Determinants and Prognostic Implications of Persistent ST-Segment Elevation After Primary Angioplasty for Acute Myocardial Infarction

Importance of Microvascular Reperfusion Injury on Clinical Outcome

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Background—Despite early recanalization of an occluded infarct artery, reperfusion at the level of the microcirculation may remain impaired owing to a process of microvascular reperfusion injury.

Methods and Results—Microvascular reperfusion injury was studied in 91 patients with acute myocardial infarction (AMI) by evaluation of the resolution of ST-segment elevation after successful PTCA. Impaired microvascular reperfusion, defined as the presence of persistent (≥50% of initial value) ST-segment elevation (ST $\geq 50\%$) at the end of coronary intervention, was observed in 33 patients (36%) and was independently correlated with low systolic pressure on admission and high age. Patients ≥55 years of age with systolic pressures $\leq 120$ mm Hg were at high risk for development of impaired reperfusion compared with patients not meeting these criteria (72% versus 14%, $P<0.001$). Impaired microvascular reperfusion was associated with a more extensive infarction and worse clinical outcome at the 1-year follow-up: cardiac death rate, 15% versus 2% (ST $\geq 50\%$ versus ST $<50\%$, $P=0.01$); nonfatal MI rate, 9% versus 2% ($P=0.1$); and total major adverse cardiac event (MACE) rate, 45% versus 15% ($P<0.005$). ST $\geq 50\%$ was the most important independent determinant of MACE with an adjusted risk ratio of 3.4.

Conclusions—Impaired microvascular reperfusion, as evidenced by ST $\geq 50\%$ after successful recanalization, occurs in more than one third of our AMI patients, especially in older patients with low systolic pressure. Its detrimental implications on clinical outcome reinforce the need to develop adjunctive agents that attenuate the process of reperfusion injury. (Circulation. 1999;99:1972-1977.)

Key Words: reperfusion ■ infarction ■ angioplasty

Early recanalization of an occluded coronary artery has become the main goal in the care of acute myocardial infarction (AMI). However, despite successful recanalization by either thrombolytic agents or PTCA, a substantial number of patients still fail to obtain complete and sustained myocardial reperfusion and remain at risk of developing large infarcts.1

There is concern that at the time of reperfusion, further injury occurs to the myocardium. Restoration of blood flow to a previously ischemic zone causes profound physiological and anatomical changes, including neutrophil infiltration, tissue edema, microvascular damage, and subsequent impairment of microcirculatory flow.2-4 This so-called low-reflow phenomenon was first described in 1974 by Kloner et al5 in an animal model and observed in humans in 1992 by Ito et al6 using intracoronary contrast echocardiography during primary angioplasty for AMI. Myocardial reperfusion injury has also recently been studied by serial ST-segment analysis during primary angioplasty. Persistent ST-segment elevation shortly after recanalization reflects sustained electrical transmural injury and has been shown to correlate well with impaired myocardial reperfusion at the microcirculatory level and with further extension of myocardial damage after successful primary angioplasty.7,8

The additional prognostic value of microvascular reperfusion injury beyond the well-established prognostic determinants, such as age, extent of myocardial damage, and severity of coronary artery disease, however, is less known. Also, identification of patients at risk for development of impaired microvascular reperfusion has not been determined previously but is important for physicians to tailor more properly adjunctive therapy.

Accordingly, the goal of this study was to identify early determinants of impaired microvascular reperfusion by evaluating the resolution of ST-segment elevation in patients with AMI treated successfully with primary angioplasty and to...
verify the independent prognostic implications of microvascular reperfusion injury on mortality and morbidity at a 1-year follow-up.

Methods

Patient Population

Between January 1995 and January 1998, a total of 91 patients with AMI, in whom successful primary PTCA for an occluded infarct artery was performed at our institution, were consecutively included in this study. Successful PTCA was defined as adequate restoration of coronary patency (TIMI flow grade ≥2) and postprocedural diameter stenosis (%DS) of the infarct artery <50%. All included patients showed initial ST-segment elevation of >1 mm in ≥2 contiguous ECG leads and had 12-lead ECGs available before and at the end of the angioplasty procedure. Patients with left bundle-branch block or poorly interpretable ST segments were excluded.

All patients received acetylsalicylic acid, and in case of systolic blood pressure >100 mm Hg, intravenous isosorbide dinitrate (0.5 μg · kg⁻¹ · min⁻¹) was started. Cardiogenic shock was defined as persistent low systolic pressure (<90 mm Hg) with clinical signs of left- or right-sided cardiac failure.

