Frequency and Clinical Significance of Myocardial Ischemia Detected Early After Coronary Stent Implantation

Josep Rodés-Cabau, Jaume Candell-Riera, Enric Domingo, Joan Castell-Conesa, Inocencio Anívarro, Juan Angel, Santiago Aguadé-Bruix, Ferran Padilla, Adriana Soto, and Jordi Soler-Soler

Servei de Cardiologia and Servei de Medicina Nuclear, Hospital General Universitari Vall d’Hebron, Barcelona, Spain

A high number (30%–50%) of reversible defects have been detected early after coronary balloon angioplasty. Inadequate luminal enlargement despite a good angiographic appearance has been suggested as a possible mechanism of these perfusion abnormalities, and some reports have shown better coronary flow reserve after coronary stent implantation than after balloon dilatation. The primary objective of this study was to evaluate the frequency of early ischemic defects detected by maximal exercise (plus dipyridamole) with $^{99m}$Tc-tetrofosmin SPECT after successful coronary angioplasty with stent implantation. A secondary objective was to determine the prognostic value of these early ischemic defects.

Methods: Thirty patients without previous myocardial infarction who successfully underwent 1-vessel coronary angioplasty with stent implantation were studied. Maximal-exercise $^{99m}$Tc-tetrofosmin myocardial SPECT, with simultaneous dipyridamole if exercise was suboptimal, was performed at 6 ± 1 d (mean ± SD) after percutaneous transluminal coronary angioplasty. At 8 ± 3 mo, all patients were followed up clinically, and 77% of them underwent follow-up angiography.

Results: The percentage of stenosis decreased from 68.5% ± 12.6% of luminal diameter to 9.3% ± 8.8% after stent implantation, and minimal luminal diameter increased from 0.89 ± 0.36 mm to 2.85 ± 0.45 mm. Mild-to-moderate reversible myocardial defects in the territory of the dilated artery were detected in 5 patients (17%), with no angiographic or procedural differences occurring between them and patients without ischemic defects. At follow-up, the target lesion revascularization rates depending on the presence or absence of early ischemic defects were 40% and 8%, respectively ($P = 0.18$). Angiographic restenosis occurred in 3 of 4 patients who had early ischemic defects and underwent follow-up angiography and in 3 of 19 patients who had no early ischemic defects and underwent follow-up angiography (restenosis rate, 75% and 16%, respectively; $P < 0.05$). Conclusion: Coronary angioplasty with stent implantation is associated with a 17% rate of ischemic defects early after the procedure. Patients with early myocardial perfusion defects after coronary stent implantation had a high rate of restenosis.

Key Words: coronary disease; stents; perfusion imaging


Received Dec. 18, 2000; revision accepted Aug. 2, 2001.
For correspondence or reprints contact: Josep Rodés-Cabau, MD, Servei de Cardiologia, Hospital General Universitari Vall d’Hebron, Passeig Vall d’Hebron, 119-129, Barcelona 08035, Spain.
cardiac infarction, bypass surgery, or death) had occurred. Angiographic measurements were performed off line, using a compact disk medical 3500 view station (Philips Medical Systems, Best, The Netherlands), by an experienced observer unaware of the scintigraphic findings. Measurements were obtained from a single projection that showed the most severe stenosis. The type of stent selected and the technique of implantation were left to the discretion of the operator. All patients were treated with ticlopidine for 1 mo and aspirin. Exclusion criteria were the presence of other lesions in the dilated vessel or of severe stenosis (>70% stenosis of the diameter by visual estimation) in the nondilated vessels, previous myocardial infarction, previous coronary bypass surgery, and local vascular complications precluding exercise within the week after PTCA. The Institutional Ethics Committee approved the study, and all patients gave written informed consent.

**Exercise Test**

The symptom-limited exercise test was performed within the week after PTCA (3–7 d). Twenty-one patients used a bicycle ergometer, and 9 used a standard treadmill. All antiangial drugs were withdrawn >24 h before the exercise test. When the bicycle ergometer was used, the test started with an initial load of 50 W, and 25 W were added every 3 min. When the exercise treadmill was used, the Bruce protocol was applied. Exercise testing was stopped if exhaustion, symptoms, or >2 mm ST-segment depression developed. Exercise testing was considered adequate if >80% of the maximal predicted heart rate or >5 metabolic equivalents of oxygen consumption were achieved without angina or ST-segment depression. Patients unable to exercise adequately were withdrawn if exhaustion, symptoms, or 1 mm appeared 0.08 s after the J point.

