Early and intermediate term clinical outcome after multiple coronary stenting

Anoop Chauhan, Erik Vu, Donald R Ricci, Christopher E Buller, Michael D Moscovich, Stephanie Monkman, Ian M Penn

Abstract

Objective—To examine the immediate and intermediate term clinical outcome of multiple coronary stenting.

Design—Consecutive patients were prospectively entered on a dedicated database. Follow up information was obtained from outpatient and telephone interviews with patients and family physicians.

Setting—A tertiary referral centre.

Patients—140 consecutive patients underwent multiple coronary stenting between April 1994 and November 1996. Most patients had unstable coronary syndromes.

Main outcome measures—Death, cerebrovascular accidents, myocardial infarction (MI), coronary artery bypass surgery (CABG), and repeat angioplasty (PTCA).

Results—The angiographic success rate was 100% and the clinical procedural success rate 93%. The mean (SD) follow up was 11.9 (7.2) months (range 2–32). The mean (SD) number of stents per patient was 2.4 (0.7). The mean (SD) number of lesions treated per patient was 1.4 (0.6). There were four in-hospital deaths (2.9%) and five patients (3.6%) had a MI before hospital discharge. All in-hospital deaths occurred in patients presenting with an acute MI and cardiogenic shock. Three patients (2.2%) had a late MI. One patient with stent thrombosis underwent emergency CABG. Three patients (2.2%) underwent late CABG. Eight patients (5.7%) had a repeat PTCA. Eighty three patients (61.5%) were asymptomatic at follow up and 121 (86.4%) were free from major clinical events.

Conclusion—In an era of increased operator experience, high pressure stent deployment, and reduced anticoagulation with antiplatelet treatment alone, multiple coronary stenting may be performed with a high procedural success rate and good intermediate term outcome.

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Keywords: angioplasty; stents; clinical outcome; interventional cardiology

The implantation of an intracoronary stent improves the clinical success rate of percutaneous transluminal coronary angioplasty (PTCA) and reduces the rate of restenosis. 1 2 Intracoronary stenting is also an accepted treatment for failed angioplasty in the setting of a suboptimal result, threatened closure, or acute closure (bailout stenting). 3 4 The clinical outcome after multiple coronary stenting, however, has not been established. Some early studies have suggested an adverse outcome after multiple coronary stent implantation 5–7 and others have reported outcome in only selected patients. 8 The aim of this study was to review the procedural and late clinical outcome in unselected patients undergoing multiple coronary stenting in an era of high pressure stent deployment and reduced anticoagulation at a single high volume angioplasty centre.

Patients and methods

The clinical outcome of 140 unselected, consecutive patients undergoing multiple coronary stenting at our institution between April 1994 and November 1996 was reviewed. Anatomical characteristics other than a reference vessel diameter of less than 3 mm were not considered as contraindications.

Definitions

Multiple coronary stenting—The implantation of two or more stents in one or more vessels during the same procedure.

Bailout stenting—Coronary stenting for balloon angioplasty complicated by abrupt occlusion or threatened closure.

Suboptimal result—A residual stenosis of greater than 50% with or without intimal dissection.

Unstable angina—Crescendo pattern of angina to include an episode of rest pain, angina at rest of greater than 20 minutes duration in the absence of myocardial infarction (MI), or persistent postinfarction angina (Canadian Cardiovascular Society angina classes III and IV). 10

Vessel disease—One vessel disease was present if there was more than 50% diameter luminal narrowing in the left anterior descending, left circumflex, or right coronary vessels, or a major branch. Multiple vessel disease was defined as the presence of more than 50% diameter luminal narrowing in more than one of these major epicardial vessels.

Major complications—Death, cerebrovascular accidents, Q or non-Q wave MI, repeat PTCA, or urgent coronary artery bypass surgery (CABG).

Q wave MI—Development of new pathological Q waves (40 ms) in two or more contiguous leads, associated with a rise in creatine kinase (CK) activity of more than twice the upper limit of normal with an elevated CK-MB fraction.

Non-Q wave MI—An increase in peak CK activity to more than twice the upper limit of...
normal without the development of pathologicaL Q waves or a significant R wave in lead V1. 

**Angiographic success rate**—The rate of achievement of less than 50% residual stenosis.

**Procedural success rate**—Successful stent delivery to the intended site with greater than a 20% reduction in the percentage diameter stenosis, with a final residual stenosis of less than 50% and freedom from major complications during hospitalisation.