Total ischemic time, including the time from beginning of pain to hospital admission (prehospital ischemic time) and the time from admission to first balloon inflation (hospital ischemic time), could be registered in 82 patients. During hospitalization, β-blocking agents or ACE inhibitors were started according to evidence-based practice guidelines.

Serial measurements of cardiac enzyme release (creatinine kinase [CK] with CK-MB isoenzymes) were available in 85 patients, and the maximum level was used as an enzymatic marker of infarct size. Samples were obtained at 4-hour intervals up to 18 hours and later at 8-hour intervals up to 72 hours after intervention.

ECG Analysis

To assess the extent of microvascular reperfusion injury, serial ST-segment analysis on a 12-lead ECG recording just before and at the end of the coronary intervention was done by 1 observer blinded to clinical data. The sum of ST-segment elevations was measured manually with lens-intensified calipers 20 ms after the end of the QRS complex from leads I, aVL, and V1 through V6 for left anterior descending coronary artery occlusions and leads II, III, aVF, V5, V6, and reciprocal ST-segment depressions in V1 and V2 for right coronary artery and left circumflex artery occlusions. Inadequate resolution of ST-segment elevation after successful recanalization was expressed as a percentage of the initial ST-segment elevation (%ST). Persistent ST-segment elevation ≥50% of the initial value (ST ≥50%) was defined as a marker of impaired microvascular reperfusion. On the other hand, ST-segment elevations <50% indicated good myocardial reperfusion.

With regard to the reproducibility of ST-segment measurements, we demonstrated in a previous report a close correlation (R²=0.94) between 2 measurements analyzed by 2 independent cardiologists. In addition to ST-segment measurements, the 32-point Selvester QRS score was calculated from the standard 12-lead ECG to assess the amount of myocardial damage. This QRS score has been validated in AMI patients and has been shown to correlate well with infarct size. The QRS score is scaled according to the size of Q waves and R and S amplitudes. A QRS score of ≥8 corresponds to a marked reduction in ejection fraction (<50%). The QRS score was calculated from baseline ECG just before primary angioplasty (pre-QRS) and from the ECG recording at a median of 41 days (6 and 68 days) after angioplasty (post-QRS). The difference between post- and pre-QRS scores predominantly reflects the amount of necrotic myocardial tissue related to the process of reperfusion injury.

The QRS score was manually calculated by a cardiologist without knowledge of reperfusion state or other clinical data. The intraobserver and interobserver variabilities were 0.6±0.7 (absolute mean difference ±SD) and 0.7±0.7, respectively, and were determined by recalculating the QRS score in 40 randomly selected study ECGs.

Angiographic Data

Coronary angiography and coronary angioplasty were performed with standard catheters by use of nonionic, low-osmolality contrast agents after administration of 150 U/kg heparin IV. In case of suboptimal post-PTCA results, a coronary stent was implanted. No drugs with potentially rheological capacities (eg, ILb/IIa receptor blockers or adenosine) were used in study patients.

Coronary angiographic data were quantitatively analyzed with a computer-based cardiovascular angiography analysis system (CAAS II, Pie Medical Data). Stenosis severity after PTCA was calculated from the minimal luminal diameter and a computer-estimated reference diameter and expressed as percent DS. Multivessel disease was defined as the presence of a lesion with >50% DS in a non–infarct-related coronary artery.

The TIMI angiographic scale was used to determine the recanalization status of the infarct-related artery and was assessed visually.

Clinical Follow-Up

After hospital discharge, patients were followed up for 1 year, with data recorded from clinic visits and/or telephone calls to the referring physician.

Three major adverse cardiac events (MACEs) were identified: cardiac death, including sudden death without evidence of a noncardiac origin; nonfatal MI; and hospitalization because of cardiac failure, life-threatening arrhythmias, or recurrent ischemia caused by angiographically documented progression of coronary artery disease. Myocardial infarction was defined by enzymatic or ECG documentation during hospital admission.

For purposes of analysis, elective rehospitalization for cardiac surgery in patients with severe multivessel disease documented at the time of AMI was not considered a MACE. The date of the first event was used in calculating event-free survival. Only 1 event, the most serious in the above order, was tabulated for each patient.

