Small vessel stenting is safe, but still waiting for a well-proven antirestenotic effect

See page 1785 for the article to which this Editorial refers

Since the first intracoronary stent placement in patients in 1986, mainly for treating acute closure, coronary stenting indications have expanded remarkably. Coronary artery stents have been shown to reduce restenosis following coronary angioplasty as compared with balloon angioplasty alone in short coronary lesions of vessels >3 mm. Other trials generally demonstrated benefits of stenting over balloon angioplasty in various other conditions. Coronary stenting is now being used in many centres in patients with focal lesions in large vessels, in total occlusions, in long lesions, in saphenous vein grafts, in acute myocardial infarctions and in restenotic lesions[1]. These achievements were made possible thanks to new and better stent designs, improvements in stent implantation techniques and effective antiplatelet therapy with a low rate of stent thrombosis. However, the role of stents in other challenging situations, such as diffuse disease, small arteries, bifurcation lesions, and within heavy calcification, is less clear.

It is estimated that in 30–40% of all interventions the reference vessel diameter is less than 3 mm. Women, diabetics and patients with a small surface area usually have small coronary vessels. With ongoing worldwide experience it became clear that two of the most powerful predictors of restenosis are angiographic–geometric in nature: the arterial diameter and lesion length[2–5]. The likelihood of restenosis can almost be calculated from these two parameters alone.

Using models of restenosis based on late loss/acute gain ratio for small coronary vessels, stenting small vessels may offer some advantages in the immediate and late outcome. Although stenting in small coronary arteries remains an indication subject to controversy, it is currently performed in a significant number of procedures. In fact, even in strictly controlled clinical trials where only arteries of 3 mm and larger are allowed[4–5], the post procedural quantitative coronary angiography analysis has revealed that a substantial number of vessels treated are smaller than the 3 mm threshold. Yet, data from prospective randomized trials that specifically address the issue of clinical and angiographic benefit in small vessels are still lacking, although various clinical trials have been initiated and are currently underway.

The results of the study by Park et al[6] in this issue outline important data on this frequent problem faced by interventional cardiologists every day. In this study, 120 patients with type A and B lesions in small vessels (mean reference vessel diameter of 2.52 mm) were prospectively randomized into balloon angioplasty alone or elective stenting. The procedure was successful in all patients with no stent thrombosis; however, 12/60 (20%) patients in the balloon group were stented because of suboptimal results or major dissection. During follow-up there were no differences in clinical events. Angiographic restenosis at 6 months was similar (31·9% for balloon

References


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angioplasty vs 35.7% for stents); in the stented group the minimal lumen diameter was larger but the late loss was greater. In this randomized, small, single-centre study, no differences were seen between the two strategies. The 1998 ACC Expert Consensus\(^7\) states that stenting of small vessels ‘is safe but it does not result in improved long-term outcome compared with conventional percutaneous transluminal coronary angioplasty (PTCA), provided that dilatation gives a satisfactory initial result.’ However, stents remain useful when PTCA results are suboptimal.

The early availability of coil-type stents for bailout use in small (<2.5 mm) vessels was associated with high thrombosis and restenosis rates (in certain circumstances exceeding 50%)\(^8\). There are now several registries and non-randomized studies describing stenting in small vessel disease as feasible and safe, with a high procedural success, low subacute occlusion rate and low incidence of adverse events during follow-up. Elezi et al\(^9\) subdivided 2602 patients with successful Palmaz-Schatz stent implantation for symptomatic coronary artery disease into three equally sized groups according to vessel size. Event-free survival at 1 year was 69.5% in the group <2.8 mm, 77.5% in the 2.8–3.2 mm, and 81% in the >3.2 mm vessels (\(P<0.001\)). Late lumen loss was similar between the three groups and not unsurprisingly the angiographic restenosis rate was significantly higher in the small-vessel group (38.6%, 28.4%, and 20.4%, respectively). When stenting coronary arteries <2.8 mm diabetics and those with complex lesions were found to have a different restenosis rate than those with less complex, focal ‘de novo lesions’ (53.5% vs 29.6%). It was concluded that in the absence of such adverse characteristics, stenting may be safely performed and favourable long-term results are to be expected with a lower restenosis rate. In that report\(^9\) the Palmaz-Schatz stent, which is not designed for smaller vessels, was used. New stents are being designed to obtain an optimal radial force at a smaller diameter with a lower metal-to-vessel surface ratio, thus improving long-term results. The importance of stent shape and structure are at present under investigation.

Miketic et al.\(^10\) prospectively evaluated the safety, efficacy and 6 month angiographic follow-up patency of the NIR stent in 67 patients with complex (type ‘C’) lesions <3 mm vessel diameter. Procedural success was high, 98.2% with a subacute stent thrombosis rate of 0%. Restenosis at 6 months occurred in 21 patients (36.2%). Akiyama et al.\(^11\) had a subacute stent thrombosis of 1.5% in 602 patients in whom different types of stents were implanted in vessels <3 mm. They found an angiographic follow-up restenosis rate of 32.6%. Morice et al.\(^12\) described a procedural success rate of 98% and a subacute occlusion rate of 2.6% in a single-centre registry report on 190 patients stented with 2.5 mm balloons. Clinical follow-up showed a 24.5% repeat intervention rate.