**Stent thrombosis**—Stent thrombosis was assumed when either occlusive thrombus formation was visualised angiographically within the stented vessel segment or clinical symptoms and electrocardiographic changes revealed acute MI six weeks after stent implantation.

**Major vascular complications**—Bleeding or haematoma formation requiring transfusion or vascular repair, or both.

### STENT PROCEDURE

Conventional over the wire and monorail balloon catheters were used for angioplasty. The stents were either hand crimped onto the angioplasty balloon or premounted with or without a delivery system. The balloon stent assembly was advanced through 8 F guiding catheters selected to offer sufficient back-up support. Angiography was repeated and further inflations performed inside the stent if necessary to produce an optimal result. Both compliant and non-compliant balloons were used and inflated to a pressure of up to 18–20 atm within the stent.

### ANTIPLATELET AND ANTICOAGULATION TREATMENT

All patients received 80–325 mg aspirin 24 hours before the procedure. The post-stenting anticoagulation regimen evolved during the study and patients received either conventional anticoagulation with warfarin and aspirin or a combination of aspirin and ticlopidine. All patients received a bolus of 10 000 units intravenous heparin before angioplasty (if they were not already receiving a heparin infusion) with repeat boluses to maintain an activated clotting time of greater than 300 seconds. Most patients (94%) were treated with only ticlopidine and aspirin after stent implantation and heparin was discontinued immediately after the procedure. The femoral sheaths were removed six hours after discontinuation of heparin. Ticlopidine was continued for four weeks. A complete blood count was performed at two and four weeks to check for neutropenia.

In patients treated with warfarin the femoral sheath was left in place and removed six hours later. Intravenous heparin was restarted two hours after haemostasis was achieved. Oral anticoagulation with warfarin was started on the day of stent implantation. Intravenous heparin was continued until warfarin dosing produced an international normalised ratio (INR) of more than 2.5. All patients received warfarin for a minimum of one month unless there were complications, and aspirin was continued long term. Anticoagulation was continued to maintain the INR between 2.5 and 3.

### Results

Table 1 shows the patient demographics. Most patients had unstable coronary syndromes, with 8.6% of patients presenting with an acute MI and 78.6% with unstable angina. Only 18 (12.9%) of the 140 patients presented with stable angina. Thirty eight (27.1%) had post-infarction angina (MI less than 30 days). Table 2 shows the angiographic and procedural characteristics. A total of 201 vessels were stented; nine patients (4.5%) had left main coronary artery disease (four with protected left circulation). Bailout coronary stenting for threatened or abrupt closure was undertaken in 32.8% of the lesions with a further 8.5% undergoing stenting after a suboptimal result following balloon angioplasty. High pressure (>12 atm) inflation was used to optimise stent deployment in 332 (99%) of the 336 stents. Warfarin anticoagulation was used in only a few patients (6.4%). Intravascular ultrasound guidance was used only in 4% of patients.

Multiple coronary stenting of a single coronary artery was undertaken in 111 of the 140 patients. A total of 139 lesions were treated with 276 stents (mean (SD) 2.5 (0.8)). The indication for stenting was elective in 50%, bailout in 40%, and suboptimal result in 10%. This is similar to the indication for stenting in the overall group.

### IN-HOSPITAL OUTCOME

The angiographic success rate was 100%. The procedural success rate was 93%. No patients suffered a cerebrovascular accident.

<table>
<thead>
<tr>
<th>Clinical presentation (%)</th>
<th>Number of patients (n=140)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute MI</td>
<td>12 (8.6%)</td>
</tr>
<tr>
<td>Post-MI angina*</td>
<td>38 (27%)</td>
</tr>
<tr>
<td>Unstable angina†</td>
<td>110 (78.6%)</td>
</tr>
<tr>
<td>Stable angina</td>
<td>18 (12.9%)</td>
</tr>
</tbody>
</table>

*myocardial infarction within 30 days; †includes the 38 patients with postmyocardial infarction angina.

