Coronary Artery Stents

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The introduction and widespread use of coronary stents have been the most important advancement in the percutaneous treatment of coronary artery disease (CAD) since the initial introduction of balloon angioplasty. There have been several phases in the evolution of stent practice, some of which occurred simultaneously: (1) initial use limited by the need for multiple medications to prevent subacute thrombosis; (2) recognition that these antithrombotic regimens prolonged hospitalization, increased bleeding complications, and failed to prevent acute or subacute artery closure; (3) recognition of the importance of stent implantation for treatment of acute or threatened artery closure after balloon angioplasty; (4) documentation of decreased restenosis in narrowly defined populations; (5) a shift from anticoagulant to antiplatelet therapies; and (6) widespread use of stents for many clinical presentations and lesion types. Throughout these phases, stent technology has improved with more flexible and deliverable stents, allowing an increasing number of angiographic lesion subsets to be treated.

Scientific knowledge about stents has expanded rapidly. In 1996, the American College of Cardiology (ACC) published an evidence-based expert consensus document that included the initial 2 randomized trials using the prototype Palmaz-Schatz stent and registry experiences that led to US Food and Drug Administration approval of the first 2 stents for the treatment of discrete, de novo lesions to prevent restenosis and for treatment of acute or impending artery closure with angioplasty. By the time the ACC document was published, stents were being used in more than 50% of all percutaneous coronary artery procedures. Subsequently, stent technology and research continued to advance and by the time the second ACC consensus document was published just 2 years later, neither of the 2 stents on which the first document was based were used, having been replaced by improved stents.

Since 1996, the number of randomized clinical trials and other studies evaluating stents has increased rapidly, and stents are now used in the...
overwhelming majority of percutaneous coronary revascularization procedures. Herein we review all the studies relevant to this practice pattern.

**METHODS**

The MEDLINE database was searched for articles from 1990 through January 2000 for randomized clinical trials and observational studies for the treatment of CAD using the index terms stents, coronary artery disease, and angioplasty. Recently completed but not yet published clinical trials also were included after review by all 3 authors. Multicenter randomized trials were given more weight in recommendations than single-center observational studies. Studies were classified according to the strength of the available data into proven and unproven indications for stent use and whether presented at recent national and international cardiology conferences.

**STENT DESIGNS AND INDICATIONS**

Balloon-expandable stents are the most commonly used, although a small number of self-expanding stents are available. Stents range from 8 to 38 mm in length and from 2.5 to 4.0 mm in diameter. Stents differ in interunit connections, flexibility, radiopacity, surface area coverage, metal content, and metal composition (although the overwhelming majority are 316L stainless steel) (FIGURE). Selection of a specific stent for a specific application is rarely based on the results of any specific randomized clinical trial. Different stents have been compared with one another in 8 randomized trials using an equivalence design, and in most of these studies, stent performance has been found equivalent. Therefore, selection of a specific stent for a patient is generally made based on the operator’s experience with that stent, and lesion characteristics for which it is being used (such as ease of stent deliverability, need for side-branch access, size of the target vessel, lesion length) and the stent delivery system (eg, monorail or over-the-wire). There are 2 broad groups of indications for stent implantation. The first is treatment of acute or threatened artery closure following balloon angioplasty. Stent placement in this setting has been documented to result in decreased need for emergency surgery in multiple observational studies. The second, more common indication is elective stent implantation for optimizing the initial and longer-term revascularization result.

**LESIONS AND SITUATIONS FOR WHICH STENTING IS BENEFICIAL**

**Native Coronary Artery Lesions in Vessels ≥3 mm in Diameter**

There have been 12 randomized trials comparing stents with balloon angioplasty in more than 6300 patients (TABLE 1). Although the adjunctive therapy administered with both stents and angioplasty has changed over time, the results of these trials have been consistent: adverse cardiac events were reduced with use of stents by about 30% in the 6 months following the procedure. This reduction was mainly due to a decreased need for repeat revascularization, with a risk reduction of approximately 50%, a benefit that persists over time.

