Impaired Myocardial Perfusion Is a Major Explanation of the Poor Outcome Observed in Patients Undergoing Primary Angioplasty for ST-Segment–Elevation Myocardial Infarction and Signs of Heart Failure

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Background—The aim of the present study was to investigate the prognostic implication of myocardial perfusion in patients with ST-segment–elevation myocardial infarction (STEMI) and signs of heart failure, treated with primary angioplasty.

Methods and Results—Our population is represented by 1548 consecutive patients undergoing primary angioplasty for STEMI. Congestive heart failure was defined as Killip class ≥1 at admission. Killip class was linearly associated with myocardial perfusion, enzymatic infarct size, predischarge ejection fraction, and 1-year mortality rate. Myocardial blush was an independent predictor of 1-year mortality (RR [95% CI]=2.92 [1.37 to 6.23], \(P=0.005\)) in patients with advanced Killip class at presentation.

Conclusions—Our study shows that patients with heart failure complicating STEMI have impaired myocardial perfusion, which accounts for the poor outcome observed in these patients. Further efforts should be aimed at improving myocardial perfusion, beyond epicardial recanalization, to further improve the outcome of these high-risk patients. (Circulation. 2004;109:958-961.)

Key Words: angioplasty ■ heart failure ■ perfusion

The benefits of primary angioplasty in patients with ST-segment–elevation myocardial infarction (STEMI) have been demonstrated in randomized trials. However, the outcome in patients with STEMI and heart failure at presentation remains poor, particularly in those with cardiogenic shock.

The aim of the present study was to investigate the implication of myocardial perfusion on outcome in patients with STEMI and signs of heart failure, treated with primary angioplasty.

Methods

From April 1997 to October 2001, 1548 consecutive patients with STEMI underwent primary angioplasty at our institution. The institutional review board approved our study, and all patients gave informed consent. Congestive heart failure was defined as Killip class ≥1 at admission. Angiograms were analyzed by an independent core laboratory (DIAGRAM, Zwolle, the Netherlands). Angiographic success was defined as postprocedural TIMI 3 flow and a residual stenosis <50%. Myocardial blush grade (MBG) and enzymatic infarct size were evaluated, as previously described. Distal embolization was defined as an abrupt “cutoff” in one of the coronary branches of the infarct-related artery, distal to the angioplasty site. Intra-aortic balloon pump (IABP) was routinely used in patients with severe multivessel disease and/or proximal left anterior descending artery occlusion, left main stenosis, or patients at higher risk for reocclusion, independent of the grade of Killip class at presentation.

Continuous data were expressed as median and interquartile ranges and categorical data as percentages. ANOVA and the \(\chi^2\) test were appropriately used for continuous and categorical variables, respectively. Multivariate analysis was performed by use of the Cox proportional hazard method to identify independent predictors of 1-year mortality in patients with heart failure at presentation.

Results

Demographic, clinical, and angiographic characteristics according to Killip class at presentation are reported in Table 1. Patients with Killip class ≥1 were older, with higher prevalence of female gender, anterior myocardial infarction, and multivessel disease. A higher prevalence of distal embolization was observed in patients with advanced Killip class. Killip class was linearly associated with the rate of MBG 2 to 3, angiographic success, and, consequently, with enzymatic infarct size, predischarge ejection fraction, and 1-year mortality rates (Table 1 and Figure 1).
The prognostic implication of myocardial perfusion beyond optimal epicardial recanalization in patients with heart failure at presentation is shown in Figure 2. In fact, in the analysis restricted to patients with optimal epicardial recanalization (TIMI 3 flow and residual stenosis <50%), myocardial perfusion significantly affected 1-year mortality rates (RR [95% CI]=2.54 [1.01 to 6.68], P=0.049). As reported in Table 2, at multivariate analysis restricted to patients with heart failure at presentation, MBG 0 to 1 was found to be an independent predictor of 1-year mortality rates (RR [95% CI]=2.92 [1.37 to 6.23], P=0.005).