**99mTc-Tetrofosmin SPECT**

All patients received an intravenous dose of $^{99m}$Tc-tetrofosmin (220 MBq) 30–60 s before the end of exercise. The stress and rest studies were performed 1–2 h apart, and the dose for the rest study was 650 MBq. Images were acquired 1 h after administration of the radiopharmaceutical using an SP4 scintillation camera (Elscint Ltd., Haifa, Israel) with a high-resolution collimator and a semicircular orbit starting at a 30° right anterior oblique position, with detection performed every 3°. Reconstruction was performed (Butterworth filter; order, 5; section frequency, 0.4), and short-axis, horizontal long-axis, and vertical long-axis sections were obtained. Twelve segments were evaluated: anterobasal, midanterior, anterolateral, septobasal, midseptal, septalapical, inferobasal, midinferior, inferolateralobasal, midlateral, and posterolateral. Myocardial uptake was assessed by 2 experienced observers, who interfered with the dilated vessel and were unaware of the diameter by visual estimation) in the nondilated vessels, previous myocardial infarction, previous coronary bypass surgery, and local vascular complications precluding exercise within the week after PTCA. The Institutional Ethics Committee approved the study, and all patients gave written informed consent.

**Statistical Analysis**

Categoric values are expressed as frequencies. Continuous variables are expressed as mean ± SD or median with superior and inferior range. Univariate analyses were performed using the Fischer exact test for categoric values and the Student t test or the nonparametric Mann–Whitney test for continuous variables. $P < 0.05$ was considered statistically significant.

**RESULTS**

The baseline clinical characteristics of the study population are listed in Table 1. The mean age was 60 y, and 19 patients (63%) underwent coronary angiography and PTCA because of unstable angina (10 patients had class I or II unstable angina, and 9 patients had class III). Myocardial ischemia before PTCA was evidenced by positive treadmill results in 12 patients (40%), positive myocardial scintigraphy results in 9 patients (30%), and spontaneous ECG changes in 9 patients (30%).

**Angiographic Characteristics and PTCA Results**

Most patients (n = 21; 70%) underwent PTCA of the left anterior descending artery. The results of PTCA are described in Table 2. Thirty-four stents were implanted (26 patients received 1 stent and 4 patients received 2 stents), with a median diameter of 3.0 mm (range, 2.5–4.0 mm) and a median length of 15 mm (range, 8–24 mm). The majority of stents implanted were tubular (MultiLink [10 stents]; Guidant/ACS, Santa Clara, CA; Jostent [2 stents]; JOMED International AB, Helsingborg, Sweden; NIR stent [2 stents]; Medinol Ltd., Tel Aviv, Israel; MiniCrown [1 stent]; Johnson & Johnson Interventional Systems, Warren, NJ; Bestent [1 stent]; Medtronic InStent, Minneapolis, MN), 7 stents had a sinusoidal ring design (AVE GFX stent; Arterial Vascular Engineering Inc., Santa Rosa, CA), 4 stents comprised zigzag modules mounted on a flexible spine (XT coronary stent; Bard Ireland Ltd., Galway, Ireland), 3 stents were a self-expanding wire mesh (Wallstent; Schneider AG, Bulach, Switzerland), and 4 stents had a coil design (Crossflex; Johnson & Johnson).

**TABLE 1**

Patient Demographics (n = 30)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>60 ± 10</td>
</tr>
<tr>
<td>Female</td>
<td>8 (27%)</td>
</tr>
<tr>
<td>Smoker</td>
<td>6 (20%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14 (47%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>10 (33%)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>22 (73%)</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>19 (63%)</td>
</tr>
<tr>
<td>Demonstration of ischemia</td>
<td>12 (40%)</td>
</tr>
<tr>
<td>Treadmill testing</td>
<td>9 (30%)</td>
</tr>
<tr>
<td>Myocardial scintigraphy</td>
<td>9 (30%)</td>
</tr>
</tbody>
</table>
Before the intervention, the mean minimal luminal diameter at the culprit lesion was 0.89 ± 0.36 mm and the mean stenosis grade was 68.6% ± 12.6%. After stent implantation, the corresponding values were 2.82 ± 0.45 mm and 9.3% ± 8.8%, respectively (P < 0.001).

