The recent advances in stent technology and implantation technique expanded indications in coronary stenting, resulting in the liberal use of stents in different patient settings. Small coronary arteries are generally defined as vessels with angiographical diameter size of less than 3.0 mm. These small vessels, when treated by balloon angioplasty (PTCA) or stents have quite distinct immediate (for PTCA) and long-term results (for PTCA and stents) than the results in vessels ≥ 3.0 mm.1–3 In this review, we will address the major features and characteristics of small vessel interventions, discussing the results of currently available studies comparing the use of different percutaneous revascularization modalities in this patient population.

Defining small vessels: Intravascular ultrasound or angiography? Even an experienced angiographer may have problems in recognizing the exact vessel size when dealing with small vessels. There is a definite discrepancy between angiographic and intravascular ultrasound (IVUS) measurement of the size of the vessel. The angiographic measurement of the vessel size can underestimate the true vessel size when compared to the IVUS evaluation. This discrepancy originates from the plaque burden in the segment close to the lesion. The diffuse disease present in the reference vessel will make this segment as small as the lesion itself. This limitation may lead to two errors:

1) The size of the reference segment is underevaluated because we measure the lumen (plaque and vessel wall) rather than vessel (diameter of the vessel without the plaque).
2) We underevaluate the severity of the index lesion because we compare the narrow segment (the lesion) to a reference segment which is also narrowed.

The use of IVUS can give information concerning the amount of plaque present and distinguish between lumen and vessel wall diameters. In addition, IVUS can also assess the immediate success of stent deployment.4

These IVUS measurements are also important to influence long-term results. In a study of Akiyama et al.,1 the balloon to artery ratio (angiographic measurement) was not predictive for restenosis, while the final cross-sectional area within the stent (IVUS measurement) was a predictor of restenosis.

The bigger the better — The smaller the worse. Previous studies in small vessels have found a lower success with balloon angioplasty compared to stents. In a study by Shunkert et al.,6 a total of 2,306 patients undergoing percutaneous coronary revascularization was divided into two groups with reference diameters of ≤ 2.5 mm (n = 813) or > 2.5 mm (n = 1,493). Success and in-hospital major adverse cardiac event rates (death, Q-wave myocardial infarction and emergency coronary artery bypass graft) between groups were compared. Success rate after angioplasty was lower in the small vessel group (92% vs. 95%; p = 0.006) and major adverse cardiac events occurred more frequently (3.4% vs. 2.0%; p = 0.03; the odds ratio for the occurrence of adverse events was 2.1; p = 0.02 for small vessels). Stents were used less in small vessels than in the large vessels (18.5% vs. 41.9%) but there was no difference in immediate success. When stents are used more liberally, the results are significantly better.

The old fear for stent thrombosis in vessels of 2.5 mm or less, which was up to 10% despite usage of ticlopidine,7 is no longer present due to better stent deployment. In our study on coronary stenting beyond standard indication,8 we compared several groups of lesions with different characteristics and we did not see any short-term difference in the results and complications following stenting large vessels versus small vessels.

The American College of Cardiology guidelines9 do not recommend vessels < 3.0 mm for stenting. We think that this position is related to the lack of proof of superior long-term results rather than to concern regarding short-term complications.
A study by Elezi et al.1 identified subgroups of patients with increased risk for restenosis with small vessels. Restenosis occurred in 53.5% of lesions in patients with diabetes and complex lesions located in small vessels compared to a restenosis rate of 29.6% in patients undergoing stenting in small vessels but without additional risk factors. Unfortunately, other treatment modalities such as surgery or rotational atherectomy are not superior to coronary stenting in this indication. Use of radiation to prevent in-stent restenosis could be advocated in small vessels with long lesions, but further data are needed. At present there is only one study (SMARTS: SMall Artery Radiation Therapy Study) in the form of a registry which will evaluate the incidence of angiographic restenosis in 180 patients with lesions shorter than 25 mm in length, located in vessels < 2.75 mm, and treated with Ir-192.

The randomized trials. A subanalysis of the STRESS study (Stent Restenosis Study), one of the first stent versus balloon randomized trial conducted by Savage suggested that stenting performed better than angioplasty (restenosis rate: 55% for angioplasty, 34% for stenting; p < 0.001) when evaluated in vessels < 3 mm in reference diameter.10

The best way to answer the question concerning the most appropriate approach (PTCA vs. stenting) for lesions located in small vessels is to conduct dedicated randomized trials. These studies11–14 have been performed and the results are summarized in Table 1. Unfortunately, the results of these trials do not permit us to draw a definite conclusion. In general, we can say that PTCA did not perform inferiorly compared to stenting, provided a strategy of 20% provisional stenting is incorporated in the angioplasty approach. On the other hand, we need to recognize that if stenting is not inferior to PTCA, stenting a lesion in a small vessel may be a safer and quicker approach compared to attempting angioplasty first. One possible concern regarding the strategy of routinely stenting all lesions located in small vessels may originate from the high rate of second recurrence of in-stent restenosis. Another more definite concern comes from the higher cost of a stenting procedure compared to PTCA with provisional stenting. In summary, we are still left with the need to find the most appropriate strategy to approach lesions located in small vessels.