These results are not necessarily applicable to all patient and angiographic subsets. Among patients with more complex lesion morphology, restenosis rates after stent placement are increased, but appear to be increased even more if angioplasty alone is used. Several important lessons have been learned: (1) Stents decrease restenosis by providing the largest initial angiographic gain and by preventing early recoil and late negative remodeling (constriction) of the treated vessel. However, neointimal hyperplasia is increased with stent use compared with angioplasty alone. (2) Even when an initial optimal angiographic result is obtained with angioplasty alone, placement of a stent in coronary arteries 3 mm or greater in diameter improves clinical outcome and reduces restenosis. (3) There is a distinct difference between angiographic and clinical restenosis, both of which are reduced by stent placement.

The performance of subsequent revascularization is influenced by routine follow-up angiography. In the Benestent II study, patients were randomized to undergo either angioplasty or stenting and also randomized to undergo either clinical follow-up or clinical and angiographic follow-up. In the patients without protocol angiographic follow-up, repeat revascularization was substantially less frequent (6.0%) compared with patients with protocol angiographic follow-up (12.3%, P = .02).

**Chronic Total Occlusions**

Success rates for treatment of chronic total coronary artery occlusions are lower than for nonoccluded arteries. Even when an occlusion is crossed and dilated successfully, restenosis and reocclusion are more frequent than in nonoccluded arteries. Nine randomized trials have compared angioplasty alone...
CORONARY ARTERY STENTS

with stent placement in coronary artery occlusions in more than 1000 patients (Table 2). These studies revealed a reduction in angiographic and clinical restenosis and reocclusion in stented patients. Accordingly, current clinical restenosis and reocclusion in chronic total artery occlusions should have a stent placed if the runoff vascular bed is of sufficient size ($\geq 2.5$ mm).

**Stenotic Vein Grafts**

Treatment of stenotic vein grafts accounts for up to 10% of percutaneous interventional procedures. Major problems associated with balloon dilatation in vein grafts include increased acute complications such as distal embolization and “no reflow” (which can cause myocardial infarction [MI]) and also high restenosis rates. Observational studies have revealed a higher procedural success rate with stenting compared with that of angioplasty alone, higher long-term patency, and improved in-hospital clinical outcome. Two randomized trials evaluated the role of stent placement in vein grafts. In the SAVED trial, 110 patients were randomly assigned to receive stent placement along with warfarin plus aspirin and 110 to receive balloon angioplasty. Stent placement resulted in higher procedural success (92% vs 68%, $P<.001$) and lower rates of angiographic restenosis (37% vs 46%), target vessel revascularization (17% vs 26%), and the combined end point of death, MI, or target vessel revascularization (26% vs 39%) at 6 months. Preliminary data from the Venestent trial showed comparable success between the 2 groups in an intention-to-treat analysis, although crossover to stents was required in 24% of the balloon angioplasty group. At 6 months,

**Table 1. Studies Comparing Balloon Angioplasty With Stents for Native Coronary Artery Lesions**

<table>
<thead>
<tr>
<th>Study, y</th>
<th>Follow-up, mo</th>
<th>No. of Patients</th>
<th>Stent Angioplasty</th>
<th>Angiographic Restenosis, %</th>
<th>Stent</th>
<th>Angioplasty</th>
<th>P Value</th>
<th>Target Vessel Revascularization (TVR), %</th>
<th>Stent</th>
<th>Angioplasty</th>
<th>P Value</th>
<th>Death, MI, or TVR, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>STRESS, 1994†</td>
<td>6</td>
<td>205/202</td>
<td>31.6</td>
<td>42.1</td>
<td>.046</td>
<td>10.2</td>
<td>15.4</td>
<td>.06</td>
<td>19.5</td>
<td>23.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benestent, 1994†</td>
<td>7/60‡</td>
<td>259/257</td>
<td>22</td>
<td>32</td>
<td>.02</td>
<td>13.5/17.3‡</td>
<td>23.3/27.6</td>
<td>.05/0.006</td>
<td>20.1/65.5</td>
<td>29.6/59.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TASC I, 1995§</td>
<td>6</td>
<td>270 (Overall)</td>
<td>31</td>
<td>46</td>
<td>.01</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Versaci et al, 1997</td>
<td>12</td>
<td>60/60</td>
<td>19</td>
<td>40</td>
<td>.02</td>
<td>6.6</td>
<td>22</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td></td>
</tr>
<tr>
<td>STRESS II, 1998</td>
<td>12</td>
<td>100/89</td>
<td>. . .</td>
<td>. . .</td>
<td>10</td>
<td>20</td>
<td>. . .</td>
<td>. . .</td>
<td>17</td>
<td>34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benestent II, 1998</td>
<td>6</td>
<td>413/410</td>
<td>16</td>
<td>31</td>
<td>.001</td>
<td>8‡</td>
<td>13.7</td>
<td>.02</td>
<td>12.8</td>
<td>19.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OCEAS, 1998</td>
<td>7</td>
<td>57/59</td>
<td>18.8</td>
<td>16.6</td>
<td>. . .</td>
<td>17.5</td>
<td>9.2</td>
<td>. . .</td>
<td>19.2</td>
<td>16.9</td>
<td></td>
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</tr>
<tr>
<td>WIN, 1998§</td>
<td>6</td>
<td>299/287</td>
<td>38</td>
<td>37</td>
<td>. . .</td>
<td>39</td>
<td>39</td>
<td>. . .</td>
<td>28.1</td>
<td>26.8</td>
<td></td>
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<tr>
<td>BOSS, 1998§</td>
<td>8</td>
<td>40/40</td>
<td>. . .</td>
<td>. . .</td>
<td>21.4</td>
<td>23.5</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td></td>
<td></td>
</tr>
<tr>
<td>EPISTENT, 1998‡</td>
<td>6</td>
<td>1603/796</td>
<td>. . .</td>
<td>. . .</td>
<td>8.7</td>
<td>15.4</td>
<td>.001</td>
<td>13</td>
<td>20.5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OPUS, 1999§</td>
<td>6</td>
<td>480 (Overall)</td>
<td>. . .</td>
<td>. . .</td>
<td>4.0</td>
<td>10.7</td>
<td>.056</td>
<td>6.1</td>
<td>14.9</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