**Myocardial SPECT Exercise Test**

The results of the exercise test are shown in Table 3. Exercise testing was performed at a mean of 6 ± 1 d after PTCA. Three patients (10%) could not exercise adequately and received an intravenous dose of dipyridamole. The findings were positive for 4 patients (2 with ECG changes and 2 with ECG changes added to angina). No complications occurred.

Myocardial SPECT showed myocardial defects in the territory of the dilated artery in 5 patients (17%). The dilated artery was the left anterior descending artery in 2 patients, the left circumflex artery in another 2, and the right coronary artery in 1. The myocardial defect was evaluated as moderate in all but 1 patient, in whom it was mild. Only 1 of these 5 patients had significant ST depression during exercise. As shown in Table 4, no angiographic or procedural differences were seen between patients with and patients without early ischemic defects in the territory of the dilated artery.

Another 5 patients had mild myocardial perfusion defects remote from the dilated artery. Two of these patients had presented with moderate coronary stenosis in the distal segment of a nondilated artery, and 3 had significant ECG changes during exercise (2 with added angina). The results of the exercise test are shown in Table 3. Exercise testing was performed at a mean of 6 ± 1 d after PTCA. Three patients (10%) could not exercise adequately and received an intravenous dose of dipyridamole. The findings were positive for 4 patients (2 with ECG changes and 2 with ECG changes added to angina). No complications occurred.

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**Follow-Up**

Four patients (13%) underwent target lesion revascularization because of clinical restenosis (3 had recurrent angina, and 1 had a non-Q wave myocardial infarction). No deaths occurred before follow-up. Angiographic restenosis was detected by follow-up angiography in 6 (26%) of 23 patients.

**Relationship Between Early Ischemic Defects in Territory of Dilated Artery and Restenosis**

Angiographic restenosis occurred in 3 of 4 patients who had ischemic defects and underwent follow-up angiography (restenosis rate, 75%) and in 3 of 19 patients who had no ischemic defects and underwent follow-up angiography (restenosis rate, 16%) (P = 0.04). Two of the 5 patients with early myocardial defects underwent target lesion revascularization (40%), compared with only 2 of 25 patients without early ischemic defects (8%) (P = 0.18; Fig. 1). At the time of follow-up, none of the patients with significant ECG changes during exercise testing had experienced clinical events.

Maximal exercise (plus dipyridamole) 

**Table 2**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of dilated vessels</td>
<td>21 (70%)</td>
</tr>
<tr>
<td>LAD</td>
<td>21 (70%)</td>
</tr>
<tr>
<td>LCX</td>
<td>5 (17%)</td>
</tr>
<tr>
<td>RCA</td>
<td>4 (13%)</td>
</tr>
</tbody>
</table>

**Reference diameter (mm)**

| Before PTCA | 2.93 ± 0.59 |
| After PTCA  | 3.11 ± 0.48 |

**Minimal luminal diameter (mm)**

| Before PTCA | 0.89 ± 0.36 |
| After PTCA  | 2.85 ± 0.45 |

**Stenosis (% diameter)**

| Before PTCA | 68.5 ± 12.6 |
| After PTCA  | 9.3 ± 8.8   |

LAD = left anterior descending coronary artery; LCX = left circumflex coronary artery; RCA = right coronary artery.

**Table 3**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time after angioplasty (d)</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>Metabolic equivalents of oxygen consumption</td>
<td>7 ± 1.9</td>
</tr>
<tr>
<td>Peak heart rate (bpm)</td>
<td>129 ± 25</td>
</tr>
<tr>
<td>% Predicted heart rate</td>
<td>79 ± 13</td>
</tr>
<tr>
<td>Peak systolic blood pressure (mm Hg)</td>
<td>180 ± 20</td>
</tr>
<tr>
<td>Peak rate-pressure product (bpm · mm Hg · 10)</td>
<td>23.5 ± 1.9</td>
</tr>
<tr>
<td>No. of patients taking dipyridamole</td>
<td>3 (10%)</td>
</tr>
<tr>
<td>No. of patients with ST depression ≥ 1 mm</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>No. of patients with angina</td>
<td>2 (7%)</td>
</tr>
</tbody>
</table>

