Impact of cardiac and renal dysfunction on inhospital morbidity and mortality of patients with acute myocardial infarction undergoing primary angioplasty

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Background Risk stratification of patients with ST-elevation myocardial infarction (STEMI) undergoing primary angioplasty is important in order to predict outcomes and to delineate targeted therapeutic strategies. Although the prognostic implications of reduced left ventricular ejection fraction (LVEF) and creatinine clearance (CrCl) have been recognized, the clinical and prognostic impact of their combination has never been prospectively evaluated.

Methods We stratified 467 patients with STEMI undergoing primary angioplasty according to LVEF and CrCl values at admission: CrCl > 60 mL/min and LVEF > 40% (group 1, n = 261); CrCl < 60 mL/min and LVEF > 40% (group 2, n = 113); CrCl > 60 mL/min and LVEF < 40% (group 3, n = 60); CrCl < 60 mL/min and LVEF < 40% (group 4, n = 33).

Results Inhospital mortality was different in the 4 groups (1% in group 1, 3% in group 2, 15% in group 3, 30% in group 4) (P < .001). The incidence of combined end point of death, acute pulmonary edema, cardiogenic shock, and acute renal failure requiring mechanical support increased progressively from group 1 to group 4 (5%, 17%, 33%, and 48%, respectively) (P < .001). We found a significant gradient of risk in terms of inhospital mortality and combined end point when patients outcome was evaluated according to the presence of both normal LVEF and CrCl (group 1), impairment in only 1 of these 2 parameters (group 2 and 3 pooled together), and combined LVEF and CrCl reductions (group 4).

Conclusions Reduced LVEF and CrCl are strong independent predictors of increased inhospital morbidity and mortality, and their combined evaluation provides a simple tool for early risk stratification in patients with STEMI treated with primary angioplasty. (Am Heart J 2007;153:755-62.)

In patients with ST-segment elevation acute myocardial infarction (STEMI), primary angioplasty represents the best strategy for acute coronary reperfusion.1,2 Although the average mortality rate of patients with STEMI treated with primary angioplasty has been progressively reduced, it still varies significantly among different patient subgroups. Hence, several clinical scores have been introduced as useful tools for bedside risk stratification of patients and for identification of high-risk subsets in which targeted therapeutic strategies should be considered.3-7

Mortality risk during STEMI has been proved to be increased in patients with renal dysfunction8-11 and in those with a lower left ventricular ejection fraction (LVEF).12-15 With regard to renal dysfunction, a number of studies have demonstrated that even mild renal impairment is associated with an increased risk and that patients with renal insufficiency develop more adverse cardiac events, including atrial fibrillation, congestive heart failure, and mechanical complications.8-11 Renal dysfunction has been shown to worsen the prognosis of patients with STEMI treated medically9 with thrombolysis16 and, more recently, with primary angioplasty.17,18 In patients with STEMI, however, diminished renal function at hospital presentation may be the consequence of impaired cardiac function, rather than the expression of chronic renal insufficiency. Thus, despite the fact that the mechanism(s) by which renal impairment worsens the prognosis of patients with STEMI has not fully elucidated, it is possible that acute impairment in kidney perfusion may play an important role. Indeed, LVEF reduction and renal dysfunction are recognized as the most powerful prognostic determinates of STEMI. However, they have been seldom used and almost never considered together in the prognostic assessment of patients undergoing primary angioplasty. Therefore, the question as to whether renal and cardiac insufficiency...
are independent prognostic risk factors or, if instead, renal dysfunction is merely a marker of a more extensive left ventricular impairment and hemodynamic compromise remains unclear. In the era of primary angioplasty, information regarding the interplay of these 2 organ impairments on clinical outcome is still lacking.

In this study we evaluated the impact of renal insufficiency and cardiac impairment, when they are present singularly or in combination, on the prognosis of patients with STEMI treated with primary angioplasty.

Methods

Study population

This prospective, observational study was conducted at the Centro Cardiologico Monzino between January 1, 2001, and July 31, 2005. We enrolled 467 consecutive patients with STEMI who were treated with primary angioplasty. According to our institute protocol, patients were included if they presented within 12 hours from the onset of symptoms. Patients in chronic peritoneal or hemodialysis treatment were excluded. Patients undergoing cardiac surgery for emergency coronary revascularization were also excluded. The ethics committee of our institute approved the study.

