Stents for Intracoronary Placement: Current Status and Future Directions

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The technique of intracoronary stenting has achieved remarkable progress over the last few years. Improved stent deployment techniques and optimization of postprocedural management have dramatically improved the safety of intracoronary stent placement. At present, the incidence of early vessel closure after stenting is even lower than after standard angioplasty, and, as most operators no longer prescribe aggressive anticoagulation, bleeding complications are uncommon.

Stenting has become an extremely effective treatment for abrupt or threatened vessel closure or for any suboptimal angiographic result during conventional angioplasty. Furthermore, large prospective trials have demonstrated that its efficacy is superior to that of conventional angioplasty for primary restenosis prevention in focal lesions of some native coronary arteries. Ongoing trials tend to extrapolate these conclusions to saphenous vein graft lesions.

Mechanical support of the vessel wall explains the sustained angiographic benefit observed after stenting. Future developments may include the use of stents as a vehicle for local drug delivery in an attempt to further reduce the incidence of restenosis.

In view of these results, coronary stents should be considered a new standard therapeutic modality in interventional cardiology.

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Historical Overview

History: part 1 (1986 to 1991). In 1986, Sigwart (Lausanne, Switzerland) and Puel (Toulouse, France) first implanted, almost simultaneously, a stent in human coronary arteries (4). In 1987, Roubin (Birmingham, Alabama) (5) and Schatz (La Jolla, California) (6) and their coworkers performed the first stent implantation in the United States. Stents were initially implanted for the treatment of restenosis. Abrupt or threatened vessel closure after coronary angioplasty and treatment of saphenous vein graft narrowings were the next indications. As always with a new technique, these initial experiences were reported in rather small observational trials or presented as uncontrolled data. Only 5 years after the initial implantation, the first two important studies, reporting registry results of observational multicenter trials, were published. Serruys et al. (7) reported data on the European Wallstent (Schneider AG, Zürich, Switzerland) and Schatz et al. (8) reported on use of the U. S. Palmaz-Schatz (Johnson & Johnson) device. These pioneer works pointed out several problems: 1) the occurrence of subacute stent thrombosis, which had an unacceptably high rate (20%) in the European study; 2) technical hazards related to implantation of the device with risk for stent loss or embolization (Palmaz-Schatz stent) or wrong positioning (Wallstent), requiring implantation of multiple stents; 3) bleeding problems related to anticoagulation; and 4) different results according to the type of stent being used. At that time, it was concluded that the place of this technique for the treatment of obstructive coronary artery disease remained to be determined because of the high incidence of complications.

History: part 2 (1991 to 1993/1994). Nevertheless, a persistent belief of certain investigators in their technique, better patient selection and more adequate postprocedural management reduced the incidence of the aforementioned complications in the early 1990s, and randomized trials comparing...
stenting with angioplasty were initiated for primary and secondary restenosis prevention and for the treatment of saphenous vein graft narrowings and sudden or threatened vessel closure during angioplasty. These randomized trials were started much earlier than studies comparing angioplasty and coronary artery bypass grafting. At present, only primary restenosis prevention trials (Benestent I [Belgium/Netherlands] [9] and STRESS I [Stent REStenosis Study] studies) [10] have been completed and their data published. These data show favorable results for stenting, as will be discussed later.

History: part 3 (1993/1994 to ?). If the second part of stent history was characterized by a clear reduction of procedure-related complications and the completion of the first randomized trials, the third part is characterized by better stent deployment techniques and abolition of oral anticoagulation after the intervention. Goldberg (11) and Colombo (12) and co-workers demonstrated by means of intravascular ultrasound that, with conventional implantation techniques, stent deployment was suboptimal in up to 87% of cases with incorrect apposition of the device with the vascular surface. They therefore suggested additional high pressure noncompliant balloon angioplasty to fully expand the stent. Although a relation between stent underexpansion and subacute thrombosis has never been clearly documented, several investigators (13), using ultrasound, progressively diminished and finally stopped their postintervention anticoagulation regimen and observed, simultaneously, very low closure rates with combined aspirin-ticlopidine treatment. French investigators (14), in contrast, started a multicenter feasibility study on stenting without coumadin and without mandatory ultrasound in March 1992. In December 1992, after adding ticlopidine (250 mg twice daily) to postprocedural treatment with aspirin and low molecular weight heparin, they observed (15,16) a reduction in suboptimal outcome after angioplasty. These data will be discussed later. A new generation device with proximal and distal markers on the stent, capable of passing in large lumen GF guiding catheters, will soon be available.

