'Real world' small vessel coronary artery stenting: an analysis

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Abstract

The objective of this study was to describe the context, procedural outcome and long-term results of contemporary small vessel (SV) coronary artery stenting. It was set in a tertiary cardiology centre. The study was designed as a retrospective analysis of the procedural and long-term results in a consecutive series of patients undergoing implantation of an SV stent (defined as ≤ 2.5 mm) in 1999–2000.

Of the 1,130 percutaneous coronary interventions (PCIs) in the study period, 138 (12%) involved placement of SV stents. Of these interventions 58% consisted of SV stents as sole treatment. Some 69% of patients were male and their mean age was 58 years; 46% were hypertensive, 13% diabetic, 84% hypercholesterolaemic and 18% were smokers. Of these patients 54% were in anginal classes III and IV. Of the SV stents fitted, 94% were 2.5 mm and 6% were 2.0 mm. 75% of SV stents were implanted in main epicardial vessels. The mean follow-up for these patients was 17 months. Long-term symptomatic benefit was achieved in 76%. The major adverse cardiac events (MACE) rate was 15%, comprising 1% acute myocardial infarction (AMI) and 14% re-PCI. There were no deaths.

In conclusion, SV stenting in the modern era, in an unselected series of patients, is performed in 12% of PCI procedures. It comprises the sole treatment in 58% of these interventions. The majority of SV stents are 2.5 mm and are placed in main coronary arteries. Procedural and long-term results are excellent. These data may inform the choice of treatment for patients with SV disease and may be useful in planning studies in stenting SVs.

Key words: small vessel, coronary artery, stent.

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Introduction

The use of stents for the treatment of stenoses in small vessel (SV) coronary arteries remains controversial because the published data reveal disparate results. Early stent versus balloon studies included only 10–13% vessels ≤ 2.50 mm.[1,2] Subgroup analysis showed that the restenosis rate for SVs was acceptable, although the numbers were small: in the STRESS (Stent Restenosis Study) study, for vessels < 2.50 mm the restenosis rate was 30% and for vessels ≥ 3 mm it was 31.6%.[3] However, this result may be flawed by the small numbers in the SV category and by the fact that this was not a SV study – the operators labelled the vessel as within the inclusion criteria of STRESS but quantitative angiography labelled the vessel as small (the operators may have been right).

Akiyama *et al.*, in a cohort of 1,298 patients, reported restenosis rates of 19.9% in vessels ≥ 3 mm and 32.6% in vessels < 3 mm (p=0.0001).[4] Kastrati *et al.*, using univariate analysis of 1,753 lesions, found that a reference diameter < 3.08 mm conferred a relative risk of restenosis of 1.5 compared with larger vessels.[5] A recent study by Koning *et al.* prospectively randomised stent placement and POBA (plain old balloon angioplasty) in vessels ≤ 3 mm. Angiographic restenosis was 21% in the stent group, compared with 47% in the POBA group (p=0.0001).[6]

The production of second and third generation pre-mounted stents has stimulated a re-evaluation of the efficacy of SV stenting. There have been at least eight randomised trials of SV stents versus balloon angioplasty.[1,2,6-13] The emerging message from these trials, overall, is that stenting is worthwhile in terms of acute and long-term results. There have also been at least six non-controlled series or registries.[14-19] Interestingly, in the SOPHOS study (Study of Phosphorylcholine coating On Stents), using the Bio*divYsio* stent

Table 1. Implantation sites of SV and non-SV stents

Vessel	SV stent group n=138 (%)	Non-SV stent group n=992 (%)
LAD	60 (44)	45 (46)
Circumflex	25 (18)	188 (19)
OM	11 (8)	99 (10)
Diagonal	15 (11)	109 (11)
RCA	18 (13)	99 (10)
PDA	6 (4)	30 (3)
Vein graft/LIMA	3 (2)	10 (1)

Key: SV = small vessel; LAD = left anterior descending; OM = obtuse marginal; RCA = right coronary artery; PDA = posterior descending artery; LIMA = left internal mammary artery.

