Prognostic Value of Persistent ST-Segment Elevation after Successful Primary Angioplasty

Francisco Pomar Domingo, José V. Albero Martinez, Enrique Peris Domingo, Ildefonso Echanove Errazti, Juan V. Vilar Herrero, Emilio Pérez Fernández and José A. Velasco Rami


Introduction and objectives. A variable percentage of patients with myocardial infarction treated with successful primary angioplasty and restoration of coronary flow show persistent ST-segment elevation, probably due to inadequate cellular reperfusion. We studied if persistent ST-segment elevation was a predictor of worse prognosis.

Patients and method. We comparatively studied the clinical and angiographic results of 116 acute myocardial infarction patients after successful primary angioplasty, which were classified into two groups depending on the persistence (> 50%) or reduction (≤ 50%) of ST-segment elevation between the electrocardiograms recorded before and after coronary angioplasty.

Results. In 96 patients (Group I) the ST-segment elevation improved after angioplasty and in 20 patients (Group II) there was no improvement. Baseline characteristics were similar in both groups except for Killip class 4, which was more prevalent in group II (7.2 vs. 25%; p = 0.01). There were no differences in the characteristics or results of the procedure. There was more myocardial damage in group II (CK 3,149 ± 1,636 vs. 2,185 ± 2,010 U/l; p = 0.02), associated with a more impaired left ventricular ejection fraction in the late angiographic control (47 ± 16 vs 55 ± 16%; p = 0.05). At a one-year follow-up the mortality was 8.3% in group I and 30% in group II (p = 0.01).

Conclusions. The persistence of ST-segment elevation after successful primary angioplasty identifies a group of patients that may suffer an increased risk of adverse events in spite of good epicardial flow.

Key words: Myocardial infarction. Coronary angioplasty. Reperfusion.

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Introduction and objectives. Un porcentaje variable de pacientes con infarto agudo de miocardio tratados con angioplastia primaria mantienen el segmento ST elevado a pesar de restablecer el flujo coronario, probablemente por inadecuada reperfusión celular. Analizamos si la persistencia del segmento ST elevado es un signo que puede predecir un peor pronóstico.

Pacientes y método. Comparamos los resultados clínicos y angiográficos de 116 pacientes con infarto agudo de miocardio tratados con éxito mediante angioplastia primaria, clasificados en dos grupos dependiendo de la persistencia (≥ 50%) o reducción (< 50%) de la elevación del segmento ST entre los electrocardiogramas realizados antes y después del procedimiento.

Resultados. En 96 pacientes (grupo I) el segmento ST mejoró tras la angioplastia y en 20 pacientes (grupo II) no hubo mejoria. No existieron diferencias en las características clínicas y angiográficas basales excepto mayor prevalencia de clase Killip 4 en el grupo II (7.2 frente a 25%; p = 0.01). Tampoco hubo diferencias en las características y los resultados del procedimiento. La extensión del daño miocárdico fue mayor en el grupo II (CK 3,149 ± 1,636 frente a 2,185 ± 2,010 U/l; p = 0.02) y se asoció a una peor fracción de eyeción ventricular en el estudio angiográfico tardío (47 ± 16 frente a 55 ± 16%; p = 0.05). La mortalidad al año fue del 8,3% en grupo I y del 30% en grupo II (p = 0.01).

Conclusiones. La persistencia del segmento ST elevado tras una angioplastia primaria con éxito permite diferenciar un grupo de pacientes en los que, a pesar de restablecer un buen flujo coronario epicárdico, el riesgo de acontecimientos adversos está incrementado.

Palabras clave: Infarto de miocardio. Angioplastia coronaria. Reperfusión.

