Catheterization and Cardiovascular Diagnosis 37:355–359 (1996)

Original Studies

Elective Implantation of Intracoronary Stents Without Intravascular Ultrasound Guidance or Subsequent Warfarin

Mullasari Ajit Sankardas, MD, Paul Timothy McEniery, MBBS, FSCAI, Constantine Nicholas Aroney, MD, and John Hugh Nicholas Bett, MBBS

Two hundred forty-three stents (203 Palmaz-Schatz, 40 Gianturco-Roubin) were electively implanted in 188 lesions in 168 patients (mean age 58 ± 10 years, 77% males) using angiographic but not ultrasound guidance. Patients were treated subsequently with aspirin and observed in hospital for up to 7 days. Those with acute myocardial infarction, radiolucent defects in coronary arteries suggestive of thrombus, and results that were not optimal after stent implantation were anticoagulated with warfarin and not included in the study.

Two had subacute stent thrombosis and two patients non-Q-wave myocardial infarction in-hospital. At follow-up (median 149 days) none had had subacute stent thrombosis, one suffered non-Q-wave myocardial infarction, none had died, and none had developed major complications at the vascular access site. Fourteen (8%) had undergone further revascularisation procedures.

This initial experience suggests that aspirin is sufficient to prevent subacute stent thrombosis after elective high pressure assisted coronary stent implantation without intravascular ultrasound guidance if the angiographic appearance after stent deployment is optimal.

Key words: stents, intravascular ultrasound, aspirin

INTRODUCTION

The use of balloon-expandable intracoronary stents has been shown to reduce restenosis that otherwise occurs in about 30–50% of patients after percutaneous transluminal coronary angioplasty (PTCA) [1–3]. The authors of STRESS [4] concluded that placement of intracoronary stents results in a higher procedural success rate and less angiographic restenosis and need for revascularisation of the index lesion within 6 months. The BENESTENT study [5] also showed that clinical and angiographic results were improved 7 months after elective stent implantation, but that these were obtained at the cost of a significantly higher risk of vascular complications at the access site and a longer period in-hospital. These were a consequence of prolonged anticoagulation with warfarin given to reduce the incidence of subacute thrombosis.

Intravascular ultrasound (IVUS) guidance has been used to optimise stent expansion [6–10] and has been shown to permit the deployment of stents without subsequent anticoagulation [11]. Nevertheless, the value of IVUS is limited by its cost [12]. When an optimal angiographic appearance is achieved after high-pressure assisted intracoronary stent implantation without IVUS guidance subsequent antiplatelet therapy with ticlopidine and aspirin [13–15] and dextran [16,17] or heparin [18] has been found to be safe.

We describe our initial experience with aspirin therapy after elective intracoronary stent implantation without IVUS guidance.

From the Department of Cardiology, Prince Charles Hospital, Queensland, Australia.

Received March 28, 1995; revision accepted September 19, 1995.

Address reprint requests to Dr. Paul T. McEniery, Department of Cardiology, Prince Charles Hospital, Rode Road, Chermside, Queensland 4032, Australia.

METHODS

We report the results of elective stent deployment in 188 lesions in 168 patients between August 1995 and June 1995. All had symptomatic coronary artery disease, and stents were implanted to limit restenosis. They had lesions greater than 70% in arteries at least 2.5 mm in diameter. Informed written consent was obtained prior to the procedure.

Angiograms were performed on a Philips DCI biplane system or Siemens Hicor single-plane digital system. Intracoronary nitroglycerin or sublingual isosorbide dinitrate was given before all baseline angiograms and intracoronary nitroglycerin before final angiograms. The position of the tube gantry was similar at baseline and final angiograms, and the lesions were evaluated in the single worst view. Measurements of minimal luminal diameter and reference vessel diameter followed by calculation of percentage diameter stenosis were performed with a hand-held calliper technique, using the contrast-filled 8 French guiding catheter as the calibration object. The angiographic measurements were performed by one investigator (MAS) who was not blinded. Lesion calcification was defined as radiodensities noted with fluoroscopy within the vessel wall at the site of the target lesion [19]. Lesions were classified according to the American College of Cardiology [20], and length was defined as the length of the segment of the lesion with encroachment of 50% or more of the lumen. Dissection was defined as a linear intralumunal filling defect, extraluminal opacity, or spiral dissection. No attempt was made to classify the types of dissection [21].