Study protocol

In all patients, serum creatinine concentration was measured at hospital admission (before primary angioplasty), and creatinine clearance (CrCl) was calculated by applying the Cockcroft-Gault formula. Baseline renal insufficiency was defined as a creatinine clearance ≤60 mL/min. An echocardiographic evaluation was performed in all patients in the first hours (≤6 hours) after admission, and LVEF was calculated by the Simpson rule. Left ventricular systolic dysfunction was defined as an LVEF ≤40%.

Left ventricular ejection fraction and CrCl were dichotomized and treated as binary variables, according to previous works. Based on LVEF and CrCl values, patients were allocated to 1 of the following 4 groups: LVEF >40% and CrCl >60 mL/min (group 1); LVEF >40% and CrCl ≤60 mL/min (group 2); LVEF ≤40% and CrCl >60 mL/min (group 3); LVEF ≤40% and CrCl ≤60 mL/min (group 4).

Pharmacologic treatment during hospitalization was left to the discretion of the coronary care unit (CCU) cardiologist, according to our institute’s clinical protocols and international experience guidelines.

The primary end point of the study was the occurrence of inhospital death and of a composite clinical end point of death, acute renal failure requiring renal replacement therapy, acute respiratory failure requiring mechanical ventilation, or cardiogenic shock requiring intraaortic balloon pump support. Furthermore, other inhospital major adverse clinical events were evaluated.

Primary angioplasty

Primary angioplasty was performed by a 24-hour, on-call interventional team, according to standard clinical practice. Patients received a bolus of 5000 U heparin in the CCU, followed by additional boluses during the procedure, to
maintain the activated clotting time ≥300 seconds (between 200 and 250 seconds when abciximab was used). Coronary stenting, using bare metal stents in all patients, was performed with standard technique. Poststenting antithrombotic treatment consisted of aspirin and either clopidogrel or ticlopidine at standard dosages.

Definitions

Emergency renal replacement therapy (hemofiltration or hemodialysis) was performed if there was acute renal failure with oligoanuria for ≥48 hours, despite that there had been administration of ≥1 g per 24 hours of intravenous furosemide. In the event of concomitant overt heart failure, emergency renal replacement therapy was performed earlier. Blood transfusion was initiated in the case of hemoglobin reduction <8.0 g/L. Time to reperfusion was measured as the time from symptom onset to the coronary reperfusion obtained with balloon inflation. Cardiogenic shock was defined as prolonged hypotension (systolic blood pressure <85 mm Hg), with evidence of decreased organ perfusion caused by severe left ventricular dysfunction, right ventricular infarction, or mechanical complications of infarction. Intratracheal intubation and mechanical ventilation were performed in the case of prolonged cardiac arrest due to ventricular arrhythmias or severe respiratory failure (arterial oxygen saturation ≤80% despite optimal oxygen administration) due to acute pulmonary edema or cardiogenic shock.

Statistical analysis

The χ² or the Fisher exact test for categorical variables and the analysis of variance test for continuous variables were used to compare characteristics across groups of patients. A multivariate logistic regression model, which included all the potential confounding factors, that is, age, sex, anterior infarct location, anemia, diabetes, and time to reperfusion, was applied to assess the association among LVEF and CrCl reduction and inhospital mortality and morbidity. The value of LVEF (≥40% and ≤40%) and of CrCl (≥60 and ≤60 mL/min) was included as categorical variables. Linear regression analysis was used for obtaining correlation coefficient between CrCl and LVEF. Receiver operating characteristic analysis was performed to assess the predictive value of LVEF and CrCl and other risk scores versus inhospital mortality. Data are expressed as mean ± SD or percentages. A P value <.05 was considered to indicate statistical significance. All calculations were computed with the aid of the SAS software package (Version 8.02; SAS Institute Inc, Cary, NC).

Results

According to LVEF and CrCl values, 261 patients (56%) were included in group 1, 113 (24%) in group 2, 60 (13%) in group 3, and 33 (7%) in group 4.

The clinical and demographic characteristics of the 4 study groups are given in Table I. Coronary risk factors, infarct location, abciximab use, infarct-related artery, and contrast agent volume were similar in the 4 groups. Patients with renal insufficiency (groups 2 and 4) were older, more likely to be women, and had a higher incidence of anemia when compared to patients without renal insufficiency (groups 1 and 3). Notably, the serum creatinine value, although significantly higher in patients with renal insufficiency (groups 2 and 4) than in those without renal insufficiency, was, on the average, normal or only slightly increased in these 2 groups (1.2 ± 0.3 mg/dL in group 2 and 1.3 ± 0.5 mg/dL in group 4).