**Table 4**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Present</th>
<th>Absent</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of stents per patient</td>
<td>1.0</td>
<td>1.1</td>
<td>0.35</td>
</tr>
<tr>
<td>Stent length (mm)</td>
<td>17.0 ± 4.8</td>
<td>16.3 ± 3.4</td>
<td>0.72</td>
</tr>
<tr>
<td>Stent diameter (mm)</td>
<td>3.0 ± 0.35</td>
<td>3.09 ± 0.36</td>
<td>0.61</td>
</tr>
<tr>
<td>Maximum inflation pressure (atm)</td>
<td>11.8 ± 1.7</td>
<td>12.9 ± 1.5</td>
<td>0.15</td>
</tr>
<tr>
<td>Reference diameter before angioplasty (mm)</td>
<td>2.92 ± 0.54</td>
<td>2.92 ± 0.60</td>
<td>0.98</td>
</tr>
<tr>
<td>Stenosis (% diameter)</td>
<td>65.1 ± 15.9</td>
<td>69.2 ± 12.1</td>
<td>0.51</td>
</tr>
<tr>
<td>Minimal luminal diameter after angioplasty (mm)</td>
<td>1.02 ± 0.45</td>
<td>0.86 ± 0.34</td>
<td>0.38</td>
</tr>
<tr>
<td>Reference diameter after angioplasty (mm)</td>
<td>3.08 ± 0.47</td>
<td>3.11 ± 0.49</td>
<td>0.87</td>
</tr>
<tr>
<td>Residual stenosis (%)</td>
<td>12.5 ± 7.5</td>
<td>8.6 ± 9.1</td>
<td>0.38</td>
</tr>
<tr>
<td>Minimal luminal diameter after angioplasty (mm)</td>
<td>2.70 ± 0.52</td>
<td>2.84 ± 0.44</td>
<td>0.54</td>
</tr>
</tbody>
</table>
implantation.

.. events occurred in patients with residual ischemia after stent

.. graphic restenosis rate, although only half of the restenotic

.. ional ischemic defects was associated with a high angio-

.. foci extruded plaque in an adjacent vessel with no stent

.. unapparent stent-edge dissections or new accumulations of

.. fects after balloon angioplasty (16,17). Similar results have

.. been reported for measurement of coronary flow reserve

.. immediately after balloon angioplasty and stent implanta-

.. tion. Coronary flow reserve remained abnormal in nearly

.. 60% of patients after balloon angioplasty, whereas only

.. % of patients had an inadequate flow reserve after coro-

.. nary stent implantation (14). Likewise, the coronary flow

.. reserve determined by PET in 15 patients within the first 3 d

.. after coronary stent implantation showed normalization of

.. myocardial blood flow in all cases (18). However, other

.. studies using coil stents have reported lower rates (13%–

.. 60%) of functional recovery after coronary angioplasty

.. (19,20). In this study, differences in the rate of coil stent

.. implantation between patients with and patients without

.. early myocardial defects were not statistically significant

.. (20% vs. 12%, respectively).