*MI indicates myocardial infarction. Ellipses indicate data were not reported for that category. For expansions of study names, see the corresponding reference. Data are for lesions in coronary arteries with vessel diameter $\geq 3.0$ mm. †Later follow-up at 60 months. ‡Any repeat procedure. §Only preliminary data are available. ¶One hundred twenty-two patients in the TASC I trial and 43 in the WIN trial had restenotic lesions treated. *Six months angiographic follow-up and 48 months clinical follow-up.

**Table 2. Studies Comparing Balloon Angioplasty With Stents for Ocluded Coronary Arteries**

<table>
<thead>
<tr>
<th>Study, y</th>
<th>Follow-up, mo</th>
<th>No. of Patients</th>
<th>Angiographic Restenosis, %</th>
<th>Reocclusion, %</th>
<th>Target Vessel Revascularization, %</th>
<th>Adverse Cardiac Events, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SICCO, 1996†</td>
<td>6</td>
<td>119</td>
<td>32</td>
<td>74</td>
<td>.001</td>
<td>12</td>
</tr>
<tr>
<td>Thomas et al, 1996§</td>
<td>6</td>
<td>60</td>
<td>37.5</td>
<td>60</td>
<td>. . .</td>
<td>. . .</td>
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<tr>
<td>GISSCO, 1998</td>
<td>9</td>
<td>110</td>
<td>32</td>
<td>68</td>
<td>.001</td>
<td>8</td>
</tr>
<tr>
<td>CORSICA, 1998§</td>
<td>6</td>
<td>142</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>SPACTO, 1999</td>
<td>6</td>
<td>85</td>
<td>32.4</td>
<td>63.6</td>
<td>.01</td>
<td>2.9</td>
</tr>
<tr>
<td>STOP, 1999§</td>
<td>6</td>
<td>96</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>TOSCA, 1999</td>
<td>6</td>
<td>410</td>
<td>55</td>
<td>70</td>
<td>.01</td>
<td>10.9</td>
</tr>
<tr>
<td>SARECCO, 1999</td>
<td>24</td>
<td>110</td>
<td>26</td>
<td>62</td>
<td>.05</td>
<td>2</td>
</tr>
<tr>
<td>MAJIC, 1999‡</td>
<td>6</td>
<td>221</td>
<td>57</td>
<td>56</td>
<td>.90</td>
<td>1.2</td>
</tr>
</tbody>
</table>

*Ellipses indicate data were not gathered for that category. †Warfarin and aspirin given to stent patients. ‡Late clinical follow-up (33 months). §Only preliminary data are available.
adverse cardiac events had occurred less frequently in the stent group (n = 78) than in the angioplasty group (n = 72), primarily due to less frequent target lesion revascularization (17% vs 26%), and a lower rate of the composite end point of death, MI, or target vessel revascularization (26% vs 39%).