Discussion

The main finding of the present study is that among patients with STEMI undergoing primary angioplasty, poor myocardial perfusion is a major explanation of poor outcome observed in patients with heart failure at presentation. The Killip classification still represents a simple and accurate tool for early risk stratification of patients with STEMI.1

Despite the significant improvement in survival of patients undergoing primary angioplasty, the mortality rate in patients with heart failure at presentation remains disappointingly high, particularly in those with cardiogenic shock.2–6

Data from registry studies have shown that in patients with Killip class II and III6 or cardiogenic shock,2 mechanical revascularization was associated with a significantly better survival in comparison with a less aggressive strategy. The role of adjunctive IABP in these high-risk patients remains controversial,3 with benefits observed mainly in patients treated with thrombolysis and not in those treated with primary angioplasty. Thus, IABP may potentially play an important role in terms of coronary flow and perfusion, mainly in the presence of residual stenosis (after thrombolysis), and less after mechanical recanalization. This finding has been confirmed in our previous report.11 Furthermore, there are no data available on the impact of IABP on MBG, whereas the potential role of other ventricular assist devices has yet to be investigated.12

A major explanation of the poor outcome observed in patients with more advanced Killip class is the linear association found in our study between myocardial perfusion and the degree of heart failure at presentation. A linear association between Killip class and postprocedural TIMI 3 flow was also observed in the Shock Trial Registry.2 As shown by our previous report,8 an optimal myocardial reperfusion beyond optimal epicardial flow is required to further improve clinical outcome, particularly in high-risk patients. In our study, among patients with heart failure at presentation and angiographic success, optimal myocardial perfusion (MBG 2 to 3) significantly affected 1-year mortality rates. Several factors may explain our results. In patients with heart failure at presentation, a larger infarction may be associated with more severe damage of microcirculation, and thus impaired perfusion. On the other hand, the larger infarct size shown by our study may be a consequence of impaired perfusion. Several factors may be regarded as being responsible for impaired myocardial perfusion after primary angioplasty. For several years, microvascular reperfusion damage has been regarded as the main determinant of the no-reflow phenomenon.13 Several additional pharmacological therapies have been studied to reduce the ischemia-reperfusion injury. Previous reports showed significant benefits from intracoronary administration of adenosine or verapamil in reducing microvascular reperfusion damage and infarct size and improving outcome.14,15 Recent interests have been focused on nitric oxide synthase inhibitors.16 Results of a randomized trial17 showed

| TABLE 1. Demographic, Clinical, and Angiographic Characteristics According to Killip Class at Presentation |

<table>
<thead>
<tr>
<th>Killip Class</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>1418</td>
<td>72</td>
<td>35</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Age (70 y), %</td>
<td>22.6</td>
<td>31.9</td>
<td>40.0</td>
<td>42.9</td>
<td>0.005</td>
</tr>
<tr>
<td>Male gender, %</td>
<td>78.0</td>
<td>75.0</td>
<td>57.1</td>
<td>67.9</td>
<td>0.009</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>10.1</td>
<td>9.7</td>
<td>14.3</td>
<td>19.0</td>
<td>NS</td>
</tr>
<tr>
<td>Time delay (&gt;4 h), %</td>
<td>37.9</td>
<td>34.7</td>
<td>37.1</td>
<td>33.3</td>
<td>NS</td>
</tr>
<tr>
<td>Multivessel disease, %</td>
<td>51.5</td>
<td>63.9</td>
<td>80.0</td>
<td>71.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Preprocedural TIMI 0–1 flow, %</td>
<td>50.8</td>
<td>70.8</td>
<td>80.0</td>
<td>76.2</td>
<td>NS</td>
</tr>
<tr>
<td>Collateral circulation, %</td>
<td>10.3</td>
<td>6.9</td>
<td>8.6</td>
<td>4.8</td>
<td>NS</td>
</tr>
<tr>
<td>Postprocedural TIMI 3 flow, %</td>
<td>89.0</td>
<td>84.7</td>
<td>77.1</td>
<td>55.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Stent, %</td>
<td>57.0</td>
<td>61.1</td>
<td>65.7</td>
<td>57.1</td>
<td>NS</td>
</tr>
<tr>
<td>IABP, %</td>
<td>5.6</td>
<td>19.4</td>
<td>42.9</td>
<td>66.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LDH48, U/L</td>
<td>1273 (702–2346)</td>
<td>2057 (569–3719)</td>
<td>3621 (1085–4875)</td>
<td>4619 (1119–5764)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>45 (36–52)</td>
<td>39 (30–48)</td>
<td>36 (30–46)</td>
<td>36 (25–49)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