Patients with impaired LVEF (groups 3 and 4) had a longer time to reperfusion and a higher creatine kinase-MB peak than those without significant LVEF reduction (groups 1 and 2).

No relationship was found between baseline LVEF and CrCl values in the entire population (Figure 1).

Overall, inhospital mortality was 5.3% (n = 25). Table II reports the inhospital clinical complications in the 4 study groups. Most adverse events, including inhospital death and the combined end point of death and major clinical complications, were more frequently observed in patients with renal insufficiency than in those without it. A significant gradient of increasing inhospital mortality (Figure 2) and of the combined end point (Figure 3), going from no dysfunction in both organs (group 1), to dysfunction in only one of the organs (groups 2 and 3 pooled together) and ending with dysfunction in both of them (group 4), was observed when patients outcome was analyzed according to cardiac and renal function.

At multivariate analysis adjusting for age, sex, infarct location, anemia, diabetes, and time to reperfusion, the odds ratio of inhospital mortality in patients with either renal or cardiac dysfunction, as compared with patients without dysfunction of these organs, was 7.9 (95% CI 2.0-31.0, P = .003), whereas for patients with both renal and cardiac dysfunction, it was 51.2 (95% CI 9.9-263.8, P < .0001). The odd ratios of combined end point were 8.3 (95% CI 3.9-17.9, P < .0001) and 25.9 (95%
for combined end point). As shown in Table III, the increased mortality rate include elderly patients22,27,28; patients with STEMI treated with primary angioplasty at ent patient subgroups may vary significantly. Subsets of women29; those with renal insufficiency,17 anemia,23 survival.1,2,26 However, the mortality rate across differ-

When CrCl and LVEF were considered together, the area under the receiver operating characteristic curve was 0.91 (P < .001), a value similar to that obtained by applying previous risk scores to our patients (Figure 4). As shown in Table III, the association of reduced CrCl and LVEF was the strongest predictor for clinical outcomes among other possible combinations.

When CrCl and LVEF were considered together, the area under the receiver operating characteristic curve was 0.91 (P < .001), a value similar to that obtained by applying previous risk scores to our patients (Figure 4).

**Table II.** Inhospital clinical complications

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 261)</th>
<th>Group 2 (n = 113)</th>
<th>Group 3 (n = 60)</th>
<th>Group 4 (n = 33)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPR, VT, or VF</td>
<td>18 (7%)</td>
<td>14 (12%)</td>
<td>14 (23%)</td>
<td>7 (21%)</td>
<td>.001</td>
</tr>
<tr>
<td>High-rate atrial fibrillation</td>
<td>17 (7%)</td>
<td>6 (5%)</td>
<td>4 (7%)</td>
<td>5 (15%)</td>
<td>.25</td>
</tr>
<tr>
<td>High-degree conduction disturbances</td>
<td>14 (5%)</td>
<td>5 (4%)</td>
<td>4 (7%)</td>
<td>3 (9%)</td>
<td>.74</td>
</tr>
<tr>
<td>Acute pulmonary edema requiring mechanical ventilation</td>
<td>6 (2%)</td>
<td>6 (5%)</td>
<td>17 (28%)</td>
<td>6 (18%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cardiogenic shock requiring intraaortic balloon counterpulsation</td>
<td>8 (3%)</td>
<td>11 (10%)</td>
<td>17 (28%)</td>
<td>13 (39%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Major bleeding requiring blood transfusion</td>
<td>10 (4%)</td>
<td>2 (2%)</td>
<td>2 (3%)</td>
<td>2 (6%)</td>
<td>.62</td>
</tr>
<tr>
<td>Acute renal failure requiring renal replacement therapy</td>
<td>0 (0%)</td>
<td>3 (3%)</td>
<td>5 (15%)</td>
<td>&lt;.001*</td>
<td></td>
</tr>
<tr>
<td>Patients with ≥2 major clinical complications</td>
<td>16 (6%)</td>
<td>18 (16%)</td>
<td>19 (32%)</td>
<td>10 (36%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Inhospital death</td>
<td>3 (1%)</td>
<td>3 (3%)</td>
<td>9 (15%)</td>
<td>10 (30%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Combined end point</td>
<td>12 (5%)</td>
<td>19 (17%)</td>
<td>20 (33%)</td>
<td>16 (48%)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

CPR, Cardiopulmonary resuscitation; VF, ventricular fibrillation; VT, ventricular tachycardia.

*By Fisher exact test.