CAD, coronary artery disease.
Multiple coronary stenting

Table 2 Angiographic and procedural characteristics

<table>
<thead>
<tr>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion location (n=201)</td>
</tr>
<tr>
<td>Left main</td>
</tr>
<tr>
<td>Left anterior descending artery</td>
</tr>
<tr>
<td>Right coronary artery</td>
</tr>
<tr>
<td>Circumflex coronary artery</td>
</tr>
<tr>
<td>Vein graft</td>
</tr>
<tr>
<td>Diagonal</td>
</tr>
<tr>
<td>Ramus</td>
</tr>
<tr>
<td>De novo lesions</td>
</tr>
</tbody>
</table>

Indication for stenting of lesions

<table>
<thead>
<tr>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective</td>
</tr>
<tr>
<td>Sub-optimal PTCA result</td>
</tr>
<tr>
<td>Bailout</td>
</tr>
</tbody>
</table>

Number of stents

<table>
<thead>
<tr>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
</tr>
<tr>
<td>Mean (SD) per patient</td>
</tr>
<tr>
<td>Mean (SD) lesions stented per patient</td>
</tr>
<tr>
<td>Mean (SD) maximum pressure (atm)</td>
</tr>
<tr>
<td>Use of high pressure (&gt;12 atm)</td>
</tr>
<tr>
<td>Warfarin anticoagulation</td>
</tr>
<tr>
<td>Antiplatelet therapy alone</td>
</tr>
<tr>
<td>Intra-aortic balloon pump support</td>
</tr>
</tbody>
</table>

Deaths

There were four (2.9%) deaths. The first occurred in a 46 year old man who presented with an acute inferior MI and cardiogenic shock. Angiography showed critical lesions in the left main artery, dominant right coronary artery, and left anterior descending artery. Successful stenting of all lesions with intra-aortic balloon pump support was undertaken. However, the patient developed electromechanical dissociation and died during the procedure despite an excellent angiographic result. The second death occurred in a 64 year old man who presented with cardiogenic shock and underwent emergency PTCA and multiple stenting to the left main and circumflex coronary artery with intra-aortic balloon pump support. He remained in cardiogenic shock, however, and died four days later despite an angiographically successful result. The third death occurred in a 69 year old man who presented with cardiogenic shock and an acute right ventricular MI leading to a cardiac arrest. Emergency angiography showed an occluded right coronary artery. Emergency PTCA and multiple stenting were performed to this vessel with intra-aortic balloon pump support. He continued to remain in cardiogenic shock, however, and died the next day despite an angiographically successful result. The fourth death occurred in a 72 year old man who presented with an acute MI and cardiogenic shock with a history of previous MI and severe peripheral vascular disease. He had three vessel coronary artery disease including left main stenosis with an ejection fraction of less than 20% and severe mitral regurgitation. Emergency CABG was not performed but stenting of the left main artery, circumflex artery, and two lesions in the left anterior descending coronary artery with intra-aortic balloon pump support was successful. However, he developed multi-system failure and died two days later.

Myocardial infarction

Three of four patients (2.9%) who suffered a Q wave MI before hospital discharge due to stent thrombosis required revascularisation with repeat PTCA (two) or CABG (one). The fourth patient received thrombolysis and repeat angiography showed patent stents with good antegrade flow. No further intervention was undertaken. One patient suffered a non-Q wave MI with a peak CK of 280 units due to the loss of a small marginal branch after bailout stenting of the circumflex coronary artery.

CABG

No patient required procedural emergency CABG. A 72 year old woman with a history of CABG performed on two previous occasions was referred for surgery before hospital discharge. She had undergone multiple stenting of a right coronary artery saphenous vein graft with three stents. She suffered a Q wave MI due to stent thrombosis on the third day after the procedure and was referred for repeat CABG during the same hospital admission.

Repeat PTCA

Three patients had a repeat PTCA before hospital discharge: two had a stent thrombosis and one who had recurrent chest pain after multiple bailout stenting required an additional half stent to cover a distal dissection beyond two patent stents.

Vascular complications

Three patients suffered major peripheral vascular complications. Two underwent surgical repair of a left common femoral aneurysm following an intra-aortic balloon pump support procedure and one required a blood transfusion after bleeding from his femoral access site.

Late clinical outcome

Table 3 shows clinical outcome. The mean (SD) follow up duration was 11.9 (7.2) months. Clinical follow up was available in all 135 patients discharged from hospital who underwent multiple stenting and did not require CABG. Follow up of more than six months was available for 107 (79.3%) of 135 patients and of more than 12 months in 63 (46.7%).

