Early Electrocardiographic Findings and MR Imaging-Verified Microvascular Injury and Myocardial Infarct Size

Robin Nijveldt, MD, PhD,* Pieter A. van der Vleuten, MD,‡ Alexander Hirsch, MD,†§ Aernout M. Beek, MD,* René A. Tio, MD, PhD,§ Jan G. P. Tijssen, PhD,§ Jan J. Piek, MD, PhD,§ Albert C. van Rossum, MD, PhD,*† Felix Zijlstra, MD, PhD‡ Amsterdam, Utrecht, and Groningen, the Netherlands

OBJECTIVES This study investigated early electrocardiographic findings in relation to left ventricular (LV) function, extent and size of infarction, and microvascular injury in patients with acute myocardial infarction (MI) treated with percutaneous coronary intervention (PCI).

BACKGROUND The electrocardiogram (ECG) is the most used and simplest clinical method to evaluate the risk for patients immediately after reperfusion therapy for acute MI. ST-segment resolution and residual ST-segment elevation have been used for prognosis in acute MI, whereas Q waves are related to outcome in chronic MI. We hypothesized that the combination of these electrocardiographic measures early after primary PCI would enhance risk stratification.

METHODS We prospectively included 180 patients with a first acute ST-segment elevation MI to assess ST-segment resolution, residual ST-segment elevation, and number of Q waves using the 12-lead ECG acquired on admission and 1 h after successful PCI. The ECG findings were related to LV function, infarction size and transmurality, and microvascular injury as assessed with cine and gadolinium-enhanced cardiac magnetic resonance 4 ± 2 days after reperfusion therapy.

RESULTS Residual ST-segment elevation ($\beta = -2.00, p = 0.004$) and the number of Q waves ($\beta = -1.66, p = 0.005$) were independent ECG predictors of LV ejection fraction. Although the number of Q waves was the only independent predictor of infarct size ($\beta = 2.01, p < 0.001$) and transmural extent of infarction ($\beta = 0.60, p < 0.001$), residual ST-segment elevation was the only independent predictor of microvascular injury (odds ratio: 19.1, 95% confidence interval: 2.4 to 154, $p = 0.005$) in multivariable analyses. The ST-segment resolution was neither associated with LV function, infarct size, or transmurality indexes, nor with microvascular injury in multivariable analysis.

CONCLUSIONS In patients after successful coronary intervention for acute MI, residual ST-segment elevation and the number of Q waves on the post-procedural ECG offer valuable complementary information on prediction of myocardial function and necrosis and its microvascular status. (J Am Coll Cardiol Img 2009;2:1187–94) © 2009 by the American College of Cardiology Foundation
The electrocardiogram (ECG) is the most used and simplest clinical method to evaluate the risk for patients immediately after successful reperfusion therapy for acute myocardial infarction (MI). In the early 1970s, experimental and in vivo studies established the use of ST-segment elevation as a reflection of myocardial injury (1,2), and later, ECG has proven to offer valuable prognostic information for patients treated with thrombolytic therapy or primary angioplasty (3,4). Patients with acute MI are stratified to ST-segment elevation or non-ST-segment elevation MI (5), and incomplete normalization of the ST-segment after reperfusion is associated with more extensive myocardial damage, microvascular injury, and a higher mortality rate (3,4,6–8). Similarly, patients with old infarction are divided into Q-wave and non-Q-wave MI (5), in which the presence of Q waves is related to larger infarcts and an increased mortality (9–11).

In current clinical practice, an ECG is routinely obtained shortly after percutaneous coronary intervention (PCI) for acute MI to evaluate the success of reperfusion and for initial risk stratification. Aside from ST-segment resolution and residual ST-segment elevation, the ECG offers information on early Q waves. Limited data are available on the additional value of Q-wave assessment compared with ST-segment resolution or residual ST-segment elevation early after reperfusion with respect to myocardial function and necrosis.

The purpose of this study was therefore to prospectively explore the significance of ECG findings early after primary PCI in relation to left ventricular (LV) function, extent and size of infarction, and microvascular injury as assessed by cardiac magnetic resonance (CMR).

METHODS

Patient population. We screened consecutive patients presenting with a first ST-segment elevation acute MI according to standard ECG and enzymatic criteria (5). All patients had undergone primary PCI with stent implantation within 12 h of symptom onset. Exclusion criteria were: unsuccessful PCI, hemodynamic instability, elevation of creatine kinase-myocardial band <10 times the local upper limit of normal, and (relative) contraindications for CMR. One-hundred eighty patients in 4 Dutch angioplasty centers were prospectively enrolled in the study. Patients were treated with aspirin, heparin, abciximab, clopidogrel, statins, beta-blocking agents, and angiotensin-converting enzyme inhibitors, according to American College of Cardiology/American Heart Association practice guidelines (12). All patients gave informed consent to the study protocol, which was approved by the local ethics committees of the participating centers.