Inhospital death, cardiogenic shock requiring intraaortic balloon counterpulsation, acute pulmonary edema requiring mechanical ventilation, and acute renal failure requiring renal replacement therapy.

CI 8.7-77.0; P < .001), respectively (Table III). The interaction between CrCl and LVEF did not reach significance (P = .46 for inhospital mortality and P = .14 for combined end point). As shown in Table III, the association of reduced CrCl and LVEF was the strongest predictor for clinical outcomes among other possible combinations.

When CrCl and LVEF were considered together, the area under the receiver operating characteristic curve was 0.91 (P < .001), a value similar to that obtained by applying previous risk scores to our patients (Figure 4). As shown in Table III, the association of reduced CrCl and LVEF was the strongest predictor for clinical outcomes among other possible combinations. When CrCl and LVEF were considered together, the area under the receiver operating characteristic curve was 0.91 (P < .001), a value similar to that obtained by applying previous risk scores to our patients (Figure 4).

**Discussion**

Increasing evidence indicates that primary angioplasty is the most effective treatment of STEMI, in terms of preservation of ventricular function and improvement in survival.1,2,26 However, the mortality rate across different patient subgroups may vary significantly. Subsets of patients with STEMI treated with primary angioplasty at increased mortality rate include elderly patients22,27,28; women29; those with renal insufficiency,17 anemia,23 heart failure,30 cardiogenic shock,31 diabetes mellitus,32 and acute hyperglycemia,33 and those developing contrast-induced nephropathy.34 Frequently, >1 of these conditions, comorbidities, and complications are present in the same patient, causing a further increase in cumulative mortality risk. Therefore, patient’s assessment at the time of hospital admission is a critical need for accurate risk stratification and for application of personalized therapeutic strategies in the era of primary angioplasty. Several clinical and angiographic predictors of increased mortality have been recognized, and risk scores have been recently validated.3-7,17,18,25,28,30,34-36 Serum creatinine, CrCl, and LVEF have constantly been found to be predictors of short- and long-term mortality in patients with STEMI treated with primary angioplasty.3,17,18 However, risk scores have rarely included renal function and LVEF or have incorporated a predischarge LVEF value for long-term risk assessment.3 Furthermore, the complexity of these risk scores, due to the many variables included, has made their clinical application impractical. Based on 4 PAMI trials, a risk score to predict mortality in patients undergoing primary angioplasty has been proposed.4 Moreover, the TIMI risk score has recently been applied to classify patients as low- or high-risk in the DANAMI-2 trial.5 However, neither the PAMI nor the TIMI risk scores have included LVEF and renal function among the considered variables. In one recent study by Halkin et al,5 a clinical and angiographic risk score for predicting mortality after primary angioplasty was developed, using the databases from the CADILLAC trial for score derivation and from the Stent-PAMI trial for validation. For the first time, a CrCl ≤60 mL/min and an angiographic LVEF ≤40% were identified as univariate predictors of 1-year mortality and were included among the 7 variables composing the score. Notably, renal insufficiency had the greatest odds ratio (5.99), and a quite similar relative risk was found for angiographic LVEF ≤40% (4.67). However, in the CADILLAC and in the Stent-PAMI trials, patients with renal insufficiency, as well as those with cardiogenic shock at the time of presentation (most of whom have a depressed LVEF) were excluded so that patients with the highest risk profile, such as those included in group 4 of our study, were scarcely represented. The exclusion of high-risk patients from these 2 trials is confirmed by the very low average inhospital mortality rate found in the CADILLAC (1.6%) and Stent-PAMI (2.4%) trials, as compared with our study (5.3%). Furthermore, the
30-day mortality rates in their high-risk groups (score ≥6) were only 6.6% and 8.1%, respectively, a value similar to that found for in-hospital mortality in our patients at intermediate risk (7%). In-hospital mortality in our high-risk group (group 4) was significantly higher (30%), likely because patients with cardiogenic shock at hospital presentation and those with renal insufficiency were also included in our study.