Current Stent Types

Stents can be distinguished by their type of delivery system (self-expanding, balloon-expandable), their composition (metallic—stainless steel, cobalt-based alloy or tantalum; biodegradable; polymeric) and their configuration (mesh structure; slotted tube; coil). Although most stents are placed definitively in coronary vessels, this list should be completed with the temporary retrievable bailout stent (RX Flow Support Catheter, Advanced Cardiovascular Systems) (17). The following devices are currently used or still under clinical investigation in humans:

Wallstent (Schneider AG). This device, the first stent ever implanted in human coronary arteries, was used in Europe between 1986 and 1990. The self-expanding, wire mesh structure covers ~20% of the vascular surface, making it the densest stent. This high metallic density has been held responsible for the high early vessel closure rate (20%), as reported in the European Registry in 1991 (7), and the stent was therefore withdrawn from clinical investigation in 1990 (7,18). However, since 1994, the Wallstent has gained new interest, especially for treatment of vein graft lesions, in which stents may be placed without predilatation, a strategy that may diminish the risk for distal embolization. Controlled multicenter trials, examining the safety and efficacy of this stent for restenotic native and new-onset vein graft lesions, will soon be initiated in Europe and the U.S. The investigators believe that with better deployment techniques, the incidence of subacute closure will be much lower.

Flexstent (Gianturco-Roubin, Cook). This balloon-expandable, stainless steel, single-wire structure has been used since 1987, initially only for the treatment of acute vessel closure during angioplasty (19). The largest experience has been gained in the U.S., and observational trials (20) as well as risk factors analyses on adverse long-term outcome (21) have been published. Recently, favorable results were reported in a small, randomized trial (22) of this stent for the treatment of suboptimal outcome after angioplasty. These data will be discussed later. A new generation device with proximal and distal markers on the stent, capable of passing in large lumen 6F guiding catheters, will soon be available.

Palmaz-Schatz stent (Johnson & Johnson International Systems). This balloon-expandable, stainless steel, slotted tube device, introduced in 1987, is the most studied and widely used stent in the world. The Benestent I and STRESS I trials were carried out with this stent, and ongoing trials of secondary restenosis prevention, bailout and graft stenting are being performed with this device. The first-generation Palmaz-Schatz stent comprised, in addition to the short stent, two tubes connected by a metallic bridge (articulated stent). This weaker part of the stent has been held responsible for restenosis by some investigators and the manufacturer has now released a spiral-like intersection that contains more metal but also makes it more rigid and less trackable (23). A heparin-coated form of this newly designed Palmaz-Schatz stent will be used in future stent trials. A “biliary” type of Palmaz-Schatz
stent, with the same design but a slightly larger strut thickness, is available for implantation in large (>4.5 mm) saphenous vein grafts.

**Wikiton stent** (Medtronic Interventional Vascular). This balloon-expandable, helicoid coil, radiopaque (tantalum) device was the first of a new generation of stents released for clinical investigation in the early 1990s (24). It has mainly been used for restenotic lesions, bailout situations and vein graft disease. A fibrin-coated and a new small wave design stent (with more surface coverage) will be under evaluation.

**Micro stent** (Applied Vascular Engineering Inc., Richmond, Canada). This balloon-expandable, stainless steel stent is composed of different 4-mm segments of a continuous wire in zigzag design. Although this device has been widely used since 1994 in different settings, no large scale long-term angiographic follow-up data are available (25). The stent is characterized by excellent trackability and is available in different lengths.

