Randomized Comparison of Coronary Stenting With Balloon Angioplasty in Selected Patients With Acute Myocardial Infarction

Harry Suryapranata, MD, PhD; Arnoud W.J. van’t Hof, MD; Jan C.A. Hoornjte, MD, PhD; Menko-Jan de Boer, MD, PhD; Felix Zijlstra, MD, PhD

Background—Although the benefits of primary angioplasty in acute myocardial infarction have been demonstrated, several areas for improvement remain. Therefore, a prospective randomized trial comparing primary stenting with balloon angioplasty in patients with acute myocardial infarction was conducted.

Methods and Results—Patients with acute myocardial infarction were randomly assigned to undergo either primary stenting (n=112) or balloon angioplasty (n=115). The clinical end points were death, recurrent infarction, subsequent bypass surgery, or repeat angioplasty of the infarct-related vessel. The overall mortality rate at 6 months was 2%. Recurrent infarction occurred in 8 patients (7%) after balloon angioplasty and in 1 (1%) after stenting (P=0.036). Subsequent target-vessel revascularization was necessary in 19 (17%) and 4 (4%) patients, respectively (P=0.0016). The cardiac event-free survival rate in the stent group was significantly higher than in the balloon angioplasty group (95% versus 80%; P=0.012).

Conclusions—In selected patients with acute myocardial infarction, primary stenting can be applied safely and effectively, resulting in a lower incidence of recurrent infarction and a significant reduction in the need for subsequent target-vessel revascularization compared with balloon angioplasty. (Circulation. 1998;97:2502-2505.)

Key Words: stents • myocardial infarction • angioplasty
TABLE 1. Reasons for Exclusion in Candidates for Primary Angioplasty (n = 225)

<table>
<thead>
<tr>
<th>Clinical exclusion criteria</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged CPR or cardiogenic shock</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Factors making follow-up unlikely</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Life expectancy &lt; 1 year</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Angiographic exclusion criteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small IRV (&lt; 3.0 mm)</td>
<td>77</td>
<td>34</td>
</tr>
<tr>
<td>Diffuse sclerotic IRV</td>
<td>47</td>
<td>21</td>
</tr>
<tr>
<td>Target lesion involving a major side branch</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>No-reflow phenomenon or extensive thrombus throughout IRV</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>Left main or severe 3-vessel disease necessitating subsequent surgery</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Excessive proximal vessel tortuosity</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Inability to cross target lesion with a guidewire</td>
<td>5</td>
<td>2</td>
</tr>
</tbody>
</table>

CPR indicates cardiopulmonary resuscitation; IRV, infarct-related vessel.

International Normalized Ratio values had reached therapeutic levels. Warfarin was given for ≥3 months and aspirin (80 mg/d) indefinitely. However, because it became clear that ticlopidine was more effective in preventing stent thrombosis,4,5 and given the fact that anticoagulation therapy increases the risk of major bleeding complications,6,7 our poststenting regimen protocol was modified accordingly. From January 1996, only ticlopidine (250 mg/d for ≥2 weeks) and aspirin were given after stenting, and warfarin derivates were no longer used. Heparin infusion (1 mg/kg/h) and aspirin were given after stenting, and warfarin derivates were no longer used. Heparin infusion (1 mg·kg⁻¹·h⁻¹) or subcutaneous low-molecular-weight heparin (0.6 mL·BID) was given for 48 hours after sheath removal in all patients, regardless of initial treatment allocation. Thrombolytic therapy, platelet glycoprotein IIb/IIIa receptor antagonists, and intravascular ultrasound were not used.

Clinical end points were death of any cause, recurrent MI, subsequent bypass surgery, or repeat angioplasty of the IRV. Recurrent MI was defined as previously described.1 The indication for a second intervention had to be substantiated by symptoms or by ECG or scintigraphic evidence of ischemia at rest or during exercise. Subsequent revascularization involving other coronary arteries did not constitute an end point. All events were reviewed by 2 cardiologists blinded to treatment assignments.