ECG. The ST-segment resolution was evaluated on a 12-lead surface ECG acquired on admission and 1 h after PCI. The total degree of ST-segment resolution was determined 60 ms after the J point, and categorized as complete (≥70%), partial (30% to <70%), or none (<30%) ST-segment resolution (3). Residual ST-segment elevation and the presence of Q waves were assessed on the postprocedural ECG. Residual ST-segment elevation was stratified as 0.0 to 0.2, 0.3 to 0.5, 0.6 to 1.0, and >1.0 mV of persisting ST-segment elevation. The presence of a Q wave was defined as an initial negative deflection of the QRS complex of >30 ms in duration and >0.1 mV, if it was preceded by elevation of the ST-segment of more than 0.1 mV in the same lead on the ECG at diagnosis, and with exclusion of AVR (13). The number of Q waves was categorized as 0 to 2, 3, 4, and ≥5.

CMR. The CMR examination was performed on a 1.5-T clinical magnetic resonance scanner (Symphony/Sonata/Avanto, Siemens, Erlangen, Germany) using a phased-array cardiac receiver coil, at 4 ± 2 days after reperfusion. The ECG-gated images were acquired during repeated breath-holds. Contiguous short-axis slices were acquired using a segmented steady-state free-precession pulse sequence in multiple short axis views every 10 mm covering the entire LV from base to apex, to examine global and segmental LV function. Typical in-plane resolution was 1.6 × 1.9 mm², with slice thickness 5.0 to 6.0 mm (repetition time/echo time 3.2/1.6 ms, flip angle 60°, matrix 256 × 156, temporal resolution 35 to 50 ms). Late gadolinium enhancement (LGE) was performed 10 to 15 min after administration of a gadolinium-based contrast agent (Dotarem, Guerbet, Roissy, France; 0.2 mmol/kg) with a 2-dimensional segmented inversion recovery gradient-echo pulse sequence, to examine infarct size and segmental transmural extent of infarction. Typical in-plane resolution was 1.4 × 1.7 mm², with slice thickness 5.0 to 6.0 mm (repetition time/echo time = 9.6/4.4 ms, flip angle 25°, triggering to every
other heartbeat). The inversion time was set to null the signal of viable myocardium.

The CMR data were analyzed using a dedicated software package (Mass 2008beta, Medis, Leiden, the Netherlands). On short axis cine slices, the endocardial and epicardial borders were outlined manually in end-diastolic and -systolic images. From these, left ventricular end-systolic volume (LVESV) and left ventricular end-diastolic volume (LVEDV), left ventricular ejection fraction (LVEF), and mass were calculated. The assessment of LGE images for infarct size and microvascular injury (microvascular obstruction [MVO]) was done as previously described (7). Total infarct size was expressed as percentage of LV mass. MVO was defined as any region of hypoenhancement within the hyperenhanced area (Fig. 1) and was included in the calculation of total infarct size. The standard 17-segment model was used for segmental analysis of myocardial function and transmural extent of infarction (14), excluding segment 17 (apex), because segmental evaluation in the short-axis orientation is not considered reliable because of the partial volume effect and longitudinal shortening of the heart. Segmental wall thickening was calculated by subtracting end-diastolic from end-systolic wall thickness. Dysfunctional segments were defined as segments with systolic wall thickening of <3 mm. The transmural extent of infarction was calculated by dividing the hyperenhanced area by the total area of the pre-defined segment. Segments with more than 50% hyperenhancement were considered segments with transmural enhancement.

**Statistical analysis.** Values are reported as mean ± SD or median (25th to 75th percentile) for continuous variables and as frequency with percentage for categorical variables. For the comparison of continuous and categorical variables between anterior and nonanterior infarcts, the Mann-Whitney U test and chi-square test were used, as appropriate.

Correlations were calculated with simple linear and logistic regression analysis. To identify independent predictors of global and regional LV indexes, and size and extent of infarction, multivariable linear regression analysis was used. Because ST-segment resolution and residual ST-segment elevation may have important collinearity, multivariable linear regression analysis with a forward selection procedure was performed. The ST-segment resolution, residual ST-segment elevation, number of Q waves, and anterior MI entered the model if p < 0.10. Similar analysis was performed using multivariable logistic regression for the relation with the presence of MVO.