**Cordis stent** (Cordis). This balloon-expandable, tantalum, single-wire, helicoid stent is currently undergoing safety and efficacy evaluation in controlled studies (26).

**Multi Link stent** (Advanced Cardiovascular Systems). This balloon-expandable, stainless steel device is characterized by multiple serial rings connected by several links. The stent is currently under evaluation.

### Modalities of Stent Placement

**Role of intravascular ultrasound.** As mentioned previously, this technique had imposed the use of additional high pressure, noncompliant balloon angioplasty in tubular and some coil stents that enabled the concept of no anticoagulation—full antplatelet therapy (12,27). At present, controlled trials (such as the STRUT [Stent Treatment Region assessed by Ultrasound Tomography] study) are examining the impact of ultrasound on further decision-making (more additional angioplasty) after high pressure angioplasty (28). Current “blind high pressure” practice, which has resulted in very low subacute stent thrombosis rates, is probably as safe as ultrasound-guided stent placement. Intravascular ultrasound, an essential research tool, does not seem imperative from this point of view. Completion of the STRUT (and similar) trials will elucidate whether ultrasound may improve the long-term efficacy of stenting by further reducing the incidence of restenosis.

**Role of ticlopidine and other new antplatelet agents.** Ticlopidine, a thiophene-pyridine derivative, has been shown to have a broad antplatelet activity that is maximal after 3 days of treatment and that persists for >10 days after its withdrawal (29). Historically, this drug was used as premedication for conventional angioplasty in patients with aspirin intolerance. Since the end of 1992, it has been used after stent implantation in a nonrandomized fashion with excellent results (15,16,32). These observations have stimulated investigators over the world to use this drug in combination with aspirin in most ongoing stent trials. One small randomized ultrasound-controlled single-center study by Blengino et al. (31) compared the utility of aspirin alone versus aspirin plus ticlopidine and found no more benefit with ticlopidine. Nevertheless, it seems useful, on the basis of larger French experiences, to prescribe ticlopidine 3 to 5 days before elective stent placement.

New antithrombotic drugs have been developed and used in patients with unstable syndromes undergoing conventional angioplasty (32). In view of the very low subacute stent thrombosis rates currently being reported, the indication for these drugs after stenting is unclear. Future planned investigations may indicate categories of patients (large visible thrombus, acute myocardial infarction) who will benefit from this treatment.

**Role of transradial approach.** In 1994, Kiemeneij et al. (33) first described the use of the radial artery as an entry site for elective placement of the Palmaz-Schatz stent. In the era of full anticoagulation and antplatelet therapy, this alternative approach was very promising because bleeding problems were virtually absent. At present, with the overall reduction in bleeding complications, the transradial technique seems less attractive, although it remains an elegant technique in the hands of experienced operators.

**Technical aspects.** Intracoronary stenting is technically more challenging than standard angioplasty. Stents are less trackable than modern angioplasty catheters and the stent delivery systems have a far larger profile. Incorrect judgment of the accessibility of the lesion is the major cause of deployment failure and stent embolization. Data are lacking, but one may assume that ±5% of balloon-expandable stents are lost during implantation, mostly without sequelae as operators commonly retrieve in one movement guide wire, delivery system and guiding catheter in the descending aorta. Delivery systems with a stent-protective membrane, mostly used in the United States, appear safer but are less trackable. In general, if stent placement is intended, adequate backup (by an appropriate guiding catheter) and support (by use of extra support guide wires) is essential.

Specific measures may facilitate the intervention. Correct positioning is easier with radiopaque stents (Wikiton, Cordis stent) or with these delimited by double markers (Micro, new Gianturco-Roubin stent). Overall, the self-expanding Wallstent remains the most difficult device to implant correctly because it lacks radiopacity and important shortening occurs during pullback of the protective membrane.