Multiple patterns of vein graft disease, including ostial lesions, discrete and diffuse body lesions, and distal anastomotic lesions, may not benefit equally from stent implantation. In general, however, stent implantation improves initial success rates and reduces the need for target vessel revascularization in vein grafts compared with angioplasty alone.

Restenotic Lesions
Following balloon angioplasty of restenotic lesions, the recurrent restenosis rate is 30% to 50%; treatment with other devices is no more successful at reducing recurrent restenosis. In the REST trial,383 patients with restenosis following balloon angioplasty were randomized to receive either stenting or balloon angioplasty alone. There was a significant decrease in angiographic restenosis (18% vs 32%, P = .03) and the need for target lesion revascularization (10% vs 27%, P = .001) with stent use.

Acute MI
Nine randomized trials compared stenting with balloon angioplasty in acute MI53-61 (Table 3). Using an intention-to-treat analysis, stent placement was associated with a similar rate of angiographic success as angioplasty alone, although approximately 20% of patients randomized to receive angioplasty required crossover to stent placement to achieve angiographic success. However, these trials indicate that stent use led to a slightly lower rate of achieving Thrombolysis In Myocardial Infarction (TIMI) grade 3 flow, probably due to distal embolization of platelet-rich debris. The administration of an intravenous platelet glycoprotein (Gp) Ib/IIa inhibitor prior to stent placement improved the frequency with which TIMI grade 3 flow was achieved. Stenting also resulted in a decreased need for target lesion revascularization in the months after treatment. In the Stent-PAMI trial,61 stents were associated with a significant reduction in the combined end point at 6 months of death, reinfarction, disabling stroke, or target vessel revascularization from 20.1% in the angioplasty group to 12.6% in the stent group (P < .01). The difference was due entirely to the different rates of target vessel revascularization (17.0% vs 7.7%, P < .001). Subsequently, preliminary data from the CADILLAC trial (Greg Stone, MD, oral presentation at the American College of Cardiology, March 2000) confirmed a lower in-hospital target vessel revascularization rate with stents, and a similar high rate of TIMI grade 3 flow when Gp Ib/IIa inhibitors were administered prior to stenting.

Table 3. Studies Comparing Balloon Angioplasty With Stents in Acute Myocardial Infarction*

<table>
<thead>
<tr>
<th>Study, y</th>
<th>Follow-up, mo</th>
<th>Stent/Angioplasty</th>
<th>Success, %</th>
<th>Crossover, %</th>
<th>Early Events (0-30 Days), %</th>
<th>Late Events (Cumulative), %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Death</td>
<td>Reinfarction</td>
</tr>
<tr>
<td>GRAMI,54</td>
<td>12</td>
<td>52/52</td>
<td>98/94.2</td>
<td>25†</td>
<td>3.8/7.6</td>
<td>0/7.6</td>
</tr>
<tr>
<td>FRESCO,55</td>
<td>1998</td>
<td>6</td>
<td>75/75</td>
<td>99‡</td>
<td>...</td>
<td>0/0</td>
</tr>
<tr>
<td>STENTIM 2,57</td>
<td>1998</td>
<td>1</td>
<td>211</td>
<td>97/97</td>
<td>35.5†</td>
<td>1/0</td>
</tr>
<tr>
<td>Suryapranata et al,60</td>
<td>1998</td>
<td>6</td>
<td>112/115</td>
<td>98/96</td>
<td>2/13</td>
<td>2/3</td>
</tr>
<tr>
<td>PASTA,53</td>
<td>1999</td>
<td>12</td>
<td>67/69</td>
<td>99/97</td>
<td>1/10</td>
<td>3/7</td>
</tr>
<tr>
<td>PRIASM,56</td>
<td>1999</td>
<td>6</td>
<td>222</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>PSASM,57–59</td>
<td>1999</td>
<td>1</td>
<td>44/44</td>
<td>...</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Stent-PAMI,61</td>
<td>1999</td>
<td>6</td>
<td>452/448</td>
<td>89.4/92.7</td>
<td>1.5/15</td>
<td>3.5/1.8</td>
</tr>
<tr>
<td>CADILLAC,61</td>
<td>1999</td>
<td>...</td>
<td>1036/1045</td>
<td>92.1/94.8</td>
<td>15-20†</td>
<td>1.4</td>
</tr>
</tbody>
</table>