.. Despite the functional improvement obtained after coro-

.. nary stent implantation, compared with that obtained after

.. balloon angioplasty, a minority of patients still had func-

.. tional abnormalities. These early defects may be related to

.. impairment of the microvascular response, microvascular

.. stunning because of particulate embolization, or unapparent

.. angiographic obstruction at or adjacent to the stent. To

.. determine the potential mechanisms of flow abnormalities

.. immediately after stent implantation, Kern et al. (21) mea-

.. sured the coronary flow velocity reserve in the artery con-

.. taining the stent and in an angiographically normal refer-

.. ence vessel and found that at least half of the functional

.. abnormalities after stent implantation were caused by global

.. microvascular disease. According to our results, only 16% of

.. the studied patients had myocardial flow abnormalities

.. that could be attributed to residual vessel obstruction or to

.. regional microvascular stunning caused by distal emboliza-

.. tion in the territory of the dilated artery. Intravascular

.. sonography studies have shown that stent expansion is often

.. inadequate despite a satisfactory angiographic appearance

.. after stent implantation (22,23). Other mechanisms of un-

.. appreciated luminal obstruction after stent implantation are

.. unapparent stent-edge dissections or new accumulations of

.. focally extruded plaque in an adjacent vessel with no stent

.. (24). A high correlation has been shown between intravas-

.. cular sonographic assessment of stent expansion and func-

.. tional evaluation of coronary blood flow, and no correlation

.. has been shown between quantitative angiographic assess-

.. ment of stent expansion and coronary blood flow measure-

.. ments (20). Moreover, an inverse relationship between

.. optimal stent expansion, as assessed by intravascular sonog-

.. raphy, and the probability of restenosis has been reported,

.. suggesting that suboptimal stent deployment has an impor-

.. tant role in the restenotic process (25,26). Nevertheless,

.. absence of early myocardial ischemia may not exclude the

.. possibility of restenosis, because half of angiographic re-

.. stenosis in our study occurred in patients without residual

.. ischemic defects.

.. There has been some doubt as to the safety of performing

.. a functional test within the first few days after coronary

.. stent implantation. This doubt is based on previous case

.. reports documenting stent thrombosis within hours after

.. stress testing (27,28). No episodes of stent thrombosis or of

.. local vascular complications were observed in our study.

.. Furthermore, a large, randomized study has shown that

.. functional testing early after implantation of a coronary

.. stent is safe (29).

.. This study had some limitations. Intravascular sonogra-

.. phy was not routinely used to guide stent deployment.

.. Sonography would have detected stent underexpansion or

.. focal obstructions adjacent to the stent explaining some of

.. the early myocardial defects. Also, determination of frac-

.. tional flow reserve by pressure sensor wires would have

.. differentiated the potential role of residual obstructions after

.. DISCUSSION

.. Coronary angioplasty with stent implantation was associ-

.. ated with a 17% rate of myocardial defects early after the

.. procedure, as assessed by maximal exercise (plus dipyr-

.. idamole) 99mTc-tetrofosmin SPECT. Detection of these resi-

.. dual ischemic defects was associated with a high angio-

.. graphic restenosis rate, although only half of the restenotic

.. events occurred in patients with residual ischemia after stent

.. implantation.

.. This study compares favorably with the 30%–50% inci-

.. dence of myocardial perfusion abnormalities reported early

.. after coronary balloon angioplasty, suggesting that some of

.. the myocardial defects present early after balloon angio-

.. plasty were caused by inadequate luminal enlargement and

.. that the greater luminal area achieved with stent implanta-

.. tion resulted in a better functional result after angioplasty.

.. Also, stents prevent elastic recoil and spasm at the dilated

.. site, mechanisms that can contribute to early ischemic de-

.. fects after balloon angioplasty (16,17). Similar results have

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.. tional flow reserve by pressure sensor wires would have

.. differentiated the potential role of residual obstructions after

.. floatation.
stent implantation from the role of microvascular dysfunction, because the latter does not affect values obtained with pressure wires (30). Incomplete angiographic follow-up prevents accurate assessment of the restenosis rate. There may be some asymptomatic patients with angiographic restenosis; identifying these patients could change the restenosis rate and alter the final results. However, the angiographic restenosis rate and clinical events at follow-up were similar to those observed in other studies (31,32), and rates of angiography at follow-up were nearly equal in patients with and patients without early ischemic defects (80% and 76%, respectively). Finally, the most important limitation of the study was the small sample size, which significantly lessened the potential of the results, especially those concerning the clinical significance of the test. The small number of patients with residual ischemic defects prevented us from reaching definite conclusions about their prognostic value.

CONCLUSION

In most patients, coronary stent implantation results in complete normalization of myocardial perfusion, as evaluated by maximal exercise (plus dipiridamole) myocardial $^{99m}$Tc-tetrofosmin SPECT. However, 17% of patients were found to have persistent myocardial defects despite successful stent implantation and good angiographic results. Furthermore, the study findings suggest that detection of these early ischemic defects is associated with a high restenosis rate and that normal myocardial perfusion results identify a group of patients with a low risk of restenosis at follow-up. However, the clinical value of these findings has to be confirmed by larger studies.

REFERENCES


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