Deaths

One late death (0.7%) occurred in a 78 year old man with a history of previous CABG and impaired left ventricular function. He underwent multiple stenting of a right coronary artery saphenous vein graft. There were no

<table>
<thead>
<tr>
<th>In-hospital events (n=140)</th>
<th>Hospital discharge/late follow up (n=135)</th>
<th>Total (n=140)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4 (2.9)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Any MI</td>
<td>5 (3.6)</td>
<td>3 (2.2)</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>4 (2.9)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Non-Q wave MI</td>
<td>1 (0.7)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>CABG</td>
<td>1 (0.7)</td>
<td>3 (2.3)</td>
</tr>
<tr>
<td>Repeat angioplasty</td>
<td>3 (2.1)</td>
<td>5 (3.7)</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>4 (2.9)</td>
<td>0</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>3 (2.1)</td>
<td>0</td>
</tr>
<tr>
<td>Any major cardiac event*</td>
<td>10 (7.1)</td>
<td>9 (6.7)</td>
</tr>
<tr>
<td>Event free patients</td>
<td>130 (92.9)</td>
<td>126 (93.3)</td>
</tr>
</tbody>
</table>

The results are presented as number (%).

*death, stroke, MI, CABG, or repeat angioplasty.
The Benestent and STRESS trials have shown the effectiveness of elective coronary stenting using single stents in selected de novo lesions. There are no data available from controlled clinical trials for clinical outcome after multiple coronary stenting. An increased incidence of in-hospital ischaemic complications has been reported after bailout stenting with multiple stents. In our study the in-hospital major cardiac event rate (7.1%) is similar to that previously reported in randomised trials of single stents despite over 30% of our patients receiving multiple bailout stents after failed PTCA. There was a higher in-hospital death rate (2.9%) than in the Benestent and STRESS trials. However, all the deaths occurred in patients presenting with acute MI and cardiogenic shock, conditions that are normally considered as very high risk and such patients are not represented in the randomised trials that have only reported outcome in highly selected patients. Our study represents everyday practical experience at a busy tertiary centre involving unselected, consecutive patients in whom anatomical characteristics other than a reference vessel diameter of less than 3 mm were not considered as contraindications for stenting. Multiple stenting in the presence of acute MI and cardiogenic shock was associated with a high mortality. Four of the five patients who received multiple stents in the setting of acute MI and cardiogenic shock died before hospital discharge.

The use of multiple stents has also been identified as a predictor of stent thrombosis, particularly when other risk factors are also present. The stent thrombosis rate was 2.9%, which is favourable with that reported in previous studies of single stents. A higher restenosis rate has also been reported after multiple stenting. Multiple stents may be associated with restenosis rates of up to 40% even in the high pressure era. In our study patients did not undergo routine follow up angiography and therefore we could not assess the restenosis rate. Repeat angiography was performed only on clinical grounds. The overall (procedure to late follow up) rate of repeat PTCA or CABG (7.9%), and late (after hospital discharge) repeat PTCA or CABG rate (5%) was not increased compared to the rates reported for single stents in the randomised trials. The overall major cardiac event rate (13.6%) is also similar to the Benestent (20.1%) and STRESS (19.5%) studies.

The improved outcome after multiple stenting when compared with that of other observational studies may reflect increased operator experience and improved stent deployment techniques. Intravascular ultrasonography has recently shown that high pressure balloon inflation of 18 or 20 atm is more effective in achieving ideal apposition of the stent to the vessel wall than standard pressure balloons of larger than stent size. Several studies have also suggested that patients treated with stenting do well with a reduced anticoagulation regimen that excludes intravenous dextran, oral warfarin, and prolonged heparin when high pressure balloons result in full stent appo-

### Table 4 Clinical outcome after single vessel multiple coronary stenting in 111 patients

<table>
<thead>
<tr>
<th>Event</th>
<th>In-hospital events (n=111)</th>
<th>Hospital discharge/late follow up (n=106)</th>
<th>Total (n=111)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4 (3.6)</td>
<td>1 (0.9)</td>
<td>5 (4.5)</td>
</tr>
<tr>
<td>Cerebrovascular accident</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>MI</td>
<td>4 (3.6)</td>
<td>3 (2.8)</td>
<td>7 (6.3)</td>
</tr>
<tr>
<td>CABG</td>
<td>1 (0.9)</td>
<td>3 (2.3)</td>
<td>4 (3.6)</td>
</tr>
<tr>
<td>Repeat angioplasty</td>
<td>1 (0.9)</td>
<td>5 (4.7)</td>
<td>6 (5.4)</td>
</tr>
<tr>
<td>Stent thrombosis</td>
<td>3 (2.7)</td>
<td>0</td>
<td>3 (2.7)</td>
</tr>
<tr>
<td>Vascular complications</td>
<td>3 (2.7)</td>
<td>0</td>
<td>3 (2.7)</td>
</tr>
<tr>
<td>Any major cardiac event*</td>
<td>8 (7.2)</td>
<td>10 (9.4)</td>
<td>18 (16.2)</td>
</tr>
</tbody>
</table>

The results are presented as number (%).