All statistical tests were 2-tailed, and a value of p < 0.05 was considered statistically significant. Calculations were generated by SPSS software (version 15.0 for Windows, SPSS, Inc., Chicago, Illinois).

**RESULTS**

Patient characteristics and angiographic and ECG data are listed in Table 1. Mean LVEDV was 99.4 ± 18.3 ml/m², LVESV was 57.8 ± 16.9 ml/m², and LVEF was 42.7 ± 8.6% in the total group of patients, with a mean number of 8.4 ± 3.2 dysfunctional segments. The mean total size of gadolinium-enhanced infarction was 16.6 ± 8.9% of LV mass, with a mean number of 3.2 ± 2.4 transmural enhanced segments. In 57.8% of the patients, there was presence of MVO on the LGE images. Patients with anterior MI (n = 114, 63%) had significantly worse LVEF, more dysfunctional segments, larger infarct size, and more segments with transmural enhancement than patients with nonanterior MI (p < 0.001 for all). There was no difference in median (25th to 75th percentile) symptom-to-balloon time between patients with anterior or nonanterior MI (2.6 h, 2.0 to 4.0 h vs.
Median time to reperfusion (h) 2.9 (2.0–4.5)

Risk factors

Body mass index (kg/m²) 26.3 (±3.1)

Women 64 (37%)

Diabetes mellitus 7 (4%)

Hypertension 45 (25%)

Hyperlipidemia 39 (22%)

Current smoking 101 (56%)

Table 1. Patient Characteristics and Angiographic and Electrocardiographic Data

<table>
<thead>
<tr>
<th>n</th>
<th>180</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>55 (±10)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.3 (±3.1)</td>
</tr>
</tbody>
</table>

Men 156 (87%)

Diabetes mellitus 7 (4%)

Hypertension 45 (25%)

Hyperlipidemia 39 (22%)

Current smoking 101 (56%)

Median maximum serum creatine kinase-myocardial band divided by local upper limit of normal 44 (24–69)

Median time to reperfusion (h) 2.9 (2.0–4.5)

Platelet glycoprotein IIb/IIIa inhibitors 137 (76%)

Multivessel disease 53 (29%)

Left anterior descending artery 114 (63%)

Left circumflex artery 19 (11%)

Right coronary artery 47 (26%)

TIMI flow grade post-PCI (n = 180)

| 1 | 2 (1%) |
| 2 | 20 (11%) |
| 3 | 158 (88%) |

MBG post-PCI (n = 173)

| 0–1 | 57 (33%) |
| 2–3 | 116 (67%) |

ST-segment resolution (n = 171)

| Complete | 102 (59%) |
| Partial | 49 (29%) |
| Incomplete | 20 (12%) |

Residual ST-segment elevation (mm) (n = 178)

| 0–2 | 75 (42%) |
| 3–5 | 56 (32%) |
| 6–10 | 32 (18%) |
| >10 | 15 (8%) |

Number of Q waves (n = 180)

| 0–2 | 44 (24%) |
| 3 | 48 (27%) |
| 4 | 47 (26%) |
| ≥5 | 41 (23%) |

Values are presented as number (%), mean (±SD), or median (25th–75th percentile).

MBG = myocardial blush grade; PCI = percutaneous coronary intervention; TIMI = Thrombolysis In Myocardial Infarction.

Table 2 and 3 also show the predictive value of each ECG parameter with respect to myocardial function, size and extent of infarction, and microvascular injury. The strongest predictors of LVEF were residual ST-segment elevation and the number of Q waves in multivariable analysis. Additionally, the number of Q waves independently predicted infarct size and transmural extent, whereas residual ST-segment elevation was the single and best predictor of MVO presence. The ST-segment resolution is no longer associated with LV function or transmurality after adjustment for residual ST-segment elevation and the number of Q waves. Furthermore, anterior MI was a strong independent predictor of LVEF, the number of dysfunctional segments, infarct size, and the number of segments with transmural infarction.

