%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Smoking</td>
<td>474</td>
<td>324 (35.6%)</td>
<td>152 (44.3%)</td>
<td>.004</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>355</td>
<td>173 (19.0%)</td>
<td>181 (52.8%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous AMI</td>
<td>143</td>
<td>54 (5.9%)</td>
<td>90 (26.2%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Previous revascularization</td>
<td>120</td>
<td>40 (4.4%)</td>
<td>81 (23.6%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Antiplatelet agents</td>
<td>314</td>
<td>136 (14.9%)</td>
<td>177 (51.6%)</td>
<td>.001</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>60</td>
<td>35 (3.8%)</td>
<td>25 (7.3%)</td>
<td>.01</td>
</tr>
<tr>
<td>Nitrates</td>
<td>167</td>
<td>63 (6.9%)</td>
<td>103 (30.0%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>221</td>
<td>110 (12.1%)</td>
<td>110 (32.1%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Statins</td>
<td>230</td>
<td>100 (11.0%)</td>
<td>129 (37.6%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ACE inhibitors/ARA-II</td>
<td>244</td>
<td>128 (14.1%)</td>
<td>118 (34.4%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Verapamil/diltiazem</td>
<td>75</td>
<td>30 (3.3%)</td>
<td>45 (13.1%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Dihydropiridine</td>
<td>108</td>
<td>47 (5.3%)</td>
<td>59 (17.2%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Characteristics of pain</td>
<td>241</td>
<td>22 (2.4%)</td>
<td>219 (64.0%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Typical angina</td>
<td>193</td>
<td>105 (11.5%)</td>
<td>88 (25.7%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Atypical angina</td>
<td>679</td>
<td>324 (35.6%)</td>
<td>354 (10.2%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Non-specific</td>
<td>114</td>
<td>4 (0.4%)</td>
<td>110 (32.1%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>ECG changes</td>
<td>62</td>
<td>3 (0.3%)</td>
<td>59 (17.2%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Elevated troponin I</td>
<td>114</td>
<td>4 (0.4%)</td>
<td>110 (32.1%)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*ARA-II indicates angiotensin II receptor antagonists; SD, standard deviation; ECG, electrocardiogram; ACE inhibitors, angiotensin converting enzyme inhibitors.
patients were: myocardial infarction, 49 (14.3%); unstable angina, 129 (37.6%); secondary angina, 21 (6.1%); other cardiac causes, 50 (14.6%); and non-cardiac pain, 94 (27.4%). Patients with a final diagnosis of ACS presented significantly higher TRS than patients whose final diagnosis was not ACS (3.3±1.3 vs 2.0±1.2; P<.001).

We achieved full clinical follow-up in 1190 patients (94.9%). At 6 months, 9.6% of hospitalized patients had presented a composite endpoint versus only 1.3% of those discharged from the emergency department; moreover, all the parameters evaluated were significantly greater. Among the patients discharged from the emergency department, 45 (5.3%) were hospitalized within 6 months; 9 (1.1%) required coronary revascularization; 5 (0.6%) presented AMI; 2 (0.2%) died due to cardiovascular causes (of these, one 76 year-old man with TRS=3 died of heart failure and one 89 year-old man with TRS=5 of sudden death). Patients with high TRS (≥4) presented significantly greater risk of composite endpoint at 6 months (5 [11.1%] vs 7 [0.9%]; P<.001).

Table 4 shows the relationship between TRS and cardiac events at 6 months in the 2 study groups. Figure shows endpoint percentages according to the TRS for all patients and by group. The TRS was a good predictor of risk gradient. Patients with higher scores more frequently presented composite endpoints at 6 months (from 3.6% to 40.0% for TRS of 0/1 and 6/7, respectively, in hospitalized patients and from 0.5% to 100% for TRS of 0/1 and 5, respectively, in patients discharged from the emergency department). The relative risk of the composite endpoints in the first 6 months of follow-up per unit TRS increase among hospitalized patients was 1.72 (95% confidence inter-
val [CI], 1.32-2.24; \( P < .001 \) and 3.63 among patients discharged from the emergency department (95% CI, 2.20-6.00; \( P < .001 \)).