Conceptually, tubular stents may cause side branch closure and prohibit the application of percutaneous coronary intervention if ostial disease is present in these side branches. Reported data (34,35) show that closure occurs rarely (<5%) and that its occurrence, which appears to imply no clinical sequelae, is mostly related to the presence of ostial disease of the branch. Therefore, coil stents should be implanted in the main artery if intervention in large (>2-mm) side branches is intended.
Table 1. Angiographic Success Rates After Conventional Coronary Angioplasty

<table>
<thead>
<tr>
<th>Study (ref no.)</th>
<th>Qualitative Analysis (operator)</th>
<th>Quantitative Analysis (core laboratory)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHLBI 1977-1981 registry (36)</td>
<td>1-vessel disease: 67.3</td>
<td>80.1</td>
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<td></td>
<td>2-vessel disease: 55.2</td>
<td>85.0</td>
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<td></td>
<td>3-vessel disease: 60.9</td>
<td>85.0</td>
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<tr>
<td>NHLBI 1985-1986 registry (36)</td>
<td>1-vessel disease: 86.1</td>
<td>90.6</td>
</tr>
<tr>
<td></td>
<td>2-vessel disease: 78.0</td>
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</tr>
<tr>
<td></td>
<td>3-vessel disease: 77.5</td>
<td>89.0</td>
</tr>
<tr>
<td>M-HEART I (37)</td>
<td>CAVEAT I (38)</td>
<td>96.4</td>
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<td>STRESS I (38)</td>
<td>Angioplastin (39)</td>
<td>97.1</td>
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<tr>
<td>CAVEAT II (40)</td>
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<td>97.1</td>
</tr>
</tbody>
</table>

CAVEAT = Coronary Angioplasty Versus Directional Atherectomy; M-HEART = Multi-Hospital Eastern Atlantic Restenosis Trial; NHLBI = National Heart, Lung, and Blood Institute; ref = reference; STRESS = STent REStension Study.

Limitations of Standard Balloon Angioplasty

Angiographic success and result. Angiographic success, defined as <50% residual stenosis at the end of the intervention as assessed during off-line quantitative coronary angiographic analysis in the core laboratory, is not always present after an angioplasty that the operator has judged successful by visual assessment. Different success rates obtained after angioplasty are listed in Table 1 (9,36-40). Over the course of time, these rates have tended to increase and the discrepancy between qualitative and quantitative angiographic analysis has decreased with growing experience, insight into the utility and accuracy of quantitative angiographic analysis and the performance of randomized trials. The latter have contributed to a better execution of the angioplasty procedure, as operators try to optimize their angiographic results by conventional means. Even though we “do better than before,” angioplasty will be unsuccessful in certain patients and suboptimal in others, perhaps causing persistence of angina in some patients or exposing others to a higher risk for restenosis. Therefore, in view of this “the bigger, the better” theory, angioplasty may require new device assistance to increase angiographic success and to improve suboptimal angiographic results.

Abrupt vessel closure. Vessel closure during angioplasty is unpredictable and still occurs with an unchanged nonnegligible incidence rate of 4.4% to 8.3% (44). The immediate and long-term outcome of patients who experience abrupt vessel closure during angioplasty are impaired. Despite combined reangioplasty, thrombolysis and urgent bypass grafting, a 6% incidence of death and 33% incidence of myocardial infarction have been reported (44).

Restenosis. Restenosis, treated repeatedly by conventional angioplasty, is safe and efficient but also more expensive than primary stenting or even grafting (45). Only their greater clinical need for repeat intervention, caused by restenosis, discriminated patients treated with angioplasty from those who had undergone bypass grafting in all randomized trials that have compared these therapeutic options (46). Similar rates of death and myocardial infarction with these therapies provide an ethical basis for further transcatheter coronary therapies. However, new device assistance seems mandatory to further improve the immediate safety and the long-term efficacy of angioplasty by reducing the need for urgent or elective reintervention, or both.