INTRODUCTION

For many years, the benefits of reperfusion treatment in acute myocardial infarction (AMI) have been attributed to the re-establishment of coronary flow in the artery responsible for the infarction (ARI).1,2 Later,
various studies with angiographic control confirmed that, in addition to opening the ARI, it was necessary to achieve a flow of TIMI (Thrombolysis in Myocardial Infarction) grade 3 in order to improve survival.\textsuperscript{3,4} Currently, several studies with contrast echocardiography,\textsuperscript{5,6} magnetic resonance,\textsuperscript{7} and gammography\textsuperscript{10,12} have shown that normalization of epicardial coronary flow does not always correspond to adequate myocardial perfusion.

With primary coronary angioplasty (CA), achievement of flow of TIMI 3 means that the procedure has been successful.\textsuperscript{13} Nevertheless, in some patients, in spite of angiographic success, the ST segment remains elevated on electrocardiogram, which is probably indicative of inadequate cellular reperfusion.\textsuperscript{14} In patients treated with thrombolysis, the rapid resolution of e ST segment elevation is considered a good marker for reperfusion.\textsuperscript{15,18} In this study we attempt to evaluate whether the persistence of the ST segment elevation after primary PCA when angiographic success has been achieved is a sign that could predict a worse prognosis in the short and long term.

PATIENTS AND METHODS

Patients

From January 1995 to December 1997, 145 patients with AMI were treated in our hospital with primary CA. All the patients presented with anginous chest pain of more than 30 minutes duration and an ST elevation of 0.1 mV in 2 or more contiguous derivations. In 118 cases, which constituted our study group, the primary CA procedure was performed successfully, with re-establishment of TIMI 3 flow in the ARI with residual stenosis of less than 30%.

Electrocardiographic analysis

Analysis of the ST segment was performed by an independent observer who did not know the patient’s clinical data. In each case 2 12-lead ECG recordings were made: 1 at baseline performed before the primary CA and a second after the procedure, when the patient returned to the coronary unit. The electrocardiograms were recorded with the standard calibration of 1 mV/cm and a speed of 25 mm/second. ST segment elevation was measured at 0.08 of the J point, and was used for the analysis of the derivation where said elevation was greatest. An improvement in ST segment elevation was considered to have occurred when the post-CA value was reduced to less than 50% of the value measured pre-CA.

Coronary angiography and coronary angioplasty

Coronary angiography and CA were performed using the usual techniques. The ARI flow was defined by using TIMI criteria.\textsuperscript{19} Multiple vessel disease was defined as the presence of more than 70% stenosis in another artery that was not responsible for the infarct. CA was performed when the initial angiography of the ARI showed subtotal or total occlusion with a TIMI flow of less than grade 3. A stent was implanted according to the criteria of the surgeon who performed the CA in 76% of cases.

All patients received an intravenous bolus of 10,000 units of sodium heparin and 500 mg of acetylsalicylic acid on initiation of the procedure, followed by an intravenous perfusion of heparin to maintain an activated partial thromboplastin time (APTT) between 50 and 100 seconds. Abciximab was not used as it was not available in our center during the study period.

Clinical and angiographic follow-up

During hospitalization, a series of determinations of the CK, CK-MB, and the maximum value reached was considered an enzyme marker for the size of the AMI. A blood sample was obtained every 6 hours during the first 72 hours and, later, every 24 hours. The survivors were scheduled at the time of discharge to be clinically evaluated at 3, 6, and 12 months following the procedure.

Angiography studies were used as controls after the sixth month, and we analyzed the amount of re-stenosis and the TIMI flow level in the treated artery. Coronary angiography quantification was performed using an automatic border detection system (Ancor, Siemens) and re-stenosis was considered to exist when the stenosis was 50%.

Ventricular function

In all cases, left ventriculography was performed immediately after the CA and again after the later control angiography. The volume of the left ventricle and the ejection fraction were calculated by using the Sandler and Dodge\textsuperscript{20} area-longitude method. A segment contractility score was obtained by dividing the

<table>
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<th>ABBREVIATIONS</th>
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<tr>
<td>AMI: acute myocardial infarction.</td>
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<tr>
<td>ARI: artery responsible for the infarct.</td>
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<tr>
<td>TIMI: grade of coronary flow (Thrombolysis in Myocardial Infarction study).</td>
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<td>CA: coronary angioplasty.</td>
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<td>APTT: activated partial thromboplastin time.</td>
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left ventricle into 5 segments that were qualitatively scored as follows: 1=normal, 2=hypokinesia, 3=akinesia, and 4=dyskinesia.