Our results confirm that both LVEF and CrCl are powerful independent prognostic variables, which are able to predict in-hospital outcomes. Moreover, they indicate that accurate risk stratification can be obtained, and in-hospital morbidity and mortality can be easily predicted, when the function of only these 2 organs is considered. Assessment of cardiac and renal function in patients with STEMI undergoing primary angioplasty may have practical implications and an important impact on clinical decision making. In “low-risk” patients, namely, those without relevant cardiac and renal impairment and a predicted in-hospital mortality rate of about 1%, an early hospital discharge can be safely planned. Conversely, in “high-risk” patients, characterized by combined cardiac and renal impairment and a predicted 30% in-hospital mortality rate, a prolonged and intensive treatment period in the CCU may be required, and a poor prognosis can be anticipated. In addition to predict mortality, our study allowed for prediction of major clinical complications. We considered a composite end point which included, in addition to in-hospital death, selected major clinical adverse events (such as acute pulmonary edema, cardiogenic shock, and acute renal failure requiring mechanical support) chosen because of their close relationship with acute cardiac and renal failure. The incidence of this combined end point was accurately predicted by LVEF and CrCl values (4.6%, 22.5%, and 48.5% in low-, intermediate-, and high-risk patients, respectively). Based on these findings, the high-risk nature of patients with renal insufficiency and reduced LVEF should be appreciated and the need for preventive measures highlighted. Appropriate novel therapeutic approaches, including tailored cardioprotective and renal-protective strategies, should be implemented in high-risk patients with STEMI undergoing primary angioplasty to support cardiac and renal function, to avoid major adverse clinical complications, and to improve survival.

The additive and independent role of cardiac and renal dysfunction in patients with STEMI is also supported by the lack, in the whole population, of a correlation between these 2 parameters. This observation confirms that renal insufficiency is not purely the consequence of acute cardiac dysfunction, as reflected by a low LVEF, but that the heart and the kidney independently influence the prognosis of patients with STEMI. Although the link between a reduced LVEF and an increased mortality and morbidity in patients with STEMI can be easily explained, the reason for increased short-term morbidity and mortality in patients with renal dysfunction is not completely known, and the mechanisms underlying a worse prognosis are not fully understood. However, it is conceivable that the interplay among extensive comorbidities, paradoxical patterns of less aggressive treatment, excess toxicity from conventional therapies, and unique pathobiology of chronic kidney disease may have
a considerable role. Indeed, renal insufficiency identifies a population characterized by a clinical and metabolic or biologic status particularly vulnerable to major cardiocirculatory acute events. This hypothesis seems confirmed by our results indicating that patients with STEMI with renal insufficiency were more often elderly, women, and had a higher incidence of anemia, and those with reduced LVEF presented, later, all factors that have been associated with increased mortality after primary angioplasty. However, the contribution of these 2 variables remained relevant also after adjustment for all these factors.

In conclusion, our study shows that reduced LVEF and CrCl are strong predictors of increased inhospital morbidity and mortality in patients with STEMI treated with primary angioplasty. Evaluation of cardiac and renal function provides a simple and clinically useful tool to early predict the risk of inhospital death and of a complicated clinical course, independently from the other major recognized prognostic factors.

Table III. Odds ratio estimates of inhospital mortality and combined end point of parameters included in the logistic multivariate analysis, and of other possible high-risk combinations