Statistical Analysis

Continuous variables are presented as median value with 25th and 75th percentiles unless otherwise stated, and comparisons between groups were made with the Mann-Whitney U test. Differences between proportions were assessed by χ² analysis.

To identify the determinants of the extent of microvascular reperfusion injury, the relation between the extent of residual %ST and baseline characteristics was examined by forward stepwise linear regression analysis, with F to enter equal to 4. Clinical baseline variables included age; sex; smoking habits; cardiogenic shock; and history of diabetes, hypertension, hypercholesterolemia (cholesterol >240 mg%), or previous infarction. To define the optimal cutoff value for predictors of impaired microvascular reperfusion, receiver-operator characteristic curve analysis was applied.

Comparison of pre-QRS and post-QRS scores in patients with and without impaired microvascular reperfusion was done by 2-way repeated-measures ANOVA with a post hoc Student-Newman-Keuls test to evaluate differences.

To analyze the impact of microvascular reperfusion injury on clinical outcome, cumulative event-free survival estimates were plotted according to the presence or absence of persistent ST-segment elevation (≥50 ST% versus <50%) by use of the Kaplan-Meier technique. Differences between survival curves were tested with the log-rank test. The Cox proportional-hazards model was applied to verify the independent prognostic implication of impaired microvascular reperfusion on clinical outcome. A probability value of P<0.05 was considered statistically significant.

Results

Patient Population

A total of 91 patients (62 men; age, 64 years [54 and 70]) were admitted in the hospital with AMI. Prehospital ischemic
time and in-hospital ischemic time were 174 minutes (70 and 218 minutes) and 57 minutes (45 and 71 minutes), respectively, resulting in a median total ischemic time of 220 minutes (142 and 298 minutes). Successful restoration of the infarct artery patency was achieved in all study patients (TIMI grade 3 flow in 75 patients and TIMI grade 2 flow in 16 patients) with a median postinterventional DS of 22% (15 and 35). A coronary stent was implanted in 38 patients.

Cardiogenic shock was present in 12 patients (13%). A total of 42 patients showed multivessel disease on the initial angiogram, and 11 patients had a history of previous infarction.

**Microvascular Reperfusion Injury and Infarct Size**

The extent of microvascular reperfusion injury was variable, as evidenced by the wide range of residual %ST after primary angioplasty going of 0% to 210% with a median value of 38% (25% and 66%). Impaired microvascular reperfusion, evidenced by ST $\geq 50\%$, was observed in 33 patients (36%).

ECG evaluation of infarct size revealed more progression of myocardial necrosis in patients with impaired microvascular reperfusion: QRS score worsened from a medium value of 3.2 before intervention to 3.8 at follow-up in patients with ST $<50\%$ and from 3.2 to 6.0 in patients with ST $\geq 50\%$ ($P<0.01$, ST <50% versus $\geq 50\%$). The median difference between post- and pre-QRS scores, reflecting predominantly the amount of myocardial necrosis related to reperfusion injury, was 3±2.3 (±SD) in patients with impaired reperfusion and 0.7±2.2 in patients with good myocardial reperfusion ($P<0.001$). A marked left ventricular dysfuncion (QRS score at follow up $\geq 8$) was present in 7 patients (22%) with severe microvascular reperfusion injury and in 8 patients (14%) without severe injury ($P=0.3$).

Analysis of cardiac enzyme release revealed more extensive myocardial injury in patients with impaired microvascular reperfusion. Maximum CK-MB level was 284±248 U/L in patients with ST $\geq 50\%$ versus 188±154 U/L in patients with ST <50% ($P<0.05$). The time from first balloon inflation to peak CK-MB level did not differ between both subgroups (530±246 versus 578±311 minutes, $P=0.5$).

**Determinants of Microvascular Reperfusion Injury**

From a variety of baseline characteristics, univariate analysis identified systolic blood pressure on admission ($r=0.39$, $P=0.0001$), age ($r=0.26$, $P=0.01$), the presence of cardiogenic shock ($r=0.27$, $P=0.01$), and the presence of multivessel disease ($r=0.21$, $P=0.04$) as significant factors relating to the extent of residual ST-segment elevation after recanalization. Stepwise regression analysis selected systolic blood pressure on admission (F to remove, 17) and age (F to remove, 9) as the only independent determinants of %ST. Patients with impaired microvascular reperfusion had lower systolic blood pressure on admission (100 versus 140 mm Hg) and were older (68 versus 62 years) than patients with good myocardial reperfusion. Systolic blood pressure in the catheterization laboratory just before intervention was not significantly related to the extent of residual ST-segment elevation ($r=0.15$, $P=0.2$).