### Side-effects

Death, re-infarct, and the need for revascularization via CA or surgery that included ARI were considered adverse side-effects.

### Statistical analysis

The different variables were analyzed with the SPSS 10.0 statistical program. The continuous variables were expressed as mean±standard deviation (SD) and they were categorized by percentages, using the Kolmogorov-Smirnov test to eliminate the normal distribution of same. To analyze the differences between the groups, the Student t test was used to compare quantitative variables and the χ² test was used for the qualitative variables. Multivariate analysis was carried out by logistical regression. The Kaplan-Meier method was used to analyze the time free of adverse side-effects during the follow-up period and the logarithmic range test was used to compare the curves of both groups. A value of P<.05 was considered statistically significant.

### RESULTS

#### Patient characteristics

Based on ST segment changes, the patients were classified into 2 groups; group I, composed of 96 patients in whom the ST segment improved (<50% of baseline value) following the CA, and group II, made up of 20 patients in whom no improvement of ST segment was observed (≥ 50% of baseline value). Two patients with complete block of the left branch on baseline ECG were excluded from the study. The time that elapsed from the opening of the ARI to the post-CA ECG recording that we used for the study was similar in both groups (16±11 minutes and 15±8 minutes; P=.92).

The baseline clinical and angiographic characteristics for both patient groups are reflected in Table 1. There were no differences between the groups, with the exception of a greater prevalence of Killip 4 in group II. Although there was a greater percentage of anterior infarct and of involvement of the anterior interventricular artery in group II, this did not reach statistical significance.

### Characteristics and results of primary angioplasty

In all patients, TIMI grade 3 flow was re-established in the artery responsible for the infarct (ARI). The

<table>
<thead>
<tr>
<th>TABLE 1. Baseline clinical and angiographic characteristics</th>
<th>Group I (n=96)</th>
<th>Group II (n=20)</th>
<th>P</th>
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<tbody>
<tr>
<td>ST Improvement</td>
<td>No ST Improvement</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years (mean±SD)</td>
<td>61±12</td>
<td>61±11</td>
<td>.65</td>
</tr>
<tr>
<td>Male</td>
<td>83 (86%)</td>
<td>15 (75%)</td>
<td>.19</td>
</tr>
<tr>
<td>Active smokers</td>
<td>48 (50%)</td>
<td>9 (45%)</td>
<td>.10</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>30 (31%)</td>
<td>7 (35%)</td>
<td>.27</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>37 (38%)</td>
<td>10 (50%)</td>
<td>.34</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>22 (23%)</td>
<td>6 (30%)</td>
<td>.50</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>10 (10%)</td>
<td>3 (15%)</td>
<td>.11</td>
</tr>
<tr>
<td>Anterior location of infarct</td>
<td>62 (64%)</td>
<td>17 (85%)</td>
<td>.07</td>
</tr>
<tr>
<td>Killip Class IV</td>
<td>7 (7.3%)</td>
<td>5 (25%)</td>
<td>.01</td>
</tr>
<tr>
<td>Maximum initial ST elevation, mm (mean±SD)</td>
<td>4.8±2.4</td>
<td>4.5±2.8</td>
<td>.83</td>
</tr>
<tr>
<td>Time from beginning of pain to initiation of procedure, min (mean±SD)</td>
<td>152±101</td>
<td>150±108</td>
<td>.91</td>
</tr>
<tr>
<td>Artery responsible for the infarct</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior descending</td>
<td>62 (64%)</td>
<td>17 (85%)</td>
<td>.06</td>
</tr>
<tr>
<td>Circumflex</td>
<td>6 (6.2%)</td>
<td>0</td>
<td>.16</td>
</tr>
<tr>
<td>Right coronary</td>
<td>28 (29%)</td>
<td>3 (15%)</td>
<td>.05</td>
</tr>
<tr>
<td>TIMI grade of initial flow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-1</td>
<td>82 (85%)</td>
<td>18 (90%)</td>
<td>.61</td>
</tr>
<tr>
<td>2</td>
<td>14 (15%)</td>
<td>2 (10%)</td>
<td>.58</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>–</td>
</tr>
<tr>
<td>Multi-vessel disease</td>
<td>47 (49%)</td>
<td>8 (40%)</td>
<td>.46</td>
</tr>
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N indicates number of patients; SD, standard deviation; TIMI, grade of coronary flow (Thrombolysis in Myocardial Infarction).
the need for a new revascularization (6.2 versus 5%; \( P = .18 \)).