Using an anticipated 2-sided test for differences in independent binomial proportions at the 5% significance level with a power of 90%, 211 patients (105 in each group) were required to detect a reduction in a composite end point from 35% to 16%. Data were analyzed by use of a single comparison between groups according to the intention-to-treat principle. Continuous variables were expressed as mean±SD and compared by use of Student’s t test, whereas discrete variables were given as absolute values and percentages. The χ² test was used to compare proportions, or a Fisher’s exact test was used when appropriate. The differences in event rates between groups during the follow-up period were assessed by the Kaplan-Meier method using the log-rank test. Multivariate analysis was performed by use of the Cox proportional hazard method, permitting calculation of odds ratios that may be interpreted as relative risks with 95% CIs. All statistical tests were 2-tailed.

Results

From June 1995 to March 1997, a total of 532 patients with acute MI have been admitted to our institution, of whom 498 underwent immediate coronary angiography. One patient died before angiography could be performed, and coronary angiography was not performed in 12 patients who were involved in another trial and 21 patients who presented >24 hours after symptom onset. Of those 498 patients undergoing coronary angiography, 25 with a small patent IRV were treated conservatively and 21 with severe triple-vessel disease were referred for immediate bypass surgery. The remaining 452 patients underwent primary angioplasty. Of these, 225 were excluded from the trial for various reasons (Table 1), and 227 eligible patients were randomized to undergo primary stenting (n = 112) or balloon angioplasty (n = 115). Most (89, or 79%) of the randomized patients in the stent group and 92 (80%) in the balloon angioplasty group were recruited in the trial after the protocol was amended and the modified poststenting regimen was adopted. Baseline characteristics and in-hospital outcome are listed in Table 2 and are compared with those of patients who were excluded from the trial. Subacute occlusion occurred in 5 patients allocated to balloon angioplasty, on the same day as the initial procedure in 4 and at day 9 in 1 patient. Repeat angioplasty followed by stenting was performed in all patients, but 4 had a recurrent MI. Only 1 stent patient had subacute occlusion and recurrent MI at day 4 and underwent bypass surgery. Quantitative angiographic results are shown in Table 3.

Figure 1 shows clinical outcome at 6 months. There were only 5 deaths (2%). Recurrent MI occurred in 1 patient after stenting and in 8 after balloon angioplasty (P = 0.036). Subsequent target-vessel revascularization was necessary in 4 and 19 patients after stenting or balloon angioplasty, respectively (P = 0.0016). Consequently, the cardiac event-free survival rate of 95% in the stent group was significantly higher than the 80% in the balloon angioplasty group (P = 0.0012). Figure 2 shows the Kaplan-Meier survival curves in both groups. No patient was lost to follow-up. Non–target-vessel revascularization was performed in 6 (5%) and 4 (3%) patients, respectively. Table 4 shows multivariate analysis of predictors of cardiac events in all patients, regardless of treatment allocation.

Discussion

The present trial indicates for the first time in a prospective, randomized manner that primary stenting can be applied safely and effectively in selected patients with acute MI, resulting in a significant reduction in recurrent MI and subsequent target-vessel revascularization compared with balloon angioplasty.

However, the major limitation of the present trial is the fact that the results were obtained from a single high-volume center, involving a limited number of patients, and might be biased by the selection of those patients who were in relatively stable hemodynamic condition and in whom the IRV was considered to be technically and anatomically ideal for stenting. In fact, this limitation prevented at least half of all patients deemed suitable for primary angioplasty from being randomized. Therefore, the results may not be generalizable to all patients with acute MI. To address this limitation in our currently ongoing trial, all patients with acute MI are now randomized before coronary angiography.

Although the mortality rate (2%) was comparable to our previous trial,1 no difference could be observed between groups. In fact, it would be unlikely that stenting could
further reduce the low mortality rate achieved by balloon angioplasty. To determine the predictors of adverse events, multivariate analysis was performed by combining both study groups. Male sex, Killip class 2, and treatment with balloon angioplasty were associated with an increased risk of adverse cardiac events (Table 4). Because most patients who were excluded from the trial had more complex coronary anatomy, had multivessel disease, were in Killip class 4, and more often needed an intra-aortic balloon pump, the initial success rate was lower than that of the study population (Table 2). All of these factors may have contributed to the higher rates of death, recurrent MI, and subsequent target-vessel revascularization, as well as a longer hospital stay. Despite this fact, the mortality rate in patients excluded from the present study was increased compared to those who were included in the trial.