**Patients with persistent ST-segment elevation showed more TIMI grade 2 flow and had longer total ischemic time compared with patients with ST <50%, but this did not reach statistical significance (see Table 1).**

With receiver-operator characteristic curve analysis, a value of 120 mm Hg for systolic blood pressure on admission and 55 years for age were defined as the optimal cutoff criteria to predict the presence of severe microvascular reperfusion injury. A combination of a systolic pressure on admission $\leq 120$ mm Hg and age $\geq 55$ years identified a subgroup of patients at high risk to develop persistent ($\geq 50\%$) ST-segment elevation after successful PTCA compared with patients meeting only $\leq 1$ of these criteria (72% versus 14%, $P<0.001$). Patients $<55$ years of age with a systolic blood pressure on admission of $>120$ mm Hg showed the lowest occurrence rate of impaired microvascular reperfusion (7%), whereas patients meeting only 1 of these criteria constituted a subgroup at intermediate risk (12% and 17%) (see Figure 1).

**Microvascular Reperfusion Injury and Clinical Outcome**

During clinical follow-up, a total of 24 patients suffered from an MACE. Three patient deaths were of noncardiac origin.

### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>ST&lt;50% (n=58)</th>
<th>ST $\geq 50%$ (n=33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>62 (48–69)</td>
<td>68 (59–73)</td>
<td>0.004</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>69</td>
<td>67</td>
<td>0.8</td>
</tr>
<tr>
<td>Hypertension, %</td>
<td>36</td>
<td>47</td>
<td>0.4</td>
</tr>
<tr>
<td>Hypercholesterolemia, %</td>
<td>44</td>
<td>53</td>
<td>0.4</td>
</tr>
<tr>
<td>Diabetes mellitus, %</td>
<td>7</td>
<td>15</td>
<td>0.2</td>
</tr>
<tr>
<td>Current smoker, %</td>
<td>48</td>
<td>39</td>
<td>0.44</td>
</tr>
<tr>
<td>Previous infarction, %</td>
<td>15</td>
<td>6</td>
<td>0.2</td>
</tr>
<tr>
<td>Cardiogenic shock, %</td>
<td>5</td>
<td>27</td>
<td>0.03</td>
</tr>
<tr>
<td>Multivessel disease, %</td>
<td>38</td>
<td>60</td>
<td>0.04</td>
</tr>
<tr>
<td>Infarct vessel, %</td>
<td></td>
<td></td>
<td>0.5</td>
</tr>
<tr>
<td>RCA/LAD/LCx/ven bypass</td>
<td>48/38/12/2</td>
<td>39/52/6/3</td>
<td></td>
</tr>
<tr>
<td>TIMI grade 2/3 flow</td>
<td>12/88</td>
<td>27/72</td>
<td>0.07</td>
</tr>
<tr>
<td>%DS postintervention</td>
<td>20 (15–31)</td>
<td>25 (15–37)</td>
<td>0.3</td>
</tr>
<tr>
<td>Stent, %</td>
<td>43</td>
<td>39</td>
<td>0.7</td>
</tr>
<tr>
<td>Total ischemic time, s</td>
<td>210 (131–267)</td>
<td>236 (190–375)</td>
<td>0.07</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On admission</td>
<td>140 (120–160)</td>
<td>100 (90–122)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Before PTCA</td>
<td>127 (116–144)</td>
<td>122 (92–138)</td>
<td>0.25</td>
</tr>
<tr>
<td>ST-segment elevation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before intervention, mm</td>
<td>8 (5–13)</td>
<td>9 (4–12)</td>
<td>0.9</td>
</tr>
<tr>
<td>After intervention, mm</td>
<td>2 (1–4)</td>
<td>6 (4–12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>%ST</td>
<td>33 (20–38)</td>
<td>70 (62–100)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>QRS score, preintervention</td>
<td>2 (1–4)</td>
<td>3 (2–4)</td>
<td>0.7</td>
</tr>
</tbody>
</table>

RCA indicates right coronary artery; LAD, left anterior descending coronary artery; LCx, circumflex artery; and ven, venous. Continuous variables are presented as median value with 25th and 75th percentiles in parentheses.
There were 6 cardiac deaths, including 3 sudden cardiac deaths, 2 deaths after progressive heart failure, and 1 death in the setting of reinfarction. Nonfatal MI occurred in 4 patients, all of them due to reocclusion of the infarct artery. Cardiac death and MI always occurred within 1 month of the index infarction. In addition, a total of 14 patients had to be hospitalized because of recurrent ischemia (n = 10), cardiac failure (n = 2), or severe arrhythmia (n = 2). Recurrent ischemia was related to restenosis of the infarct artery in 8 patients. Revascularization was performed in 11 patients by either PTCA (n = 6) or CABG (n = 5).