Table 2. Characteristics of the lesions implanted with an SV stent (n=138)

Lesion characteristic	n (%)
Eccentric	72 (48)
Smooth	110 (74)
Bifurcated	27 (18)
Calcified	22 (15)
Occluded	21 (14)
Ostial	19 (13)
Angulated	14 (9)
Thrombotic	2 (1)
Accessible	139 (93)

(Biocompatibles), the restenosis rate was 17.7% overall and in vessels with reference diameter 1.25–2.64 mm it was only 20%.[19] These results are comparable to those of STRESS quoted above, in that the inclusion reference diameter for the study was > 3.0 mm. They suggest that modern stents perform better than the first generation in the context of SVs.

Despite this conflicting body of data, the recent trend towards stent implantation has extended to SVs. In the light of this, we decided to analyse current clinical practice and outcomes in stenting, in an unselected population of patients, in a single, tertiary interventional centre with multiple operators.

Methods

We retrospectively analysed all consecutive patients undergoing percutaneous coronary intervention (PCI) which included an SV stent (defined as $\leq$ 2.5 mm balloon deployment with no upsizing) at the Northern General Hospital, Sheffield, in the period July 1999 to October 2000. The catheter laboratory and hospital records were examined for procedural data and in-hospital events. Follow-up was by questionnaire and telephone. Baseline demographic, clinical and angiographic data were collected. Local ethics committee approval was obtained.

Percutaneous intervention

PCI was carried out using standard techniques. Procedural events, vessels treated and stent sizes and numbers were recorded. Success was defined as a patent artery with TIMI 3 flow. All angiograms were reviewed by one operator (JG). Standard antiplatelet treatment for our institution was used (aspirin and a loading dose of clopidogrel followed by two weeks' clopidogrel at a maintenance dose and indefinite aspirin). Intravenous heparin was used during the procedure to keep the activated coagulation time above 250 seconds and abciximab was used in selected unstable patients.

End points

The end points of the study were major adverse cardiac events (MACE), that is, death, non-fatal myocardial infarction (MI), coronary artery bypass graft (CABG) and target lesion or vessel revascularisation at long-term follow-up. MI was defined as a new presentation with chest pain with either typical electrocardiographic findings or serum creatinine kinase level more than twice the upper limit of normal. Enzymes were not routinely measured, so small subclinical infarcts may have been missed. Symptomatic status at follow-up was also measured using a simple index of asking the patients if they were worse, the same or better than before the procedure.

Statistics

Results are presented as mean (SD) or as percentage of the total unless otherwise stated. Comparisons between the SV group (one or more stents $\leq$ 2.5 mm in diameter) and the non-SV group (no stent $\leq$ 2.5 mm in diameter) were made with unpaired Student's t tests. Significance was sought at the 5% level.