Indications for Stenting

Suboptimal angiographic results. A suboptimal angiographic result after coronary angioplasty is typically caused by acute elastic recoil, residual plaque burden and dissection. In the absence of heavily calcified plaque (for which lesion pretreatment with rotational atherectomy is a valuable option), intracoronary stent placement scaffolds the vessel wall and reduces its acute elastic recoil more than does angioplasty (47). This observation by Haude et al. (47) was confirmed in prospective studies such as the STRESS I trial, which demonstrated a higher immediate angiographic success rate (99.5% vs. 92.6%) and superior results (19 ± 11% vs. 35 ± 14% residual stenosis, mean ± SD) with stenting (22). In a small randomized trial with 66 patients, Rodriguez et al. (22) showed that implantation of a Gianturco-Roubin stent after a suboptimal result (residual stenosis ≤40% 24 h after angioplasty) reduced the incidence of restenosis from 75.7% (if no further intervention was performed) to 21.2%.

Although these data suggest that unplanned stenting should be performed for suboptimal results after angioplasty, no clear residual stenosis cutoff value has been proposed. It seems reasonable to advise stent implantation (Palmaz-Schatz or Gianturco-Roubin device) for a residual stenosis >25%, as this value was obtained in the Benestent I and STRESS I trial after stenting. However, if a residual stenosis ≤20% can be obtained with conventional angioplasty, there is no rationale for additional stenting.

Abrupt or threatened vessel closure during angioplasty. After their initial description of the stenting technique in 1987 (4), Sigwart et al. (48) reported a larger experience, restricted to bailout stenting, in 1988. Numerous observational trials with different stent types have since been reported (Table 2) (19,21,49-63). These studies have shown high technical success rates but striking differences in the incidence of adverse events. Between 1986 and 1993, the incidence of subacute stent thrombosis and related myocardial infarction did not decrease. Recently, the French multicenter study on stenting without coumadin (14) reported, in the subgroup with rescue stenting, a 3.4% closure rate with the addition of ticlopidine to the
Table 2. Results of Rescue Stenting

<table>
<thead>
<tr>
<th>Stent and Study (ref no.)</th>
<th>Study Period</th>
<th>Pts (no.)</th>
<th>Implantation Success (%)</th>
<th>Early Closure (%)</th>
<th>Myocardial Infarction (%)</th>
<th>Urgent CABG (%)</th>
<th>In Hospital Death (%)</th>
<th>Restenosis (%)</th>
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<td>11</td>
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<tr>
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<td>1989-90</td>
<td>15</td>
<td>100</td>
<td>20</td>
<td>13.3</td>
<td>60*</td>
<td>6.6</td>
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<tr>
<td>Guy et al. (50)</td>
<td>1986-89</td>
<td>17</td>
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<td>5.8</td>
<td>5.8</td>
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<td>33</td>
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<td>24</td>
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<td>115</td>
<td>96</td>
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<td>8.6</td>
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<td>26*</td>
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<td>42</td>
<td>95</td>
<td>24</td>
<td>5</td>
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*Includes patients in whom stenting was considered a bridge to operation. CABG = coronary artery bypass grafting; Pts = patients; ref = reference.

postprocedural regimen. Very low closure rates have been reported by Colombo et al. (11,12) using ultrasound guidance and high pressure angioplasty.

Various other interventional strategies have been suggested for acute vessel closure during angioplasty (44). Although the results may seem promising, they were obtained in small series and in the hands of experienced operators. Repeat angioplasty and stenting remain the most commonly used and available techniques. Autoperfusion balloon angioplasty prolongs the intervention and has a nonnegligible failure rate that requires final crossover to stenting (44). In contrast to the many observational trials on bailout stenting, only two randomized trials have compared stenting (Palmaz-Schatz) with prolonged autoperfusion balloon angioplasty. The TASC II trial (Trial of Angioplasty and Stents in Canada) (64), a small study of 43 patients, found more clinical success (90% vs. 42%) and improved immediate angiographic results with stenting. The GRACE trial (Gianturco-Roubin stent Acute Closure Evaluation) (65), designed in 1992 and using the Gianturco-Roubin stent, has not yet reported results.