Patients were treated with aspirin 300 mg bid for at least 48 hr before the procedure. After placement of the femoral arterial sheath, a bolus of 10,000–15,000 units of heparin was given to maintain the activated clotting time (ACT) at 350–400 sec. Dipyridamole or dextran were not used before the procedure. The lesion was crossed primarily with a 0.014- or 0.018-inch Extra Support (Advanced Catheter Systems, Santa Clara, CA) wire and predilated at low pressure (<6 atm) with a noncompliant or semicompliant balloon equal in diameter to the reference vessel, which was then used for high-pressure dilation (12–20 atm) after the stent was implanted. Both Palmaz-Schatz (Johnson and Johnson Interventional Systems Warren NJ) and Gianturco-Roubin (Cook, Bloomington, IN) stents were used. The type and number of stents selected depended on the length and site of the lesion and the presence of major side branches. Gianturco-Roubin stents were preferred for lesions longer than 15 mm but less than 20 mm, for lesions at a bend and when major side branches arose at the lesion. A 5 French sheath delivery system was used for Palmaz-Schatz stents. Heparin was ceased immediately after the procedure and sheaths were removed when the ACT was less than 165 sec.

TABLE I. Clinical Characteristics of Patients (n = 168)

	%
Risk factors	
Hyperlipidæmia	32
History of smoking	43
Hypertension	15
Diabetes	11
Past history	
Myocardial infarction	28
Coronary artery surgery	12
PTCA	33
Presentation	
Stable angina	60
Unstable angina	40

All patients included in this study had nearly optimal results after stent placement, i.e., no residual stenosis, no dissection proximal or distal to the stent, no haziness or flap within the stent, adequate coverage of the entire lesion with one or more stents, and the lumen at the site of implantation exceeding that of the distal vessel. Those in whom stents were deployed for acute or threatened occlusion after PTCA, those in whom the post-stent angiogram was not optimal, including those with radiolucent defects suggestive of intracoronary thrombus, and those who had presented with acute myocardial infarction were anticoagulated with heparin and warfarin and were not included in the study.

Those included in the study were given aspirin (300 mg bid) and observed in-hospital for up to 7 days. Twelve patients were also given ticlopidine for 1 month. They had electrocardiograms and estimations of CKMB performed immediately and successively for 24 hr after the procedure. After discharge, all were followed for the occurrence of death, myocardial infarction, and the need for further revascularisation with PTCA or surgery.

Statistical Methods

Survival plots and box-and-whisker plots were generated with S-PLUS (S-PLUS for Windows 1994 MathSoft).

RESULTS

Patients

One hundred sixty-eight patients (77% male, mean age 58 ± 10 years) had stents implanted electively without IVUS guidance or subsequent warfarin (Table I).

TABLE II. Lesion Characteristics (n = 188)

	%
Vessel	
Native	94
Left anterior descending	50
Left circumflex	12
Right coronary	38
Saphenous vein graft	6
Site	
Proximal	44
Mid	46
Distal	8
ACC/AHA type [20]	
A	26
B_1	44
B_2	22
C	6
Calcification	7
Total occlusions	5
Restenotic lesions	5

TABLE III. Quantitative Coronary Angiography Results (n = 188)

	Baseline	Final
Reference vessel diameter (mm)	3.4 ± 0.8	3.4 ± 0.7
Diameter stenosis (%)	84.4 ± 10.5	4.6 ± 6.9
Minimal luminal diameter (mm)	0.5 ± 0.4	3.2 ± 0.8
Acute gain (mm)		2.7 ± 0.7
Lesion length (mm)	9.2 ± 7.7	
Final balloon (mm)		3.4 ± 0.5
Balloon/vessel ratio		1.0 ± 0.1

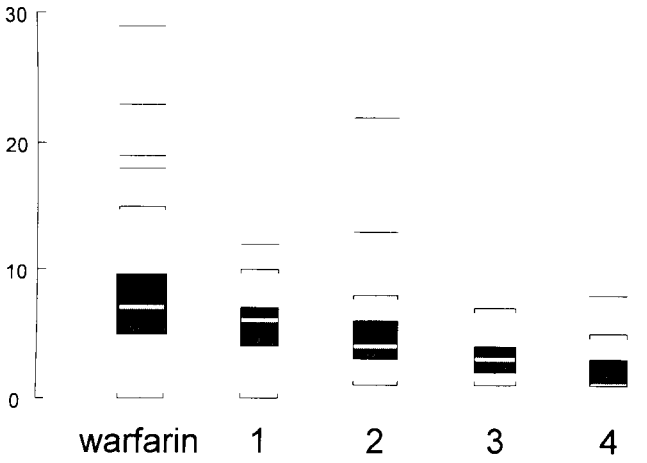

Fig. 1. Box-and-whisker plots of time spent in-hospital (days on *y*-axis) after stent implantation by (1) patients treated with warfarin (median 7 days) compared with those given only aspirin, (1) within the first 90 days of our experience (median 6 days), (2) between 90 and 180 days (median 4 days), (3) between 180 and 240 days (median 3 days), and (4) our most recent experience, after 240 days (median 1 day).