*Ellipses indicate data not gathered for that category; TVR, target vessel revascularization. All data are presented as values for stent/angioplasty groups. For expansions of study names, see the corresponding reference.
†Values for crossovers from angioplasty to stent treatment.
‡Success rate of 99% before randomization.
§Only preliminary data are available.
| Greg Stone, MD, oral presentation at the American College of Cardiology, March 2000. |
sure, and that stenting reduces the need for emergency coronary artery bypass graft (CABG) surgery. It would no longer be considered ethical to randomize patients with severe persistent coronary artery dissections or refractory acute closure to any treatment other than stent placement.

**LESIONS AND SETTINGS FOR WHICH STENTING IS OF UNPROVEN BENEFIT**

**Small Vessels (<3 mm)**

Although there is increasing information on the clinical outcome following stenting for small vessels (diameter <3 mm), the role of stenting is unclear. Early observational data suggested an increased risk of stent thrombosis, with rates of up to 7%; however, more recent, larger series have revealed a lower incidence of stent thrombosis (<2.5%). Restenosis rates after stent placement in small vessels are higher than rates for stent implantation in larger vessels (range, 30%-66%, with target vessel revascularization rates from 13%-35%). Preliminary results from 3 randomized trials (ISAR-SMART, SISA, and BESMART) revealed conflicting results. In ISAR-SMART, there were no significant differences between the stent group and the angioplasty group in the frequency of angiographic restenosis (35% vs 37%) or target vessel revascularization (20.1% vs 16.5%). However, in BESMART, angiographic restenosis (22.7% vs 48.5%, P<.001) and target vessel revascularization (13% vs 25%, P=.02) were significantly lower in the stent group. In SISA, repeat revascularization was lower in the stent group (16.6% vs 25.5%). Firm conclusions about the use of stents in small vessels cannot be made until more clinical trial data become available.

**Long Lesions**

Treatment of long lesions (≥20 mm) is associated with an increase of restenosis after both angioplasty and stent placement. There are no randomized trials comparing stents with balloon angioplasty in patients with long lesions; the only available data are from observational studies. Lesion length, stent length, and placement of multiple stents are all independent predictors of restenosis. Whether the high restenosis rates associated with stent treatment of long lesions are lower than with angioplasty alone is unknown.

**Left Main Coronary Artery Disease**

Patients with disease of the left main coronary artery (LMCA) can be divided into 2 groups: those with a “protected” LMCA (patients with a patent graft to the left circumflex or left anterior descending coronary artery), and those with an “unprotected” LMCA (patients with no patent grafts to the left coronary system). Studies of angioplasty of patients with LMCA stenoses reported varying degrees of procedural success but poor long-term results. Stenting of the LMCA is primarily performed in patients with a protected LMCA. However, stenting is also performed with increasing frequency in patients with an unprotected LMCA, and the results are improved compared with previous studies of balloon angioplasty alone.

Existing data suggest that the outcome of stent placement in discrete lesions in the middle of the LMCA, remote from the distal bifurcation and not involving the ostium, are associated with the best results. However, the potentially fatal complication of LMCA restenosis requires that patients who undergo LMCA stenting require careful follow-up, usually with repeat angiography and serial noninvasive testing. The outcome in these patients also depends on left ventricular function. In patients who undergo stent placement in the LMCA and have normal left ventricular function (ie, those who would have been excellent surgical candidates), the results of stenting are superior to results in those who undergo stenting but are poor surgical candidates or have inoperable lesions. Current evidence suggests that CABG surgery remains the treatment of choice for patients with significant LMCA disease who are surgical candidates.

**Bifurcation Lesions**

Treatment of bifurcation lesions is associated with both an increase in both early complications (particularly compromise of the main or branch vessel) and an increase in restenosis, regardless of which device approach is used. A number of stent techniques have been used to treat bifurcation lesions including “T-stenting,” “reverse Y-stenting,” “trouser-leg stenting,” and stent implantation of the major branch with angioplasty or atherectomy (or both) of the side branch. Observational studies suggest no advantage in stenting both branches of the bifurcation lesion compared with stenting 1 branch and performing angioplasty of the other branch; in fact, the outcome appears to be worse when stents are placed in both branches.