Thus, we observed a significant relationship between characteristics of the pain leading to attend the clinic and events observed in patients discharged from the emergency department. Of these, 5 (0.7%) with non-specific chest pain, 4 (3.9%) with suggestive pain and 3 (13.5%) diagnosed with angina presented composite endpoints at 6 months (\( P < .001 \) for non-specific vs suggestive/angina). However, we did not find this association in the 4 (11.4%) hospitalized patients with non-specific chest pain versus the 30 (9.9%) patients with suggestive/angina pain who presented composite endpoints (\( P = .8 \)).

**DISCUSSION**

This study of a non-selected population with chest pain confirmed the TRS as a valuable prognostic predictor and it establishes a risk gradient from 0.5% for patients with low TRS (0/1) up to 40% for patients with high scores (6/7). This risk scale had a high prognostic value both among hospitalized and discharged patients. The present study is the first to have evaluated this in a large, prospective, consecutive, non-selected group of patients attending an emergency department.

Different methods of prognostic stratification based on clinical history and complementary tests for management of ischemic chest pain have been developed. Risk prediction algorithms such as those proposed by Goldman et al\(^7\) or Pozen et al\(^7\) prove complex and are little used. Braunwald’s classification of unstable angina, much used in the last decade, has recently been revised to include cardiac enzymes levels.\(^14\) In Spain, the PEPA (Proyecto de Estudio del Pronóstico de la Angina; study project on the prognosis of angina) study, defined from clinical and electrocardiographic data the 90-day risk of death and infarction in patients with ACS without ST-segment elevation.\(^18\)

The Thrombolysis in Myocardial Infarction (TIMI) study risk score has become widely used as a tool to stratify prognosis of patients with ACS with and without ST-segment elevation.\(^19,21,23,24\) The TRS provides a simple schematic evaluation with great prognostic capacity, based on 7 variables that can be easily obtained at the patients’ bedside. This scale was developed thru the retrospective application of multivariate statistical analysis on the populations of 2 heparin trials: TIMI-11B\(^25\) and ESSENCE (Efficacy and Safety of Subcutaneous Enoxaparin in Unstable Angina and Non-Q-wave Myocardial Infarction).\(^26\) Later, it was validated in studies such as CURE,\(^27\) PRISM-PLUS,\(^28\) or TACTICS-TIMI 18\(^29\) and has proven valid to predict prognosis and response to new treatments and interventions. However, little is known about its application in daily clinical practice beyond the trials in which it was developed and in non-selected populations, where presence of electrical changes or elevation of cardiac enzymes were frequent inclusion criteria.\(^21,29,30\) Bartholomew et al\(^31\) evaluated 245 consecutive patients hospitalized for chest pain and found the TRS to be a potent predictor of events. The
very high 30-day rate of these events, 20% for TRS=2
and >50% for TRS>5, reflects a high-risk population,
higher even than that of the original TIMI study
(>70% of patients with electrical changes and 30%
presenting signs of heart failure). This contrasts with
the lower percentage of events in the present study,
which includes low-risk patients discharged after exa-
mination in the emergency department. Sample size
and differences in the profiles of patients who attend
different centers could partially explain these discre-
pancies.

The fact that our population is heterogeneous and
non-selected could explain why the general prognosis
is better even than in Antman et al’s original registry,19
even though they also included high-risk patients
(mean age, 54 years, 42% with hypertension, 17%
with diabetes, 11% with previous infarction, 10% with
previous revascularization, and 9% with high troponin
levels). The high percentages of antiplatelet treatment
(52% with a combination of 2 drugs and 12% with a
combination of 3) and revascularization (34%) pos-
sibly lowered the rate of events found among hospita-
lized patients. This could reflect the impact of recent
studies, such as CURE32 and TACTICS,29 on daily
clinical management. This is reinforced by the similitude
of our results with those of the validation of TRS in
CURE,32 which compared the efficacy of combined
antiplatelet treatment using aspirin and clopidogrel
with aspirin alone on prognosis in 12 562 patients with
ACS. Results showed 3% of events at 9 months with
TIMI=0/1 scores and 19% with TIMI=6/7 in the as-
pirin and clopidogrel group, although revascularization
was not included in the composite endpoint. Our 4.5%
(>1.5%) rate for bleeding is similar to that of CURE
and other studies such as the TOPSTAR trial33.