### Table 2. Baseline Characteristics and In-Hospital Events

<table>
<thead>
<tr>
<th></th>
<th>Randomized</th>
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<tbody>
<tr>
<td></td>
<td>Stent (n=112)</td>
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<td></td>
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<tr>
<td>Age, y</td>
<td>59±11 NS</td>
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<tr>
<td>Male</td>
<td>93 (83%)</td>
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<td>Previous infusion</td>
<td>15 (13%)</td>
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<tr>
<td>Previous bypass surgery/angioplasty</td>
<td>17 (15%) NS</td>
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<tr>
<td>Multivessel disease</td>
<td>49 (44%) NS</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Killip class 4</td>
<td>3 (3%)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Symptom-onset time to admission, min</td>
<td>217±222 NS</td>
<td></td>
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<tr>
<td>Admission to reperfusion, min</td>
<td>62±82 NS</td>
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</table>

IRV indicates infarct-related vessel. P values are between the two randomized groups. Plus-minus values are mean±SD.

### Table 3. Quantitative Angiographic Results

<table>
<thead>
<tr>
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<th>Stent (n=112)</th>
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<tr>
<td></td>
<td>Post</td>
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<tr>
<td>Minimal luminal diameter, mm Pre</td>
<td>0.23±0.45</td>
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<tr>
<td></td>
<td>Post</td>
<td></td>
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<tr>
<td>Reference diameter, mm Pre</td>
<td>3.06±0.56</td>
<td></td>
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<tr>
<td></td>
<td>Post</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Diameter stenosis, % Pre</td>
<td>92.1±15.1</td>
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</tbody>
</table>

Pre indicates preprocedure; Post, postprocedure.

*P<0.0001 Post vs Pre. Plus-minus values are mean±SD.

angioplasty were associated with an increased risk of adverse cardiac events (Table 4). Because most patients who were excluded from the trial had more complex coronary anatomy, had multivessel disease, were in Killip class 4, and more often needed an intra-aortic balloon pump, the initial success rate was lower than that of the study population (Table 2). All of these factors may have contributed to the higher rates of death, recurrent MI, and subsequent target-vessel revascularization, as well as a longer hospital stay. Despite this fact, the mortality rate in patients excluded from the present study was increased compared to those who were included in the trial.

**Figure 1.** Clinical outcome at 6 months in both study groups. re-MI indicates recurrent myocardial infarction; TVR, target-vessel revascularization.
compares favorably with patients treated with thrombolytic therapy.\textsuperscript{1–3} Although the mean diameter stenosis of 17.9% after stenting seems to be relatively high for a low incidence of target-vessel revascularization (4%), this is still lower than the 22% reported in patients with stable angina.\textsuperscript{5} In addition, patients selected for the present trial had bigger vessels than patients in other randomized trials,\textsuperscript{4,5} with poststenting reference diameter of 3.15 mm. Most (80%) of the randomized patients were included after our poststenting regimen was modified to exclude use of anticoagulants. This led to fewer bleeding complications and a shorter hospital stay compared with earlier reports.\textsuperscript{4,5} In fact, all bleeding complications occurred in the beginning of the present trial, before this strategy was adopted and aggressive anticoagulation was used. This protocol amendment was supported by studies reporting stenting in acute MI without conventional anticoagulation.\textsuperscript{4,5} Finally, the implications of the present study with respect to cost-effectiveness require a formal analysis, which will be performed after 1 year of follow-up.

\begin{table}[h]
\centering
\caption{Multivariate Analysis of Predictors of Adverse Cardiac Events}
\begin{tabular}{lll}
\hline
 & Relative Risk & 95\% CI \\
\hline
Allocated to balloon angioplasty & 3.2 & 1.2–8.5 \\
Male sex & 4.9 & 1.1–22.5 \\
Age (per year) & 1.03 & 0.99–1.07 \\
Diabetes & 1.4 & 0.3–6.6 \\
Killip class $\geq$2 at admission & 2.9 & 1.1–7.7 \\
Left anterior descending artery & 0.7 & 0.3–1.5 \\
Residual minimal luminal diameter $<$2 mm & 2.0 & 0.8–4.8 \\
Reference diameter $<$3 mm & 2.3 & 0.9–5.8 \\
\hline
\end{tabular}
\end{table}

Cardiac event was defined as any death, recurrent infarction, or subsequent target-vessel revascularization.

\section{References}


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