**Provisional Stenting**

In the early and mid-1990s the need for stent use in certain lesion types was shown to reduce the need for target lesion revascularization. However, there was concern that routine stent use without first trying to obtain “satisfactory” results with balloon angioplasty alone would increase cost as well as the frequency of in-stent restenosis, a more difficult problem to treat than restenosis after balloon angioplasty alone.

Accordingly, 5 clinical trials were performed to compare routine vs a provisional use of stents (OCBAS, OPUS-I, DEBATE II, DESTINI, and FROST). These trials included a variety of patient and lesion subsets; equally important, they used somewhat different criteria for a “satisfactory” balloon angioplasty result. OPUS-I used visual assessment of the angiographic result, whereas DEBATE II and DESTINI used angiographic stenosis and physiologic assessment of the result using Doppler flow reserve. The different trials identified some common findings, including that a satisfactory or optimal result is often not achieved with angioplasty alone, so stent implantation is common and the frequency of achieving an optimal angioplasty result varies depending on the definition used. Using angiographic cri-
teria alone (OCBAS), 13.5% of the angioplasty group crossed over to stent implantation. Using angiography and physiologic criteria for an optimal result, up to 50% of patients failed to achieve an optimal result.

The clinical outcome with a strategy of routine stenting is as good or better than that achieved with a strategy of provisional stenting. The results of these randomized trials, also supported by the EPISTENT trial,24 support the current practice of elective routine stenting for most lesions.

**ADJUNCTIVE THERAPY**

**Antiplatelet Therapy**

Five trials (ISAR, STARS, MATTIS, FANTASTIC and Hall et al)100-105 evaluated the role of aspirin, ticlopidine, and warfarin in patients with a variety of lesion types and different clinical settings. In these studies, the combination of aspirin and ticlopidine resulted in a lower rate of stent thrombosis and major adverse events, as well as fewer vascular and bleeding complications, than aspirin and warfarin or aspirin alone.

Ticlopidine has been largely replaced by clopidogrel, a thienopyridine closely related to ticlopidine in chemical structure and function, because ticlopidine caused occasionally life-threatening neutropenia in more than 1% of patients. Ticlopidine also causes thrombotic thrombocytopenic purpura (TTP) in approximately 0.3% of patients, which is fatal in 25% to 50% of cases.106 Clopidogrel does not appear to cause neutropenia and only rarely causes TTP.107,108 Another benefit of clopidogrel is that large loading doses are well tolerated, shortening the onset of action. The combination of clopidogrel and aspirin following stent placement has been studied in 3 randomized trials109-111 and in 7 registries112-118, findings suggest that the frequency of stent thrombosis with clopidogrel is low and equivalent to ticlopidine but with fewer adverse effects.

**Gp IIb/IIIa Inhibitors**

Another important adjunctive therapy used during stent placement is intravenous platelet Gp IIb/IIIa receptor block-

ers.119-121 Recent trials suggest synergy when Gp IIb/IIIa inhibitors are used during stent placement. In the EPISTENT trial,19,20 in which 2399 patients were assigned to either stent placement plus placebo (n=809), stent placement plus abciximab (n=794), or angioplasty plus abciximab (n=796), a significant reduction in cardiac events occurred in the stent and abciximab group at 6 months (5.6%) vs the angioplasty and abciximab group (7.8%) and stent with placebo group (11.4%), and the benefit persisted for at least 1 year. EPISTENT19 confirmed that even during elective percutaneous coronary revascularization, stent implantation increases the frequency of procedural myocardial enzyme elevation by 40% to 50%. In the ESPRIT trial, 2064 patients undergoing elective percutaneous revascularization with stents were randomized to receive eptifibatide or placebo. The trial was terminated early when the results of the first 1758 patients demonstrated a 43% reduction in death or MI at 48 hours with eptifibatide.79 Taken together, these data demonstrate that stents increase the frequency of procedural enzyme elevation compared with angioplasty, but the concomitant treatment with Gp IIb/IIIa inhibitors reduces the frequency of procedural enzyme elevation and other complications by 40% to 50%.