Lesions

One hundred eighty-eight lesions were treated with stents (Table II).

Stents

Two hundred forty-three stents (202 Palmaz-Schatz, 2 × 1/2 Palmaz-Schatz, and 40 Gianturco-Roubin) were deployed. One hundred forty-seven lesions were treated with single stents. The peak inflation pressure for high-pressure balloon dilation within the stent was 15.6 ± 1.9 atm (range 12–20 atm), and the inflation time was 115 ± 42 sec. The quantitative angiographic measurements are described in Table III. Although the reference vessel diameter of the vessels in which stents were implanted was 3.4 ± 0.8 mm, it was less than 3 mm for 18 (10%) of the lesions.

Outcome In-hospital

There were no deaths, and no patient had emergency coronary artery bypass surgery. Two (1%) had non-Q-wave myocardial infarction, with CKMB values exceeding twice the upper limit of the normal range and two (1%) subacute stent occlusions (days 5 and 8). Thus, the procedural success rate was 98%. Five (3%) developed haematomas at the vascular access site, but none required surgery or transfusion. The period spent in hospital after the procedure was reduced progressively as our experience grew (Fig. 1).

Outcome After Discharge From Hospital

Follow-up was carried out by telephone in all patients (median 149 days). None died, one had myocardial infarction at 78 days after PTCA, 13 (8%) required further PTCA, and two underwent bypass surgery, one of whom had had a second PTCA; thus, in all, 14 patients had further revascularisation procedures (Fig. 2).

Patients Given Warfarin

During the period these patients were treated, another 60 in whom stents were deployed were given warfarin because (1) they had presented with acute myocardial infarction, (2) stents were implanted for acute or threatened occlusion, or (3) the results were not acceptable. Gianturco-Roubin stents were used in 29 cases. In this group, sequelae included groin hæmatomas in five (8%), subacute occlusion in four (7%), Q-wave infarction in two, non-Q infarction in two, and further revascularisation in four (7%). They remained in hospital for longer than those treated without warfarin (Fig. 1).

DISCUSSION

Intracoronary stents are being used increasingly to prevent restenosis despite a subacute thrombosis rate of

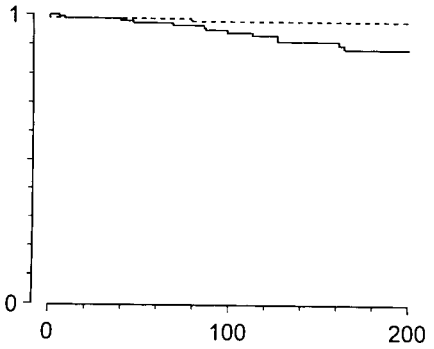

Fig. 2. Kaplan–Meier plots of freedom from revascularisation (continuous line) and from myocardial infarction (broken-line *y*-axis) during first 200 days.

4–5% [22,23] after elective use, while "bail-out" implantation is associated with an incidence of 10–30% [24–26]. Other factors which predict this complication include unstable angina, long and complex (Type C [20]) lesions with large plaques, incomplete cover of a dissection, irregularities of the vessel beyond the segment in which a stent has been implanted [27], and arteries less than 3 mm in diameter [28]. Meticulous anticoagulation with intravenous heparin and overlapping warfarin and aspirin has not reduced this risk significantly [25]. It occurs typically within 2–14 (mean 6) days [4] and may result in Q-wave myocardial infarction or death [4,27].

Anticoagulation has also been associated with a high incidence of vascular complications at the access site. In the BENESTENT study [5], this was 13.5% in those who received stents but only 3.1% in those treated with PTCA alone.

Imaging with IVUS has been used to achieve better expansion of stents and a greater acute gain [6–11,29]. No subacute thrombosis was reported in a series when this was followed by the use of ticlopidine and/or aspirin alone [30]. IVUS, however, is costly [12]. A trial conducted in 21 French institutions [31] reported an incidence of subacute thrombosis of only 1.5% using low-molecular-weight heparin (0.1 ml/10 kg bid) with aspirin 100 mg daily for 2 weeks and 250 mg of ticlopidine for 1 month. Another study [16] reported no subacute stent thrombosis using only aspirin and ticlopidine if the angiographic results were optimal after high-pressure stent implantation (without IVUS guidance).