Results

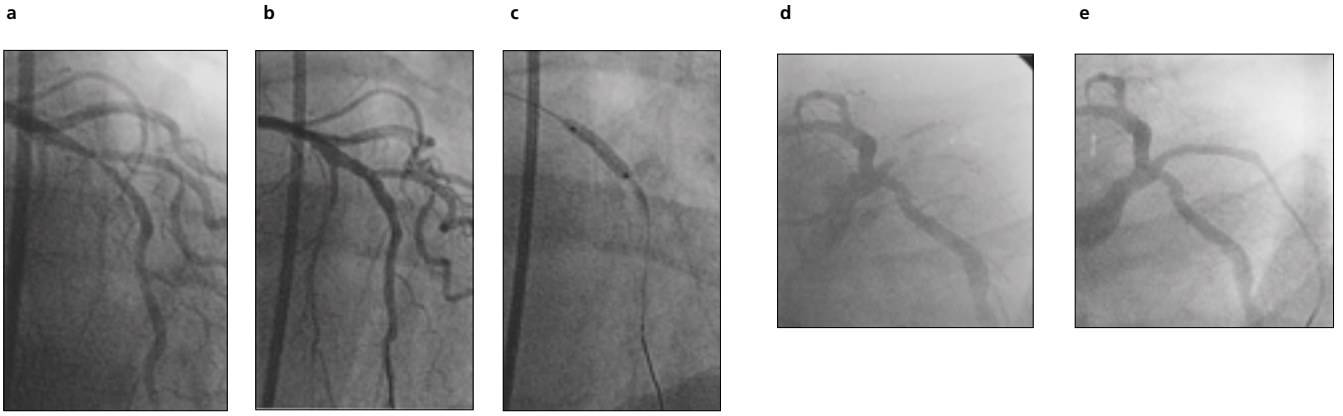
Patients

Of the 1,130 PCIs in the study period, 138 (12%) included placement of an SV stent and these patients made up the study group. Baseline characteristics of the 138 were: 95 male (69%); age 58 $\pm$ 9.6 years; 63 hypertensive (46%); 18 diabetic (13%); 116 hypercholesterolaemic (84%); 25 smokers (18%); and four with documented cerebrovascular disease (3%). Anginal class, according to the Canadian Cardiovascular Society classification, was as follows: class 0, n=4 (3%); class 1, n=7 (5%); class 2, n=48 (35%); class 3, n= 51 (37%); class 4, n=24 (17%); and acute myocardial infarction (AMI), n=4 (3%).

Vessels, lesions and stents

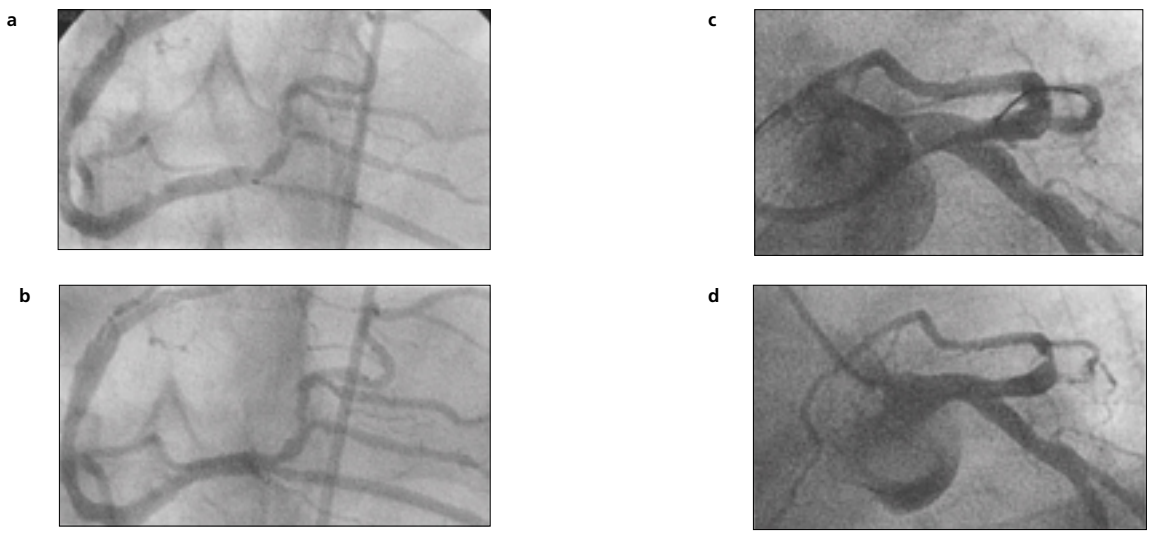
In the 138 patients studied, 80 (58%) of the procedures consisted of SV stenting alone. The remaining 42% comprised an SV stent with a larger stent or POBA in either the same vessel or another one. Some 94% of SV stents were deployed with 2.5 mm balloons and 6% with 2.0 mm balloons. Almost all the lesions (137) were new, and one was a site of restenosis. Of the lesions 131 (95%) were stented electively and seven (5%) were stented as bailout. Ten (7%) of the SV lesions were direct stented.

Figure 1. Examples of SV stents being the sole treatment in a main coronary artery. **a**) Baseline appearance of the LAD of a 78-year-old woman. **b**) Implantation of a 2.5 x 12 mm S660 stent (Medtronic). **c**) Final result. **d**) Baseline appearance of the ramus intermedius of a 64-year-old man. **e**) Final result after implantation of a 2.5 x 25 mm Coroflex stent (B-Braun)