In the multivariate logistic regression analysis adjusted for age, sex, risk factors, previous infarct, location of the infarct, time from the beginning of pain, and the characteristics of the CA procedure, the non-resolution of the ST segment was an independent predictor of mortality (OR=4.55; 95% CI, 1.1-18.78; \( P = .03 \)). Shock was not included in the model, as it was considered a mechanism of death rather than a prognostic factor requiring adjustment.

**Clinical follow-up**

Of the 107 patients surviving at discharge, during the following year there were 3 deaths in group I and 2 deaths in group II (3.1% versus 10%; \( P = .01 \)). In total, the accumulated mortality rate per year for all patients was 12%, with a significant difference between the groups (8.3% in group I and 30% in group II; \( P = .01 \)). The re-infarction rate was 1.7% (1% in group I and 5% in group II; \( P = .01 \)). A total of 14 patients required revascularization procedures (13% in group I and 12.5% in group II; \( P = .52 \)). The survival curves and absence of adverse cardiac effects is shown in Figure 1.

**Angiographic follow-up**

Angiography was performed on 89% of the patients discharged (88% of group I and 93% of group II) at 231 days±42 days after the AMI. The ARI was permeable in 96% of cases (in 1 case in group I and in 3 cases in group II it was occluded). There was no significant difference in the percentage of stenosis of the ARI (38±35% in group I and 40±27% in group II), or in the rate of re-stenosis, which was 35.8% in the patients in group I and 33% in group II.

**Ventricular function**

There were no significant differences between the 2 groups with regard to ejection fraction and segment contractility score obtained by ventriculography performed in the acute phase of AMI. Nevertheless, angiography carried out on follow-up showed significant differences, with a better ejection fraction and segment contractility in group I (Table 2).

**DISCUSSION**

Our study, performed on a series of patients with AMI treated with primary CA, confirms that, in spite of the re-establishment of the epicardic fluid to TIMI level 3 in the ARI, those patients in whom the ST segment remained elevated \( \geq 50\% \) of baseline value had a worse prognosis, with a more extensive AMI, worse long-term ventricular function, and a higher mortality rate.

**Myocardial no reflow phenomenon**

The re-establishment of a grade 3 TIMI flow in the ARI is the template for reperfusion of AMI, and primary CA has shown that this can be achieved in 75%
to 95% of cases. Nevertheless, in spite of angiographic success, some patients do not have a favorable course as a result of deficient cellular reperfusion. This phenomenon is called myocardial no reflow, first described by Klomer et al. in an animal model, and was observed later in patients with AMI treated with thrombolytic medication and primary angioplasty. There is evidence that the cause of myocardial no reflow is microvascular dysfunction caused by endothelial damage, perivascular edema, intramural hemorrhage, capillary obstruction due to accumulation of neutrophils, and spasm of the small vessels.