The group in Milan [6–13,30] proposed that high-pressure balloon inflation of intracoronary stents provides a larger vessel lumen and better application of the stent to the vessel wall. We believe that the use of this technique is more important than the choice of antiplatelet agents or the use of anticoagulants and that greater luminal gain might also reduce the restenosis rate. Indeed, aspirin alone appears to provide sufficient protection against subacute occlusion. Avoiding anticoagulants will reduce time in hospital, the risk of local vascular complications, and perhaps the effects of "paradoxical thrombosis" [32].

The use of ticlopidine is associated with more side effects than aspirin [33], including serious neutropenia, diarrhea, and skin rashes [34]. We therefore chose to use aspirin alone in almost all our patients, who were carefully selected for an optimal angiographic appearance after stents were deployed electively, but in whom IVUS guidance was not used. Our results, although preliminary, tend to confirm that this strategy is safe and cheaper than the standard anticoagulant regimen.

Limitations

Although those treated with anticoagulants during the period of the study suffered more frequent complications they cannot be regarded as a comparable group, as they were given warfarin because the results of intervention were judged to be less satisfactory. In short, this was a nonrandomised study of carefully chosen patients in whom the results of elective stent implantation were optimal. To determine whether this protocol could be extended to others or which "high-risk" patients need anticoagulation would require randomised trials.

CONCLUSIONS

Elective intracoronary stent implantation can be performed without IVUS guidance and, when optimal angiographic results are obtained, aspirin appears to be sufficient prevent subacute stent thrombosis.

ACKNOWLEDGMENTS

We thank Desley Dent for her secretarial assistance and Margaret Dahl and Monica Higgins for their help in patient follow-up.

REFERENCES

1. Holmes DR Jr, Vlietstra RE, Smith HC, et al: Restenosis after percutaneous transluminal coronary angioplasty (PTCA): A report from the PTCA Registry of the National Heart, Lung and Blood Institute. Am J Cardiol 53:77C–81C, 1984.
2. Grüntzig AR, King SB III, Schlumpf M, Seingenthaler W: Long-term follow-up after percutaneous transluminal coronary angioplasty: The early Zurich experience. N Engl J Med 316:1127–32, 1987.
3. Nobuyoshi M, Kimura T, Nosaka H, et al: Restenosis after successful percutaneous coronary angioplasty: Serial angiographic follow-up of 229 patients. J Am Coll Cardiol 12:616–623, 1988.
4. Fischman DL, Leon MB, Baim DS, et al: for the Stent Restenosis Study Investigators. A randomised comparison of coronary stent placement and balloon angioplasty in the treatment of coronary artery disease. N Engl J Med 331:496–501, 1994.