Key: SV = small vessel; LAD = left anterior descending

Figure 2. Examples of SV stents being used as adjunct treatment with standard-sized stents. **a**) Baseline appearance of a dominant RCA in a 63-year-old man after implantation of a 4.0 x 11 Bio*divYsio* stent (Biocompatibles) at the culprit lesion at the crux. **b**) Final result after implantation of a 2.5 x 18 mm Bio*divYsio* stent in the PDA. **c**) Baseline appearance in the LAO caudal view of the LAD and diagonal arteries of a 62-year-old woman. **d**) Final result after implantation of a 3.5 x 13 mm Helistent (Hexacath) in the LAD and a 2.5 x 22 Helistent in the diagonal



Key: SV = small vessel; RCA = right coronary artery; PDA = posterior descending artery; LAD = left anterior descending

The stents used were: Bio*divYsio* (Biocompatibles), n=119 (70%); S660 (Medtronic AVE), n=21 (12%); Coroflex (B-Braun), n=12 (7%); NIR (Boston), n=3 (2%); Seaquence (Nycomed), n=3 (2%); and others, n=12 (7%). Of the non-SV stents inserted, n=531 (54%) were 3.0 mm, n=388 (39%) 3.5 mm, and n=73 (7%) $\geq$ 4.0 mm. Table 1 shows the vessels treated in the SV group. (Data from the non-SV group are presented for comparison.) Table 2 shows the characteristics of the lesions treated with SV stenting.

The number of stents deployed per patient was 1.5 (0.6) in the SV group and 1.3 (0.6) in the non-SV group (p=0.006). The length of the SV stents was 10.2 (8.0) mm and maximum deployment pressure was 11.0 (2.6) atm. Of the 138 patients, angiograms were available for review in 130. In these patients, a total of 149 stents were inserted. Examples of SV stent insertion and the results achieved are shown in figures 1 and 2.

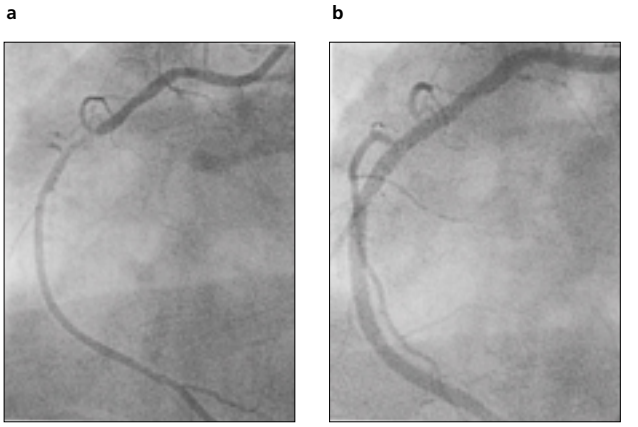
Procedural events

Of the 138 patients, angiographic success was achieved in 100%. Two procedures (1%) were complicated by acute thrombus formation. In the first case, in a 49-year-old man, thrombus was noted distal to the stent at the end of the procedure. Abciximab was used; the patient made an uneventful recovery without MI and did not require target vessel revascularisation (TVR). The second case was a 51-year-old man with unstable angina who underwent emergency PCI. Four stents were deployed in the right coronary artery (3.0 x 18 mm, 3.0 x 9 mm, 3.0 x 11 mm, and 2.5 x 9 mm). During the procedure, he had chest pain and inferior ST segment elevation on the ECG. Angiography showed thrombotic occlusion of the 3.0 x 18 mm stent, which was resistant to recanalisation. Abciximab was not given because the patient was transferred for emergency CABG, which was successful.

In-hospital events

There were no cases of in-hospital death or significant access site bleeding. There were no cases of AMI or CABG other than the two mentioned above.

Figure 3. Example of an apparent SV in a 37-year-old man. **a**) A medium-sized vessel after pre-dilatation, injection of intracoronary nitrate and implantation of a 3.0 x 15 mm Teneo stent (Biotronik) **b**) Contrast this appearance with that of a truly SV in figure 1.2



Long-term follow-up

Follow-up was 17 (6) months. Symptomatic benefit was achieved in 82% after the procedure but this proportion fell to 76% at long-term follow-up. The six-month MACE rate was 15%, comprising 1% (n=2) AMI and 14% (n=20) re-PCI. By 17 months, the MACE rate remained at 15%; no extra events had occurred.