ECG in relation to angiography and infarct size. There was no relation between incomplete Thrombolysis in Myocardial Infarction (TIMI) flow grade after primary PCI (defined as TIMI flow grade 1 to 2) and LVEF (β = −2.37, p = 0.22), the number of transmural enhanced segments (β = −0.005, p = 0.99), or the presence of MVO (odds ratio [OR]: 1.7, 25th to 75th percentile: 0.7 to 4.4, p = 0.27). An impaired myocardial blush grading (MBG) (defined as MBG 0 to 1) correlated with LVEF (β = −4.06, p = 0.003) and with transmurality (β = 1.24, p = 0.001). Also, impaired MBG was associated with the presence of MVO (OR: 3.6, 1 /H11006 1.24, p = 0.001).
Multivariable linear regression analysis of all angiographic and ECG parameters showed residual ST-segment elevation and the number of Q waves as only independent variables for prediction of LVEF and the number of Q waves for predicting transmurality. For predicting the presence of MVO, impaired MBG (OR: 2.7, 25th to 75th percentile: 1.3 to 5.7, \( p = 0.009 \)) and residual ST-segment elevation of more than 10 mm (OR: 10.5, 25th to 75th percentile: 1.2 to 88.9, \( p = 0.03 \)) were both independently associated with MVO presence in multivariable logistic regression analysis.

DISCUSSION

The principal finding of this study in patients after successful PCI for acute ST-segment elevation MI was that residual ST-segment elevation and the number of Q waves on the post-procedural ECG are complementary in predicting myocardial func-
tion and necrosis. Residual ST-segment elevation, the number of Q waves, and anterior MI were the strongest predictors of LV function. Additionally, residual elevation was the single and best predictor of microvascular injury, whereas Q-wave count and anterior infarction best predicted infarct size and transmural extent of infarction.

The changes of the electrocardiographic ST-segment in patients with ST-segment elevation MI have been associated with patency of the infarct-related artery in multiple clinical studies (15,16). Although this is no misapprehension, an important percentage of the patients does not show normalization of the ST-segment after successful revascularization despite TIMI flow grade 3 (4) because of impaired reperfusion at the myocardial tissue level. This is caused by a multitude of processes, including tissue edema, platelet plugging, neutrophil adhesion, myonecrosis, and intracapillary red blood cell stasis, resulting in MVO, which is also known as the no-reflow phenomenon (17). Experimental and clinical studies have shown that MVO is common, and that it is associated with a higher incidence of LV remodeling, congestive heart failure, and death (18,19). Thus, the ST-segment early after PCI offers prognostic information by reflecting myocardial perfusion status rather than epicardial flow and predicts clinical outcome in patients with reperfused MI (3,4). The present study extends these findings by showing that persisting elevation of the ST-segment is strongly related to LV volumes and function and is strongly correlated with the presence of microvascular injury, which is essential information during hospitalization.

In line with previous studies, residual ST-segment elevation performed better as a predictive measure than ST-segment resolution (6,20). The ST-segment elevation in acute MI may have already partially normalized on admission because of the drastically improved infarct treatment, including heparin and aspirin during transfer to the tertiary center for primary PCI. Thus, the ECG before reperfusion therapy may underestimate the true amount of ST-segment elevation and consequently may affect its prognostic power. Residual ST-segment elevation may therefore better express reperfusion injury at the myocardial tissue level than ST-segment resolution.

Early work has reported that there is a relation between the presence of Q waves on the ECG and the transmural extent of infarction in chronic MI (21). Later, human autopsy studies suggested that this association was doubtful; however, much anatomical and clinical research has shown that the distinction of Q waves in patients with previous MI is useful for prognosis because its presence predicts larger infarcts and higher mortality (10,11,22). In a report by Tousek et al. (23), a relation was found between microvascular perfusion on myocardial contrast echocardiography and the extent of Q wave formation on the ECG after mechanical reperfused acute MI. Although echocardiography using myocardial contrast can be used to predict functional outcome after reperfused acute MI, it is not capable of differentiating between the presence or absence of transmural infarction in segments with reduced myocardial perfusion. To our knowledge, the present study is the first to evaluate the significance of the number of Q waves early after primary PCI in relation to myocardial function, and in particular, to study its relation between the extent of infarction and microvascular injury. The number of Q waves strongly predicted LV end-systolic volume, LVEF, and the number of dysfunctional segments, and was the strongest independent predictor on the ECG of infarct size and its transmural extent. There was no statistically significant relation with microvascular injury.

Another important difference between the results of this study and those of earlier studies assessing

Table 2. Predictive Value of Electrocardiographic Measures on Myocardial Function and Necrosis