Although results of the GRACE trial are lacking, it may be concluded that stenting is actually the better technique for the management of acute or threatened closure during angioplasty. A wide spectrum of conditions, from suboptimal angiographic results after angioplasty to a large protruding dissection with impaired distal flow or total vessel closure, may benefit from stent placement. Because large randomized trials are lacking, the operator should choose the device with which he is most familiar and use high pressure angioplasty, depending on the stent type (66). In cases of extreme vessel tortuosity or small vessel size, membrane-protected stents or the trackable Micro stent can be considered. Even the presence of thrombus in bailout situations does not seem to be a contraindication to stenting as Sutton et al. (21) found that it was not retained as a risk factor for adverse events in a multivariate analysis. Very small vessel size (<2.5 mm) is one of the last remaining absolute contraindications to stenting. However, patients with such vessels are also poor surgical candidates and revascularization should be carefully considered before percutaneous intervention. Ticlopidine may be administered before angioplasty in order to obtain this drug's full efficacy during the intervention.

Restenosis after angioplasty. Primary restenosis prevention. Four trials comparing stenting and angioplasty for new lesions in native coronary arteries have been conducted with the Palmaz-Schatz stent; one smaller pilot study has been performed with the Witko stent (9,10,67-69).

In the Benestent I (n = 520) and STRESS I (n = 410) trials, patients with new discrete (length <15 mm) lesions in large (≥3-mm) native coronary arteries were randomized between 1991 and 1993 in 48 centers in the U.S. and Europe. At 6-month follow-up (9,10), the essential conclusions were that elective implantation of an articulated Palmaz-Schatz stent induced a sustained angiographic benefit with a reduction of the restenosis rate by ≤40% and less need for repeat intervention than that obtained with angioplasty. Further clinical
follow-up during 1 year in the Benestent I group (70) showed that these conclusions could be maintained. Despite these positive results, there were several problems. 1) The patients, to whom the preceding restrictive criteria apply, are only a small part of the general population of patients with coronary artery disease. 2) Patients who received stents had received full anticoagulation, which caused a longer hospital stay and a nonnegligible incidence of subacute thrombosis and restenosis rates, varying between 17% and 39%, has been reported. Nevertheless, restenotic lesions have a different pathologic substrate from that of new stenotic lesions and may predispose to a higher incidence of a second restenosis. Savage et al. (75) reported a higher restenosis rate after stenting of restenotic versus new lesions. Thus, the favorable results of certain primary restenosis prevention trials cannot be extrapolated to secondary restenosis prevention and it is unclear whether stenting is superior to angioplasty for restenotic lesions.

The START trial (STent versus Angioplasty Restenosis Trial) is a Spanish multicenter study that, like STRESS, included patients with unstable and multivessel disease (67). The study is about to be completed and results, which are similar to those of the preceding trials, will soon be published. A fourth, smaller, study, the Canadian TASC I study, found a very low subacute stent thrombosis rates whereas a 30% incidence rate of restenosis may be expected during follow-up. In contrast to the favorable results observed with the Palmaz-Schatz stent, primary Wiktor stenting of the right coronary artery did not show any clinical or angiographic advantage over standard angioplasty in a pilot study concerning 84 patients (69). At present, no further trials with this or other (than the Palmaz-Schatz) stents are planned.

A pilot phase with 200 patients showed the safety (no case of stent thrombosis) of a new, heparin-coated Palmaz-Schatz stent with a modified spiral articulation. This stent will be used in the Benestent II trial, which will investigate the efficacy of primary stenting in multivessel disease (71), evaluate major adverse clinical and angiographic events and perform a quality of life analysis and a financial comparison.

Secondary restenosis prevention. Stent placement has been performed for the treatment of restenotic lesions since 1986, and a limited number of observational studies with different stent types (Table 3) have been published. Many of these series, which typically are not focused on secondary stenosis prevention, appear rather outdated. A nonnegligible incidence of subacute thrombosis and restenosis rates, varying between 17% and 39%, has been reported. Nevertheless, restenotic lesions have a different pathologic substrate from that of new stenotic lesions and may predispose to a higher incidence of a second restenosis. Savage et al. (75) reported a higher restenosis rate after stenting of restenotic versus new lesions. Thus, the favorable results of certain primary restenosis prevention trials cannot be extrapolated to secondary restenosis prevention and it is unclear whether stenting is superior to angioplasty for restenotic lesions.