The first case of AMI was a 66-year-old woman who presented to another hospital three weeks after SV stenting (she had had a 2.5 mm stent to the left anterior descending artery), with sudden onset of chest pain, an old anterior infarct on the ECG and a creatinine kinase of 875 IU/L. The ECG abnormalities had been present at the time of stenting. She was treated conservatively. The second patient was a 64-year-old man who underwent successful SV stenting to the left anterior descending artery (with a 2.5 mm stent). Three weeks later he presented with an acute anterior MI and underwent successful repeat PCI to the same vessel. Three weeks later he presented with another anterior infarct and was treated conservatively. He had recently been diagnosed with chronic lymphatic leukaemia.

Of the 20 (14%) SV patients who underwent repeat PCI, 14 involved revascularisation of the SV stent only, four revascularisation of the SV stent and a non-SV stent and two revascularisation of a different vessel. Of the repeat PCI patients, two were diabetic. Five of those patients who required repeat PCI to the small vessel had received two or more SV stents in the lesion during the original procedure.

Discussion

This study reflects small vessel stenting in the 'real world', because the patients comprised a consecutive series with no exclusion or bias, and the procedures were performed by eight operators in the same institution. The main findings were that 12% of all PCIs involve the stenting of what the operator considers to be a SV. In 58% of these, the SV is the only target vessel. In this series, 20% of patients were unstable and 13% were diabetic. Symptomatic benefit was achieved in 82% but this proportion had fallen to 76% at long-term follow-up. The long-term MACE rate was 15%.

In our study 75% of lesions were in the left anterior descending, circumflex or right coronary artery. The remaining 25% of lesions were in significant branches (diagonal, marginal or posterior descending arteries). The distribution of lesions between these vessels was almost identical in the SV group compared with the non-SV group. This suggests that most SV lesions are being considered for PCI using the same criteria as non-SV lesions, and only a minority are part of a multivessel procedure in which SV stenting is an 'adjunct' treatment of small branches.

Most operators would, in the light of our data and those from the trials,[1,2,6-13] be prepared to stent 2.5 mm SVs. Very small arteries ($\leq$ 2.0 mm) might remain controversial, though in our study, 6% of SV stents were 2.0 mm (all Bio*divYsios*) and their MACE rate was 0%. The stenting of very small vessels such as these may be a promising therapy for the future. On the other hand, it could be argued that very small vessels are not important in the first place, and that restenosis is not associated with symptoms. In the six patients who received a 2.0 mm stent in our series, however, all experienced an improvement in their symptoms after stenting which was maintained during follow-up; none of this small group required TVR.

De Feyter *et al.* have constructed a reference table of the risk of restenosis after stenting. This shows that restenosis is dependent upon the stent length and in-stent area on intravascular ultrasound (IVUS).[20] In so far as the in-stent area of SV stents is, by definition, smaller than for non-SV stents, the restenosis rate for SV stents is likely to be higher. It is, therefore, important to

Key messages

- Definitions of small vessels vary: we chose ≤ 2.5 mm
- 12% of PCI procedures involve small vessel stenting
- 75% of small vessel stents are placed in the three main coronary arteries (rather then small branches)
- Long-term clinical results (70% Bio*divYsio* small vessel stents) are excellent (15% MACE at a mean of 17 months)

maximise stent size in SVs whilst inflicting as little damage as possible.

The definition of what comprises an SV involves more than an arbitrary upper limit of lumen diameter of 2.5 or 2.7 mm. In this study, we defined an SV as one in which a stent ≤ 2.5 mm was implanted. 'True' SVs may comprise only some of this group (figures 1 and 2): others may be diffusely diseased larger vessels with a focal stenosis, arteries whose lumen is underfilled after a tight lesion or mildly diseased vessels prone to spasm (figure 3).

The limitations of this study include the lack of randomisation to POBA or stent, the use of different types of stent, differences in technique of the different operators, sizing 'by eye' rather than by quantitative angiography and the lack of routine angiographic follow-up. Nevertheless, this is indeed a study of the contemporary practice of SV stenting and the clinical results achieved.

Conclusion

Small vessel coronary artery stenting in the 'real world' is safe, comprises an important proportion of PCI procedures and is feasible and effective in the long term.

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