Alternative approaches. One interesting, inexpensive and apparently effective approach to improve long-term results in interventions performed in small vessels is to combine angioplasty with Probucol. The administration of Probucol started 1 month prior to angioplasty and continued for 6 months has been associated with a 20% incidence of angiographic restenosis in arteries with a reference size < 3 mm, which was significantly lower than the 37.3% restenosis rate reported with placebo.15 Unfortunately this approach did not encounter much enthusiasm by interventionists due to the need to start the medication prior to the procedure and due to the unavailability of this drug on the market.

The use of the cutting balloon as an angioplasty device in small vessels was pioneered by Japanese interventionalists. In coronary vessels with reference diameter < 2.6 mm, comparison of matched lesions treated with cutting balloon or POBA revealed similar procedural success rates as well as the incidence of major complications, but significantly lower restenosis rates in the cutting balloon group (26% vs. 48%).16,17 The advantage of cutting balloon over POBA for treatment of coronary vessels smaller than 3 mm was confirmed in the randomized study CAPAS (Cutting balloon Angioplasty and Plain old balloon ANgioplasty in Small coronary arteries),18 showing the lower incidence of angiographic restenosis in the cutting balloon group (24% vs. 43%).

<table>
<thead>
<tr>
<th>Study</th>
<th>Vessel Size (mm)</th>
<th>Total Patients</th>
<th>Restenosis Rate PTCA</th>
<th>Stent</th>
<th>p</th>
<th>TVR PTCA Stent</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SISA</td>
<td>2.3–2.9</td>
<td>325</td>
<td>32%</td>
<td>28%</td>
<td>ns</td>
<td>25%</td>
<td>16.6%</td>
</tr>
<tr>
<td>BeSMART</td>
<td>3.0</td>
<td>381</td>
<td>48.8%</td>
<td>22.7%</td>
<td>0.001</td>
<td>25%</td>
<td>13%</td>
</tr>
<tr>
<td>ISAR-SMART</td>
<td>2.8</td>
<td>415</td>
<td>37.5%</td>
<td>35.7%</td>
<td>ns</td>
<td>16.5%</td>
<td>20%</td>
</tr>
</tbody>
</table>

SISA = Stenting In Small Arteries; BeSMART = Be-stent in SMall ARTeries; ISAR-SMART = Intracoronary Stenting or Angioplasty for Restenosis reduction in SMall ARTeries

Table 1. Main results of the principal and completed randomized studies of angioplasty versus stenting in small vessels.
Figure 2. (A) The baseline angiogram in the caudal left anterior projection of the first patient randomized in the SUSCI trial. This patient was randomized to a strategy of intravascular ultrasound, cutting balloon and stenting. (B) The final result following a stent implantation. Note that the use of intravascular ultrasound (IVUS) permitted up sizing of the cutting balloon to 3 mm, a diameter well above the reference angiographic size. This particular strategy should maximize lumen gain, maintaining the safety of accurate balloon sizing obtained by IVUS measurements.
An attempt to combine the three best strategies. We recently started a randomized trial in small vessels comparing stenting versus stenting preceded by cutting balloon sized according to the IVUS vessel size. In this group, IVUS is also employed to optimize final stent expansion (Figure 1). The rationale behind this approach is to take maximum advantage by combining two modalities (IVUS and cutting balloon) to optimize stent expansion. When stenting a small vessel, small problems can arise in underestimating the true vessel size, in this regard IVUS should help in optimizing stent expansion due to the large plaque burden. A large plaque can be considered the typical hallmark of a large or medium size vessel that appears angiographically as a small vessel. In this respect, the usage of a cutting balloon optimally sized with the help of IVUS should guarantee the best and most simple way to prepare the vessel for stent implantation. Figure 2 shows the first patient randomized in this study to the group with IVUS guidance and cutting balloon. With examination of the baseline angiography and IVUS, the mismatch between these two tools to measure vessel size is already evident. Unless guided by IVUS, it is unlikely that the operator would have used a 3 mm cutting balloon followed by a 3 mm high-pressure stent implantation in this vessel with an angiographic reference diameter of 2.13 mm. With this study we hope to answer the question of whether in a small vessel a larger acute gain has a favorable impact on follow-up minimal lumen diameter or if it is only a futile exercise completely nullified by a higher late loss. If the results of this study are positive, the field will still be open to recognize the independent value of the three elements (IVUS, cutting balloon, and stent) combined in this protocol.

It is impossible to conclude any discussion on small vessels without mentioning the role of stents coated with a specific antiproliferative drug. The future will tell us if this approach will become the best way to close in a few lines this lengthy chapter.

REFERENCES