The REST trial (REstenosis STent study), initiated in 1991 in Germany and currently extended to several European centers (77), investigates this issue in a randomized fashion. A first answer to this important topic is expected shortly.

Saphenous vein graft stenting. Conventional angioplasty of vein graft lesions is limited by the risk of distal embolization of plaque during intervention and by a high incidence of restenosis (78). For stenting, new technology has been very disappointing and the only randomized trial (CAVEAT II, Coronary Angioplasty versus Excisional Atherectomy Trial) on vein graft lesions showed similar restenosis rates and a higher incidence of periprocedural complications with directional atherectomy in comparison with angioplasty (40). Stenting of such lesions has been performed since 1986, and the experience of several centers has been reported (Table 4) (79–90). Even before the era of ultrasound and high pressure angioplasty, stenting in vein graft lesions was characterized by very low subacute stent thrombosis rates whereas a 30% incidence rate of restenosis may be expected during follow-up. It is currently unclear whether stenting results in less distal embolization during intervention. This issue as well as the impact of stenting on restenosis will be addressed in the SAVED trial (Stent versus balloon Angioplasty for aorto-
coronary saphenous Vein bypass graft Disease), the only randomized study on this subject comparing Palmaz-Schatz stenting and angioplasty. Intracrin (91) indicates that primary restenosis prevention tends to be as effective in vein grafts as in native coronary arteries. The Wallstent may be of particular interest for long lesions and for the prevention of grafts as in native coronary arteries. The Wallstent may be of primary restenosis prevention tends to be as effective in vein stenting and angioplasty. Interim analysis (91) indicates that suboptimal angioplasty results in ostial lesions should there be treated by the technique with which the operator is most familiar.

Future areas for investigation of stenting. Aortocoronary ostial lesions. New technology (laser angioplasty, directional or rotational atherectomy and stenting) is effective for ostial stenoses (93). However, substantial data are lacking and suboptimal angioplasty results in ostial lesions should therefore be treated by the technique with which the operator is most familiar.

Chronic total occlusion. Again, limited experience with stenting has been gained in patients with this indication for stenting. Goldberg et al. (94) reported a second vessel closure in 5% and restenosis in 20% of their 59 patients. Medina et al. (95) described comparable results. One randomized trial (SPECTO) (Stents versus PTCA After recanalization of Chronic Total coronary Occlusions) with the Wiktor stent is currently being undertaken.

Acute myocardial infarction. Stenting is currently being performed in patients with acute myocardial infarction who have suboptimal primary angioplasty results. Yet, large-scale data have not been published (96). The PAMI (Primary Angioplasty for Myocardial Infarction) study group is considering performing a controlled trial with the heparin-coated Palmaz-Schatz stent in patients with acute myocardial infarction.

**Conclusions.** Intracoronary stents have improved the safety and efficacy of transcatheter cardiovascular therapy. They can reverse acute vessel or graft closure during coronary intervention, and certain devices have an "antirestenosis" effect in selected patients. Most of these patients are also good surgical candidates, a group that excludes patients with distal lesions in very small vessels.

Stents will not eliminate the restenosis problem, and a persistent restenosis rate of 10% to 15% should be expected with the best of current devices. However, it is a first step in restenosis prevention and may, in the future, be part of a more global approach to preventing restenosis that may also include stent irradiation and the use of local drug delivery or gene therapy with the use of polymeric or biodegradable stents as the vehicle for application. At present, because the learning curve is short and because coronary stent placement is the most efficient means of reversing acute vessel closure during angioplasty, the ability to use these devices is mandatory in every modern catheterization laboratory.

**References**


7. Serruys PW, Serruys PR, Bentz J, et al. Angiographic follow-up after


38. Herrmann HC, Buchbinder M, Clemen MW, et al. Emergent use of