<table>
<thead>
<tr>
<th></th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>Inhospital mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age &gt;65 y</td>
<td>1.0</td>
<td>0.9-1.0</td>
<td>.07</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.2</td>
<td>0.4-3.5</td>
<td>.74</td>
</tr>
<tr>
<td>Anterior MI</td>
<td>2.5</td>
<td>0.8-7.8</td>
<td>.11</td>
</tr>
<tr>
<td>Time to reperfusion &gt;6 h</td>
<td>1.1</td>
<td>0.9-1.2</td>
<td>.31</td>
</tr>
<tr>
<td>Anemia</td>
<td>0.7</td>
<td>0.2-2.4</td>
<td>.54</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.7</td>
<td>0.9-7.8</td>
<td>.07</td>
</tr>
<tr>
<td>CrCl ≤60 mL/min or LVEF ≤40%</td>
<td>7.9</td>
<td>2.0-31.0</td>
<td>.003</td>
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<tr>
<td>CrCl ≤60 mL/min and LVEF ≤40%</td>
<td>51.2</td>
<td>9.9-263.8</td>
<td>.0001</td>
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<tr>
<td>Combined end point*</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Age &gt;65 y</td>
<td>1.0</td>
<td>0.9-1.0</td>
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<td>Male sex</td>
<td>1.2</td>
<td>0.6-2.4</td>
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<td>Anterior MI</td>
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<td>1.3-4.5</td>
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<td>Time to reperfusion &gt;6 h</td>
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<tr>
<td>Anemia</td>
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<td>Diabetes</td>
<td>1.6</td>
<td>0.7-3.5</td>
<td>.22</td>
</tr>
<tr>
<td>CrCl ≤60 mL/min or LVEF ≤40%</td>
<td>8.3</td>
<td>3.9-17.9</td>
<td>.0001</td>
</tr>
<tr>
<td>CrCl ≤60 mL/min and LVEF ≤40%</td>
<td>25.9</td>
<td>8.7-77.0</td>
<td>.001</td>
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<td>Other possible high-risk combinations (inhospital mortality)</td>
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<tr>
<td>Age &gt;65 years and LVEF ≤40%</td>
<td>6.9</td>
<td>2.8-16.9</td>
<td>.0001</td>
</tr>
<tr>
<td>Diabetes and LVEF ≤40%</td>
<td>16.8</td>
<td>5.7-49.2</td>
<td>.0001</td>
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<tr>
<td>Anterior MI and CrCl ≤60 mL/min</td>
<td>3.6</td>
<td>1.5-8.3</td>
<td>.002</td>
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<tr>
<td>Anemia and LVEF ≤40%</td>
<td>5.3</td>
<td>1.4-14.5</td>
<td>.014</td>
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<td>Other possible high-risk combinations (combined end point*)</td>
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<tr>
<td>Age &gt;65 y and LVEF ≤40%</td>
<td>6.3</td>
<td>3.2-12.4</td>
<td>.0001</td>
</tr>
<tr>
<td>Diabetes and LVEF ≤40%</td>
<td>9.6</td>
<td>3.5-26.3</td>
<td>.0001</td>
</tr>
<tr>
<td>Anterior MI and CrCl ≤60 mL/min</td>
<td>2.6</td>
<td>1.4-4.7</td>
<td>.0012</td>
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<tr>
<td>Anemia and LVEF ≤40%</td>
<td>8.7</td>
<td>2.9-26.1</td>
<td>.0001</td>
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</table>

*Inhospital death, cardiogenic shock requiring intraaortic balloon counterpulsation, acute pulmonary edema requiring mechanical ventilation, and acute renal failure requiring renal replacement therapy.

References


Figure 4

Receiver operating characteristic curves for predicting inhospital mortality in the study patients using the combined LVEF and CrCl risk model and previous risk scores. CADILLAC risk score: baseline LVEF, renal insufficiency, Killip class, final TIMI flow, age, anemia and 3-vessel disease; PAMI risk score: age, Killip class, heart rate, diabetes and infarct location; TIMI risk score: age, systolic blood pressure, heart rate, Killip class, infarct location, diabetes, history of hypertension or angina, weight, and time to treatment. AUC, Area under the curve.


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Reduction of neointimal hyperplasia after coronary stenting by pioglitazone in nondiabetic patients with metabolic syndrome

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Background This study investigates whether pioglitazone reduces neointimal hyperplasia after coronary stenting in nondiabetic patients with metabolic syndrome (MS) using intravascular ultrasound (IVUS). Pioglitazone, a novel insulin-sensitizing thiazolidinedione, has been shown to reduce neointimal hyperplasia after coronary stenting in patients with type 2 diabetes. However, the effect of pioglitazone on in-stent restenosis in nondiabetic patients with MS remains unknown.

Methods and Results Twenty-eight nondiabetic patients with MS after bare-metal stent implantation were randomized to 6-month treatment with or without 30 mg/d of pioglitazone (pioglitazone group [PIO] of 14 patients with 16 lesions and control group [CONT] of 14 patients with 16 lesions). At baseline and at 6-month follow-up, assessment of insulin resistance and visceral fat accumulation, quantitative coronary angiographic analysis, and IVUS measurements were performed. Pioglitazone treatment improved insulin resistance and decreased visceral fat accumulation without significant changes in plasma glucose levels, glycosylated hemoglobin A1c levels, and lipid profiles. Intimal index (intimal area / stent area) and intimal area were reduced in PIO compared with CONT (13% ± 7% vs 21% ± 13%, P = .033; 1.28 ± 0.76 mm² vs 1.90 ± 1.16 mm², P = .084; respectively). Binary restenosis rate was 0% in PIO versus 31% in CONT (P = .043).

Conclusions This is the first randomized, prospective IVUS study demonstrating that pioglitazone reduces neointimal hyperplasia after coronary stenting in nondiabetic patients with MS. Our data suggest that pioglitazone treatment may represent a novel therapeutic tool to target in-stent restenosis in nondiabetic patients with MS. (Am Heart J 2007;153:762.e1-762.e7.)