TIMI indicates Thrombolysis In Myocardial Infarction; LDH48, enzymatic infarct size from serial measurements of lactate dehydrogenase.

Available in *1047 and †1279 patients.
that inhibition of the complement cascade at the level of C5, which may determine a reduction in iNOS response to ischemia and reperfusion, was associated with lower rates of shock and deaths in high-risk patients undergoing primary angioplasty.

In addition to microvascular reperfusion damage, mounting interests have emerged on distal embolization. In the present study, we observed a higher rate of distal embolization in patients with advanced Killip class, which may partially explain the poor perfusion observed in these patients. Thus, adjunctive pharmacological or mechanical therapy should be used to protect the microcirculation from distal embolization during mechanical reperfusion, particularly in patients with signs of heart failure at presentation. Previous reports have also found that abciximab significantly improves the outcome in patients with cardiogenic shock treated by mechanical reperfusion. A recent retrospective analysis has shown the feasibility and efficacy of thrombus aspiration in patients with cardiogenic shock. Larger randomized trials are needed to evaluate the potential role of abciximab and distal protection devices on mortality rates in these high-risk patients.

**Limitations**

Because the benefits of adjunctive glycoprotein IIb/IIIa inhibitors have only been shown recently, less than 5% of our patients received this additional drug, and no distal protection devices were used in this series. Thus, we could not address their impact on clinical outcome in these high-risk patients. The relatively low prevalence of Killip class >1 in our study may be related to the short total ischemic time. In our daily practice, the majority of patients with STEMI undergoing primary angioplasty are in Killip class I, as previously reported in our publications. In fact, since 1993, all patients with STEMI admitted to our hospital have been treated with primary angioplasty, and thrombolytic therapy has no longer been used. Finally, our study only included patients undergoing primary angioplasty, thus excluding patients who may have died during transportation or before angioplasty.

**Conclusions**

Our study shows that patients with heart failure complicating STEMI have impaired myocardial perfusion, which accounts for the poor outcome observed in these patients. Further

**TABLE 2. Predictors of 1-Year Mortality Rates at Multivariate Analysis in Patients With Advanced Killip Class (>1)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>3.41 (1.56–7.47)</td>
<td>0.002</td>
</tr>
<tr>
<td>Time to treatment (&gt;4 h)</td>
<td>3.28 (1.5–7.22)</td>
<td>0.003</td>
</tr>
<tr>
<td>Myocardial blush grade 0–1</td>
<td>2.92 (1.37–6.23)</td>
<td>0.005</td>
</tr>
<tr>
<td>Killip class</td>
<td>2.06 (1.24–3.51)</td>
<td>0.007</td>
</tr>
<tr>
<td>Multivessel disease</td>
<td>4.07 (1.22–13.6)</td>
<td>0.023</td>
</tr>
<tr>
<td>Angiographic success</td>
<td>0.98 (0.40–2.37)</td>
<td>&gt;0.1</td>
</tr>
</tbody>
</table>
efforts should be aimed at improving myocardial perfusion beyond the restoration of epicardial flow to further improve the outcome of these high-risk patients.

References
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