Eeckhout et al.\(^13\) reported a stent thrombosis rate of 3% using the 2.5-mm AVE GFX stent in 120 patients with vessels <2.6 mm. After a mean follow-up of 9.8 months the event-free rate was 74%. Huang et al.\(^14\) reported that 29/40 (76%) patients whose small coronary vessels were treated with high-pressure 2.5-mm stents (mean reference vessel diameter 2.3 mm, mean lesion length 11.7 mm) either remained symptom-free or had patent target sites on repeat angiography, after a mean follow-up of 18 months. Kawagishi et al.\(^15\) reported that in 33 patients with coronary arteries <2.5 mm in diameter with suboptimal PTCA, the procedural success rate was 97.0% with a greater initial gain and larger post-procedural minimal luminal diameter than that in the size-matched elective PTCA patients. A significant reduction in target lesion revascularization (7-1% vs 41.9%) was observed in the stented patients.

Important data are revealed from subset analyses of the pivotal STRESS and BENESTENT randomized stent trials. These trials were supposed to include only short <15.0 mm and >3.0 mm arteries. However, a meta-analysis by Savage et al.\(^4\) of the STRESS study, found that 331 out of 598 patients had a reference vessel diameter of less than 3 mm by quantitative coronary angiography. One hundred and sixty-three patients were randomly assigned to stenting and 168 to angioplasty. Procedural success was 100% in patients assigned to stenting and 92% in patients assigned to angioplasty. Abrupt closure within 30 days occurred in 3.6% of patients in both groups. Patients treated with Palmaz–Schatz stents benefited from stenting with greater acute gain and net gain, resulting in less restenosis (34% vs 55%) and fewer events at 1 year, 22% vs 33% (\(P=0.019\)).

In the BENESTENT study\(^6\), stenting was found beneficial in 2.9–3.4 mm arteries, but not in <2.6 and >3.5 mm arteries. In a subanalysis of 236/404 (58%) patients with a reference vessel size <3 mm, the 12 month event rate was 30% for stents and 37% for PTCA. In this study, during stent implantation as well as balloon angioplasty, smaller coronary vessels were treated with relatively larger devices (higher device–vessel ratio) with consequent greater acute relative gain in lumen diameter. Smaller vessels subsequently sustained greater relative loss and a higher loss index. In both the stent and balloon groups this greater relative loss in lumen diameter was associated with a greater requirement for revascularization procedures during follow-up. In patients undergoing stent implantation, smaller vessel size was associated with a greater risk of procedural failure, subacute
stent thrombosis and myocardial infarction during follow-up, while in patients undergoing balloon angioplasty smaller vessel size was not associated with a significantly higher risk of bail-out stenting, procedural failure, abrupt vessel closure or myocardial infarction during follow-up. In both studies, the angiographic restenosis rate was higher than 30% and the long-term clinical outcome was less favourable than that of patients with large vessels.

At the last American College of Cardiology (ACC) meeting in March 2000, the 6-month data of three randomized studies of balloon angioplasty vs stents in small vessels were presented (Table 1). All three studies confirmed the safety of small vessel stenting with low complication and thrombosis rates. Two of the studies showed that both methods were equally beneficial; however the BESMART study conducted in France[10] using the beStent stent showed a considerable benefit in the stent group. This is the first and only randomized study designed to test small vessel stents against balloon angioplasty that showed a benefit for stents.

The results of the current study[6], supported by the published registry data, the STRESS and BENESTENT substudies and the last ACC meeting reports, show that small vessel stenting is safe with current stent technology. However, long-term effects in reducing restenosis have not yet been proven. Possible technological progress, in the shape of optimizing metal coverage for small vessels, or increasing the biocompatibility of metal by using various coating technologies are currently being evaluated. However, despite the lack of well-designed randomized studies we can count on the safety of stents in small vessels, and can adopt a provisional stenting approach with crossover to stenting only with suboptimal angiographic results. Currently, however, there are no conclusive data to support the routine use of stents for coronary arteries with a small vessel reference diameter.

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Table 1 Restenosis rate of randomized studies of balloon angioplasty versus stents in small vessels presented at the last American College of Cardiology (ACC) meeting, March 2000

<table>
<thead>
<tr>
<th>Study</th>
<th>Stent used</th>
<th>Stent area</th>
<th>Balloon arm</th>
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<tbody>
<tr>
<td>SISA[36]</td>
<td>beStent</td>
<td>28%</td>
<td>32%</td>
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<tr>
<td>ISAR-SMART*</td>
<td>Multilink</td>
<td>36%</td>
<td>38%</td>
</tr>
<tr>
<td>BESMART†</td>
<td>beStent</td>
<td>23%</td>
<td>49% (P&lt;0.05)</td>
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References