**Limitations**

Although the study population is large (1254 pa-
tients), the TRS distribution is not homogeneous. Only
10 patients (0.8%) presented TRS=6/7 and 38 (3.0%)
TRS=5. This may have influenced the frequency of events in this group (Figure) even though this distribu-
tion is the most common in non-selected populations.
It is important to note differences in the determination
of enzymes in our study by comparison with the origi-
nal and later validation trials. We performed serial
evaluations of troponin concentrations in all patients
as well as analyzing CK and CK-MB. Greater sensi-
tivity of troponin concentrations34-35 could have condi-
tioned TRS differences. Diagnosis of infarction using
new criteria including elevated troponin concentra-
tions could cause differences in the calculation of events. As in the original study, quantitative data on
troponin concentrations was not included, nor was the
contribution of other biological markers, such as C re-
active protein, evaluated. Finally, it may not be possi-
ble to extrapolate results of the present single-center
study to contexts with differences in population and
clinical management.

**CONCLUSION**

The TIMI risk score is an efficient tool in the stratifi-
cation of risk of cardiovascular events in patients at-
tending an emergency department for chest pain. The
TRS enables us to identify those high-risk patients
who would benefit from admission and active treat-
ment, individualized to suit each patient’s needs. Pa-
tients with TRS=0/1 and 2 who do not present electro-
cardiographic changes or enzyme elevation could be
discharged with a low probability of cardiac events at
6 months. Whereas in patients with TIMI>3, hospitali-
zation and treatment in line with current guidelines
should be considered.

**REFERENCES**

1. Marrugat J, Elouas R, Martí H. Epidemiología de la cardiopatía
ísquémica en España: estimación del número de casos y de las
2. Jesse RL, Kontos MC. Evaluation of chest pain in the emergency
3. Lee TH, Rouan GW, Weisberg MC, Brand DA, Cook EF, Acam-
pora D, et al. Sensitivity of routine clinical criteria for diagnosing
myocardial infarction within 24 hours of hospitalization. Ann In-
et al. Malpractice claims against emergency physicians in Massa-
5. Pozen MW, d’Agostino RB, Selker HP, Syktowski PA, Hood
WB Jr. A predictive instrument to improve coronary-care-unit ad-
mission practices in acute ischemic heart disease. A prospective
6. McCarthy BD, Beshansky JR, d’Agostino RB, Selker HP. Missed
diagnoses of acute myocardial infarction in the emergency depart-
7. Goldman L, Weinberg M, Weisberg M, Olshen R, Cook EF, Sarg-
ent RK, et al. A computer-derived protocol to aid in the diagno-
sis of emergency room patients with acute chest pain. N Engl J
8. Goldman L, Cook EF, Brand DA, Lee TH, Rouan GW, Weisberg
MC, et al. A computer protocol to predict myocardial infarction
1998;318:797-803.
Beshansky JR, et al. Missed diagnoses of acute cardiac ischemia
10. Sanchis J, Bodí V, Llacer A, Facila L, Pellicer M, Bertomeu V,
et al. Estratificación del riesgo de pacientes con dolor torácico sin
elevación del segmento ST en la puerta de urgencias. Rev Esp
Cardiol. 2003;56:955-62.
Nacher JJ, et al. Unidades de dolor torácico. Organización y pro-
tocolo para el diagnostico de los síndromes coronarios agudos.
12. López BL, Arós BF, Lidón Corbi RM, Cequier FA, Bueno H,
Clínica de la Sociedad Española de Cardiología en angina inestab-