Table 2 summarizes the different MACEs stratified according to the presence or absence of severe microvascular reperfusion injury. Cardiac death and reinfarction were significantly more present in patients with impaired microvascular reperfusion (P < 0.01 for combined end point). Furthermore, cardiac failure and severe arrhythmias tended to occur more frequently in patients with persistent ST-segment elevation. Clinical restenosis rate, excluding early reocclusion, seemed not to be influenced by the presence of microvascular reperfusion injury: 8% (2 of 25) in patients with ST ≥50% versus 11% (6 of 56) in patients with ST <50%.

In Figure 2, cumulative event-free survival estimates for MACE were plotted according to the presence or absence of severe microvascular reperfusion injury. Patients with ST ≥50% had worse clinical outcome than patients with ST <50% (MACE, 45% versus 15%; P < 0.01). Further analysis also revealed that in patients with TIMI grade 3 flow, the presence of persistent ST-segment elevation could discriminate between patients with poor and good clinical outcome: MACE rate, 37% in the 24 patients with ST ≥50% versus 14% in the 51 patients with ST <50% (P = 0.01).

To verify the independent prognostic implication of microvascular reperfusion injury on clinical outcome, multivariate analysis was performed, including those variables with P to enter <0.2 on univariate analysis (Table 3). The Cox proportional-hazards model selected the presence of impaired microvascular reperfusion as the most important independent determinant of MACE with an adjusted risk ratio of 3.4 (95% CI, 1.5 to 7.9). Age, the presence of cardiogenic shock, the extent of coronary artery disease, TIMI flow grading, and cholesterol level also tended to be important factors, but they did not reach significant independence in multivariate analysis model.

**TABLE 2.** Microvascular Reperfusion Injury and Clinical Outcome

<table>
<thead>
<tr>
<th></th>
<th>ST&lt;50% (n=58)</th>
<th>ST≥50% (n=33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac death, %</td>
<td>2</td>
<td>15</td>
<td>0.01</td>
</tr>
<tr>
<td>Sudden death</td>
<td>0</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Reinfarction</td>
<td>2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Nonfatal infarction, %</td>
<td>2</td>
<td>9</td>
<td>0.1</td>
</tr>
<tr>
<td>Rehospitalization, %</td>
<td>12</td>
<td>21</td>
<td>0.2</td>
</tr>
<tr>
<td>Ischemia</td>
<td>12</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>0</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Total MACE, %</td>
<td>15</td>
<td>45</td>
<td>0.002</td>
</tr>
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</table>

**TABLE 3.** Multivariate Cox Model Predicting Clinical Outcome

<table>
<thead>
<tr>
<th></th>
<th>X²</th>
<th>P</th>
<th>Risk Ratio (95% CI)</th>
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</thead>
<tbody>
<tr>
<td>%ST</td>
<td>8.4</td>
<td>0.004</td>
<td>3.4 (1.5–7.9)*</td>
</tr>
<tr>
<td>Shock</td>
<td>3.7</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>3.2</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>TIMI grade</td>
<td>2.5</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>2.2</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Cholesterol</td>
<td>2.2</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>%DS postintervention</td>
<td>1.2</td>
<td>0.28</td>
<td></td>
</tr>
</tbody>
</table>

*Risk ratio and CIs were calculated only for variables with P < 0.05; ST ≥50% vs ST <50%.

**Discussion**

This study underlines the importance and clinical relevance of myocardial reperfusion at the level of microcirculation and
conveys clinical information on the process of microvascular reperfusion injury.

The inability to adequately perfuse previously ischemic tissue has been attributed to ischemia- and/or reperfusion-induced microvascular damage and is associated with impaired microcirculatory flow with loss of its vasodilating capacity, which may last several weeks after the acute event. Previous clinical studies with contrast echocardiography or PET revealed zones of impaired tissue flow in one fourth to one third of patients with reperfused acute myocardial infarction and could demonstrate a good correlation between low myocardial reflow and extension of infarct size.