**Intravascular Ultrasound**

The role of intravascular ultrasound (IVUS) during stent placement is controversial. Information obtained by IVUS complements that obtained with angiography. In addition to aiding in selection of stent size, length, and postdilation balloon diameter, IVUS can be used to ensure complete apposition and adequate stent expansion. Using IVUS after stent implantation, Colombo et al122 demonstrated that the majority of stents (70%) were not fully expanded despite acceptable angiographic results; hence, stent thrombosis often may be due to underexpansion or incomplete opposition of the stent to the vessel wall. Colombo et al then demonstrated that high deployment pressures with IVUS guidance and dual antiplatelet therapy were associated with a stent thrombosis rate of 0.3%. However, a large French registry study123 subsequently demonstrated a low stent thrombosis rate when high deployment pressures were used and dual antiplatelet therapy was administered even without IVUS guidance, results that have since been duplicated.

It is clear that IVUS is not routinely required to achieve low rates of stent thrombosis.

Nonetheless, it has been suggested that IVUS-guided stent implantation may improve long-term outcome. An inverse relationship between minimal stent area determined by IVUS and the subsequent development of restenosis has been reported in a number of studies.124-126 In these studies, however, the magnitude of restenosis reduction with IVUS guidance is variable. In summary, IVUS has advanced the understanding of important issues surrounding stent placement and provides valuable additional information to guide stent placement over angiography alone, although it is unclear whether IVUS needs to be routinely performed.

**IN-STENT RESTENOSIS**

Although stents reduce the rate of coronary artery restenosis, in-stent restenosis (ISR) is a significant clinical problem.127 In-stent restenosis may be classified angiographically into 4 patterns according to the distribution of intimal hyperplasia in reference to the implanted stent. Pattern I includes focal (≤10 mm in length) lesions, pattern II is greater than 10 mm within the stent, pattern III is greater than 10 mm extending outside the stent, and pattern IV is totally occlusive ISR.

This classification has been found to be prognostically significant. After treatment of these different patterns of ISR, repeat target lesion revascularization ranges from 19% in pattern I to 83% in pattern IV.128 Focal restenosis typically responds well to balloon angioplasty.129 However, for diffuse ISR, multiple modalities have been studied,130-131 including excimer laser,132,133 rotational atherectomy,129,133,134 and directional atherectomy.133 None have been
showed to reduce repeat restenosis more effectively than balloon angioplasty alone. Observational studies have shown that stenting for ISR is associated with a high procedural success rate and a low complication rate, although the long-term benefit of this strategy remains unproven.135-138

The only treatment modality to provide a significant reduction in restenosis after any intervention is intracoronary brachytherapy.139,140 Randomized trials have documented reduced recurrent restenosis rates vs angioplasty alone. The benefits of brachytherapy appear to be particularly beneficial for diabetic patients, in whom dramatic reductions in angiographic restenosis (13.8% vs 63.1% with placebo) and target vessel revascularization (26.2% vs 67.7% with placebo) were seen, and for patients with long lesions.141 However, late stent thrombosis resulting in acute MI has been observed as late as 9 months following revascularization, suggesting the need for long-term thienopyridine therapy in this population.142 In addition, the importance of avoiding new stent placement at the time of brachytherapy has been emphasized. Similar benefits were seen with beta-radiation: the START trial demonstrated a 42% reduction in target lesion revascularization when compared with placebo (13% vs 22%, P = .008).79 Although radioactive stents have been developed and tested, the immediate and longer-term results appear less successful.143-148

ECONOMIC CONSIDERATIONS

Economic analysis of stent implantation is complex. The cost of each stent at approximately $1500 and the cost of adjunctive antiplatelet agents (eg, clopidogrel) must be balanced by the cost savings from the decreased need for repeat procedures. As new technologies further reduce restenosis and the need for repeat procedures, it is likely that stent implantation will become increasingly cost-effective.149-151

FUTURE STENT APPLICATIONS

Much interest has focused on loading a drug onto a stent to limit early thrombogenicity and late neoointima formation. Local stent-based drug delivery has the potential to maximize drug levels at the target site but minimize systemic effects. Many drugs have been evaluated, some of which are being tested clinically, including paclitaxel and rapamycin. The long-term role of this approach remains promising.152-154 The use of stents as drug delivery platforms remains promising, but unproven.

CONCLUSION

Coronary artery stents are essential in every modern interventional catheterization laboratory. Intracoronary stents have increased the safety of interventional procedures and have increased revascularization procedure success rates, decreasing the need for emergency CABG surgery. Data from randomized trials indicate that elective stenting of discrete lesions, de novo lesions, restenotic lesions, lesions in saphenous venous grafts, chronic totally occluded arteries, and infarct-related arteries improves clinical outcome.

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