5. Serruys PW, de Jaegere P, Kiemeneij F, et al, for the BENESTENT Study Group: A comparison of balloon expandable stent implantation with balloon angioplasty in patients with coronary artery disease. N Engl J Med 331:489–495, 1994.
6. Goldberg SL, Colombo A, Nakamura S, Alamgor Y, Maiello L, Tobis JM: Benefit of intracoronary ultrasound in the deployment of Palmaz-Schatz stents. J Am Coll Cardiol 24:996–1003, 1994.
7. Colombo A, Nakamura S, Hall P, et al: A prospective study of Gianturco-Roubin coronary stent implantation without anticoagulation. J Am Coll Cardiol 25:50A, 1995.
8. Blasani R, Mudra H, Schülen H, et al: Intravascular ultrasound guided optimized emergency coronary Palmaz-Schatz stent placement without post procedural systemic anticoagulation. J Am Coll Cardiol 25:197A, 1995.
9. Russo RJ, Schatz RA, Sklar M, et al: Ultrasound guided coronary stent implantation without prolonged systemic anticoagulation. J Am Coll Cardiol 25:50A, 1995.
10. Colombo A, Nakamura S, Hall P, et al: A prospective study of Wiktor coronary stent implantation without anticoagulation. J Am Coll Cardiol 25:239A, 1995.
11. Colombo A, Hall P, Nakamura S, et al: Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. Circulation 91:1676–1688, 1995.
12. Biengino S, Nakamura S, Hall P, et al: A cost analysis of intravascular ultrasound guided coronary stenting without anticoagulation vs. the traditional method of stenting with anticoagulation. J Am Coll Cardiol 25:197A, 1995.
13. Gaglione A, Tiecco F, Maeillo L, Nakamura S, Martini G, Colombo A: High pressure assisted intracoronary stent implantation without subsequent anticoagulation. Circulation 90:I-622, 1994.
14. Schülen H, Blasani R, Mudra H, et al: Stenting for progressive dissection during PTCA: Clinical, angiographic and intravascular ultrasound criteria to define a low-risk group not requiring subsequent anticoagulation. J Am Coll Cardiol 25:123A, 1995.
15. Barragan P, Silvestri M, Sainsous J, et al: Prevention of subacute occlusion after coronary stenting with ticlopidine regimen without intravascular ultrasound guided stenting. J Am Coll Cardiol 25: 182A, 1995.
16. Lablanche J-M, Grollier G, Danchin N, et al: Full antiplatelet therapy without anticoagulation after coronary stenting. J Am Coll Cardiol 25:181A, 1995.
17. Van Belle E, McFadden EP, Bauters C, et al: Combined antiplatelet therapy without anticoagulation: An effective alternative to prevent subacute thrombosis after coronary stenting? A 3 month follow-up. J Am Coll Cardiol 25:197A, 1995.
18. Fajadet J, Jordan C, Carvalho H, et al: Percutaneous trans radial coronary stenting without coumadin can reduce vascular access complications and hospital stay. J Am Coll Cardiol 25:182A, 1995.
19. Myler RK, Shaw RE, Stertzer SH, et al: Lesion morphology and coronary angioplasty: Current experience and analysis. J Am Coll Cardiol 19:1641–1652, 1992.
20. Guidelines for percutaneous transluminal coronary angioplasty (chairman—Ryan TJ). J Am Coll Cardiol 12:529–545, 1988.
21. Black AJR, Namay DL, Niederman AL, Lembo NJ, Roubin GS, Douglas JS Jr, King SB III: Tear or dissection after coronary angioplasty: Morphological correlates of an ischemic complication. Circulation 79:1035–1042, 1989.
22. Schatz RA, Baim DS, Leon M, et al: Clinical experience with the Palmaz-Schatz coronary stent. Circulation 83:148–161, 1991.
23. Shaknovich A, Rocha-Singh K, Tierstein P, et al: Subacute stent thrombosis in Palmaz-Schatz stents in native coronary arteries. Time course, acute management and outcome. US multicenter experience. Circulation 86:I-442, 1992.
24. Hermann HC, Hirshfield JW, Buchbinder M, et al: Emergent coronary stenting for failed percutaneous transluminal coronary angioplasty. Circulation 84:II-590, 1991.
25. Kiemeneij F, Laarman G, van der Wicken R, et al: Emergency coronary stenting with the Palmaz-Schatz stent for failed percutaneous coronary angioplasty: Results of a learning phase. Am Heart J 126:23–31, 1993.
26. Doucet S, Fajadet J, Caillard J, et al: Predictors of thrombotic occlusion following coronary Palmaz-Schatz stent implantation. Circulation 86:I-114, 1992.
27. Hande M, Erbel R, Issa H, Straub U, Rupprecht HJ, Treese N, Meyer J: Subacute thrombotic complications after intracoronary implantation of Palmaz-Schatz stents. Am Heart J 126:15–22, 1993.
28. Barragan P, Sainsous J, Silvestri M, Bouvier JL, Comet B, Siméoni JB, Charmasson C, Bremondy M: Ticlopidine and subcutaneous heparin as an alternative regimen following coronary stenting. Cathet Cardiovasc Diagn 32:133–138, 1994.
29. Mudra H, Klauss V, Blasini R, Kroetz M, Rieber J, Regar E, Theisen K: Ultrasound guidance of Palmaz-Schatz intracoronary stenting with a combined intravascular ultrasound balloon catheter. Circulation 90:1252–1261, 1994.
30. Blengino S, Maiello L, Hall P, Nakamura S, Martini G, Colombo A: Randomised trial of coronary stent implantation without anticoagulation: Aspirin vs Ticlopidine. Circulation 90:I-124, 1994.
31. Morice M-C, Bourdonnec C, Lefevre T, Blanchard D, Monassier J-P, Lienhart Y, Commeau P, Makowski S, Labrunie P, Cribier A, Joly P: Coronary stenting without Coumadin. Phase III. Circulation 90:I-125, 1994.
32. Gallerani M, Manfredini R, Morratelli S: Non-hæmorrhagic adverse reactions of oral anticoagulant therapy. Int J Cardiol 49: 1–7, 1994.
33. Hass WK, Easton JD, Adams HP, et al: A randomized trial comparing ticlopidine hydrochloride with aspirin for the prevention of stroke in high-risk patients. N Engl J Med 321:501–507, 1989.
34. Gent M, Blakely JA, Easton JD, et al: The Canadian American ticlopidine study (CATS) in thromboembolic stroke. Lancet 1:1215–1220, 1989.