The occurrence and extent of this microvascular reperfusion injury, however, seem to be variable, as could be derived from the wide range of ST-segment resolution in the present study. Old age and low systolic blood pressure on admission were identified as the most important independent determinants of persistent ST-segment elevation. It is well known that the vasodilating capacity of the microcirculation diminishes with age, most likely because of progressive atherosclerosis and endothelium dysfunction. We may postulate that ischemia/reperfusion-induced microvascular damage leads to more severe impairment of microcirculatory flow in old patients because of a preexisting endothelium dysfunction.

Low systolic blood pressure on admission was the most powerful determinant of impaired microvascular reperfusion. A direct causal relationship between low systolic pressure and impaired myocardial reperfusion is unlikely because this association disappeared when blood pressures just before intervention and after administration of blood pressure-modulating drugs were taken into account. Therefore, a common underlying pathophysiological mechanism seems to be more relevant. Inflammatory responses induced by ischemia/reperfusion are a possible but still-to-be-proved link between low systolic pressure and microvascular reperfusion injury because some proinflammatory cytokines (such as tumor necrosis factor-α) might lower blood pressure through their potent negative inotropic and vasodilating properties.

Beyond identification of determinants of reperfusion injury, the present study evaluated its prognostic implications. We could demonstrate that the well-known beneficial effect from timely coronary reperfusion on clinical outcome was offset, at least in part, by the presence of severe reperfusion injury. The detrimental effect of severe reperfusion injury was mainly related to reocclusion of the infarct artery, cardiac failure, and severe arrhythmia, including sudden death. Experimental evidence suggests that ischemia/reperfusion-related microvascular injury creates a prothrombotic environment by formation and exposure of more procoagulant factors, partial inhibition of the fibrinolytic system, and fostering of platelet aggregation mainly because of marked depression of nitric oxide levels during reperfusion. More extensive microvascular reperfusion injury with subsequently more extensive myocardial tissue necrosis may also constitute a substrate for severe arrhythmias and cardiac failure.

The detrimental and independent clinical implications of microvascular reperfusion injury reinforce the need to design adjunctive strategies that attenuate the process of reperfusion injury. Experimental models have clearly shown that the maximal beneficial effect of pharmacological intervention can be expected when blood levels are already elevated when reperfusion occurs and advocate the administration of these agents before restoration of vessel patency. Appropriate selection of patients might therefore become important. In the present study, we could identify a subgroup of patients (age ≥55 years and admission systolic pressure ≤120 mm Hg) at high risk for development of impaired microvascular reperfusion. Whether these patients will confer the most benefit from adjunctive therapy deserves confirmation in prospectively designed intervention trials.

The results of this study should be considered in light of the following limitations. First, myocardial infarct size was assessed semiquantitatively by means of a 32-point QRS score, which might be less objective and accurate than a quantitative analysis such as that done by radionuclide studies. However, serial analysis of the QRS score (before intervention and at follow-up) allowed us to study the effect of microvascular reperfusion injury on final infarct size, which other cardiac imaging techniques would not allow.

Second, our findings are derived from a select population of AMI patients with a relatively high prevalence of cardiogenic shock (13%) who were treated successfully with primary PTCA. Therefore, our results cannot be generalized to all patients presenting as emergencies with AMI.

Third, a cutoff value of 50% residual ST-segment elevation was used to stratify patients into impaired versus adequate microvascular reperfusion. In the literature, different values (eg, 50% and 70%) have been applied for evaluation of myocardial reperfusion injury. The decision to apply the 50% cutoff value in the present study was further guided by its discriminative effect on progression of myocardial necrosis, as was derived from the serial QRS score measurements. Among several cutoff values, the 50% value was associated with the highest differences in extent of infarct necrosis.

In conclusion, impaired microvascular reperfusion, as evidenced by persistent ST-segment elevation after successful mechanical recanalization, occurs in more than one third of our AMI patients, especially in older (≥55 years) patients with systolic pressure ≤120 mm Hg, and is associated with a more extensive infarction and an unfavorable clinical outcome. It can be expected that application of new adjunctive strategies that adequately attenuate the process of microvascular reperfusion injury will further improve the short- and intermediate-term prognoses of patients presenting with AMI.

References


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