*death, stroke, MI, CABG, or repeat angioplasty.

complications and he was discharged well from the hospital. However, he died following an anterior Q wave MI three months later.

**Myocardial infarction**

One patient had a Q wave MI on late follow up (see earlier). Two patients suffered a non-Q wave MI at four and six months, respectively. Repeat coronary angiography showed patent stents.

**CABG**

Three patients (2.2%) required CABG after hospital discharge. There was progression of native coronary artery disease in two. One patient underwent repeat PTCA of the stented vessel for restenosis. Restenosis recurred, however, and he was referred for CABG.

**Repeat PTCA**

Repeat angiography was performed in 17 patients (12.6%) after hospital discharge for recurrence of symptoms and five (3.7%) underwent a repeat PTCA for in-stent restenosis.

Eighty three patients (61.5%) were asymptomatic at follow up and 124 (91.9%) of 135 patients were classified as Canadian Cardiovacular Society angina class II. One hundred and twenty one (86.4%) of 140 patients were free from major clinical events. There was no significant difference in procedural, late, or overall clinical outcome in patients undergoing elective versus bailout stenting.

Table 4 shows the clinical outcome in 111 patients who underwent multiple stent implantation in a single coronary artery. There was no significant difference in clinical outcome in this group compared with outcome in the overall group (140 patients).

**Discussion**

This study shows that multiple coronary stenting can be performed with a high procedural success rate and good long term clinical outcome. It is not associated with an increased rate of stent thrombosis or late major clinical adverse events as compared to those reported previously with single stents. This favourable clinical outcome occurred despite the fact that most patients presented with unstable coronary syndromes and a high proportion underwent stent implantation as a bailout procedure for failed PTCA, conditions which are traditionally considered as high risks for coronary intervention and stent implantation.

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Multiple coronary stenting

Antiplaetlet treatment with aspirin and ticlopidine as compared to anticoagulation treatment with heparin, phenprocoumon, and aspirin is associated with a significant risk reduction in risk for MI, a reduced need for repeat intervention, decreased peripheral vascular events, and a reduction in occlusion of the stented vessel. High pressure stent deployment was undertaken in 99% of the stents implanted in our study. Most patients (94%) were treated with antiplatelet treatment alone after stent implantation despite the use of multiple stents under bailout conditions in over 50%. The low rates of stent thrombosis and vascular complications lend further support to the practice of high pressure stent deployment and reduced anticoagulation with antiplatelet treatment alone.

Our report represents a single centre observational study with no randomised comparison. The study reports early and intermediate term outcome after multiple coronary stenting. Only 12.9% of patients who underwent multiple stent implantation had stable angina. There was no significant difference in outcome between these patients and those with unstable angina. There was also no significant difference between patients who received multiple stents in a single coronary artery and those who received single stents in multiple coronary arteries or the overall outcome in the 140 patients. The numbers, however, are too small to make meaningful subgroup comparisons. This deserves further study and replication of these results is needed before clear conclusions can be drawn.

The use of abciximab in patients with an increased risk of PTCA significantly reduces ischaemic events immediately after PTCA and during the six month follow up period and is associated with a significant reduction in repeat revascularisation. This has prompted the hypothesis that combined use of a stent and abciximab will reduce further the restenosis rate and improve long term clinical outcome. This is being studied in the Epilog stent study and if benefit is confirmed then abciximab may further improve clinical outcome after multiple stenting.

We conclude that in an era of increased operator experience, high pressure stent dilatation, and reduced anticoagulation with antiplatelet treatment alone, multiple coronary stenting may be performed with a high procedural success rate and good long term outcome. Multiple stenting in the presence of acute MI and cardiogenic shock, however, is associated with a high in-hospital mortality.

References

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