**ST segment and myocardial perfusion**

For many years, normalization of ST segment elevation on 12-lead ECG has been used as a non-invasive indicator of ARI permeability. The complete resolution of ST elevation after thrombolysis has been associated with a greater than 90% probability of having a permeable ARI and with a 70% to 80% probability that the flow will be TIMI 3. At present, there is enough evidence to believe that the persistence of an elevated ST segment in the presence of completely re-established epicardial flow (TIMI grade 3) may be indicative of insufficient myocardial perfusion and, because of this, the changes observed on ECG may be a more specific indicator of myocardial perfusion that coronary angiography itself.

**Prevalence of elevated ST segment with TIMI 3 flow**

In our study of a patient cohort composed exclusively of patients in whom primary CA had achieved restoration of TIMI 3 flow, we observed that in nearly 20% of cases the ST segment remained elevated. The prevalence of this phenomenon in other studies varies from 15% to 35%, depending on the cut-off value that is used for resolution of the ST segment. We used a value of 50%, which has been used in other studies, that reported findings similar to other more complex models. Also, the time that passed from the opening of the vessel to the performance of post-CA ECG may influence the results. With the aim of obtaining early data that would allow us to differentiate patients with a worse prognosis, we have analyzed post-angioplasty ECG tracings performed when the patient arrived at the coronary unit approximately 15 minutes after the CA.

**Influence of baseline characteristics**

The reasons for deficient myocardial perfusion following primary CA are not clear. In our study, the only baseline characteristic that was associated with greater frequency to worse myocardial perfusion is Killip class IV prior to the CA, which was greater in those patients who maintained an elevated ST segment. This finding was also reported by Claes et al, who considered the low systolic arterial pressure upon admission to be the principal determinant of deficient microvascular reperfusion. The same authors suggested that age could also be a determinant of worse microvascular perfusion. Nevertheless, other recent studies coincide with our study, and we did not find difference in the ages of patient groups with better or worse myocardial perfusion. Some studies have also suggested that an anterior location of the AMI, due to the greater extent of myocardial damage, predisposes the patient to worse myocardial perfusion.

In our study, although the proportion of anterior AMI was greater in group I, this did not reach statistical significance.

**Persistence of elevated ST segment and prognosis**

Our study confirms that, with primary AC, in spite of the re-establishment of an epicardic flow of TIMI 3, the persistence of ST segment elevation >=50% of baseline value is a clear predictor of worse clinical results. Those patients with persistence of an elevated ST segment have more extensive AMI, reflected by a greater liberation of myocardial enzymes. This is a finding that coincides with the majority of studies and that translates into worse long-term ventricular function and a higher mortality rate on follow-up.

Although the subgroup of patients with cardiogenic shock was reduced in our study, it is interesting to note that in patients with cardiogenic shock who after CA had improvement of the ST segment the mortality rate (28%) was relatively low. On the other hand, those patients who maintained an elevated ST segment had a high mortality rate (80%), similar to that observed in patients with cardiogenic shock who had undergone an unsuccessful CA.

**Study limitations**

The analysis of the ST segment in a single ECG recording performed 15 to 20 minutes after the opening of the ARI could be insufficient to evaluate the state of myocardial perfusion, and could provide information that is different from that obtained at between 90 and 180 minutes as reported by other authors. There is evidence that myocardial reperfusion is a dynamic process that could be the cause of fluctuations in the ST segment and, because of this, some authors propose continuous monitoring of the ST segment via automatic analysis systems. Our study was performed on a relatively small and select cohort of patients with AMI who had been successfully treated with primary CA and, therefore, the results should only be applied to
Clinical implications

Our study suggests that ST segment monitoring obtained by simple electrocardiogram after a primary AC procedure, in combination with angiographic findings, may be of great use to differentiate a group of patients in whom, in spite of having good epicardic flow, myocardial reperfusion is insufficient and the risk of adverse events is increased. This selection of patients should encourage the use of supplemental treatment that favors microvascular perfusion, with the intention of reducing cell damage and improving prognosis.

REFERENCES