<table>
<thead>
<tr>
<th></th>
<th>Univariable</th>
<th></th>
<th>Multivariable</th>
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<tr>
<td></td>
<td>Beta</td>
<td>p Value</td>
<td>Beta</td>
<td>p Value</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-segment resolution</td>
<td>-2.47</td>
<td>0.008</td>
<td>-1.93</td>
<td>0.005</td>
</tr>
<tr>
<td>Residual ST-segment elevation</td>
<td>-3.09 &lt;0.001</td>
<td></td>
<td>-1.66</td>
<td>0.005</td>
</tr>
<tr>
<td>Number of Q waves</td>
<td>-2.61 &lt;0.001</td>
<td></td>
<td>-2.77</td>
<td>0.043</td>
</tr>
<tr>
<td>Anterior myocardial infarction</td>
<td>-5.47 &lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of dysfunctional segments</td>
<td>0.84 0.02</td>
<td></td>
<td>2.52 &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Infarct size (% of left ventricular mass)</td>
<td></td>
<td></td>
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<tr>
<td>ST-segment resolution</td>
<td>1.85</td>
<td>0.045</td>
<td>2.52</td>
<td>0.001</td>
</tr>
<tr>
<td>Residual ST-segment elevation</td>
<td>2.46 &lt;0.001</td>
<td></td>
<td>2.01</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of Q waves</td>
<td>2.77 &lt;0.001</td>
<td></td>
<td>5.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anterior myocardial infarction</td>
<td>6.91 &lt;0.001</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Number of transmural segments</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ST-segment resolution</td>
<td>0.61</td>
<td>0.02</td>
<td>1.91</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Residual ST-segment elevation</td>
<td>0.82 &lt;0.001</td>
<td></td>
<td></td>
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<tr>
<td>Number of Q waves</td>
<td>0.87 &lt;0.001</td>
<td></td>
<td>0.60</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anterior myocardial infarction</td>
<td>2.33 &lt;0.001</td>
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<td></td>
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</table>

Univariable and multivariable stepwise linear regression analysis of ST-segment resolution, residual ST-segment elevation, number of Q waves, and location of infarction for prediction of myocardial function, infarction, and transmural extent of infarction in 171 patients with complete electrocardiographic data. ST-segment resolution is categorized as complete, partial, and incomplete; residual ST-segment elevation is categorized as 0–2, 3–5, 6–10, and >10 mm; number of Q waves is categorized as 0–2, 3, 4, and ≥5 Q waves.
the predictive value of ECG measures in patients with acute MI is that both residual ST-segment elevation and the number of Q waves offered incremental information aside from angiographic measures and infarct size with respect to LV function, transmurality, and microvascular injury. Previous reports have shown that incomplete TIMI flow grade and impaired MBG predict worse clinical outcome and LV function (24,25). Although we found no statistical significant relation between incomplete TIMI flow grade and LV function in our study, impaired MBG correlated with LVEF, transmurality, and MVO. In multivariable analysis, ECG measures remained stronger predictors of LVEF and transmurality, and MBG was only predictive for the presence of MVO.

Methodological considerations. Assessment of ECG measures was done semiquantitatively. Continuous ST-segment monitoring using automated analysis systems may have improved the evaluation of myocardial reperfusion over time (16). Also, addition of ST-segment depression may have further improved the pathophysiological understanding of the ECG and its prognostic impact (6,26), reflecting reciprocal ST-segment elevation, more extensive infarction, or additional ischemia beyond the infarct zone. In this study, however, we have evaluated a clinically applicable and generally available approach. Our findings cannot be generalized to all patients with acute MI because only patients with ST-segment elevation MI were included in the study with relatively large infarcts (elevation of creatine kinase-myocardial band >10 times the upper limit of normal). Although these data suggest an incremental role for the number of Q waves in relation to LV function and infarction, it is unknown whether these results can be extrapolated to patients with acute MI without ST-segment elevation. Additionally, patients in whom revascularization was not successful, those treated conservatively, or those who underwent coronary artery bypass surgery for acute MI were not included in the study.

Clinical implications. Because residual ST-segment elevation reflects myocardial function and no-reflow, whereas the number of Q waves relates to myocardial function and size/extent of infarction, both parameters offer complementary information for patients after reperfused acute MI beyond that provided by infarct size and angiography. Therefore, we believe that the readily available and simple ECG shortly after PCI may more specifically assist the physician’s clinical decision making and risk stratification of patients after acute MI than currently known. Additionally, our findings may be relevant for selecting patients who may benefit from adjunctive therapeutic interventions (e.g., cell therapy) to limit functional deterioration and promote the repair of infarcted myocardium.

CONCLUSIONS

We found that residual ST-segment elevation and the number of Q waves on the ECG shortly after PCI for acute MI have complementary predictive value on myocardial function, size and extent of infarction, and microvascular injury.

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Reprint requests and correspondence: Dr. Robin Nijveldt, Department of Cardiology, VU University Medical Center, De Boelelaan 1117, P.O. Box 7057, 1007 MB, Amsterdam, the Netherlands. E-mail: r.nijveldt@vumc.nl.
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