Coronary Stenting

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Stents are metallic scaffolds that are deployed within a diseased segment of coronary artery to establish and then maintain a widely patent lumen. Just 6 years after the 1994 approval of the balloon-expandable Palmaz-Schatz slotted tube stent in the United States, stents are utilized in upwards of 80% of interventions and have revolutionized catheter-based treatment. Given the rapid evolution in stent design, techniques, and indications, the goal of this chapter is to highlight some of the underlying principles and concepts and to summarize the key trials on which current stent use is based, expecting that many of the nuances of stent design will continue to evolve.

HISTORICAL PERSPECTIVE

As described in Chapter 23, despite progressive improvement in the results of conventional balloon angioplasty, it remains limited by abrupt vessel closure (which leads to emergency bypass surgery in 1% of patients) and restenosis (which prompts a repeat revascularization procedure in 30% of patients). The attraction of stenting is that it addresses both of these shortcomings.

Although the concept of an endovascular prosthesis to seal dissections and overcome recoil was first proposed by the late Charles Dotter in 1964 (1), the first implantation of stents in human arteries did not occur until 1985, when Sigwart et al. (2) reported the successful placement of self-expanding Wallstents in the peripheral and coronary arteries of eight patients. One year later, however, Serruys (3) reported a much less favorable multicenter experience using this device, with 18% thrombotic occlusion and 8% mortality at 1 year. However, those patients who did not experience subacute thrombotic occlusion had a 6-month angiographic restenosis rate of only 14%, suggesting for the first time that stenting could reduce angiographic restenosis. This encouraged Gianturco and Roubin (4) to begin work on a balloon-expandable coil stent, which consisted of stainless steel wire wrapped around a deflated balloon in a serpiginous manner. A phase II study began in 1988 using this stent to reverse postangioplasty acute or threatened vessel closure (5), which led to U.S. Food and Drug Administration (FDA) approval in June 1993. Concurrently, Palmaz introduced a balloon-expandable stent in 1984 (6),(7), in which rectangular slots were cut into thin-walled stainless steel tubing, so that balloon inflation within the stent deformed these rectangular slots into diamond-shaped windows or cells. The rigidity of this design made it difficult to pass through guiding catheters and tortuous vessels, until 1989 when Schatz (8),(9) added a 1-mm central articulation to join two rigid 7-mm segments, creating the Palmaz-Schatz stent. In 1989, enrollment commenced in two randomized multicenter studies—the U.S. Stent Restenosis Study (STRESS) and the European Belgium Netherlands Stent (Benestent) trial (10),(11)—comparing balloon angioplasty with elective Palmaz-Schatz stenting, which showed a 30% reduction in angiographic restenosis compared with conventional balloon angioplasty. This led to the 1994 FDA approval of the Palmaz-Schatz stent for elective treatment of focal de novo lesions in native vessels, 3 to 4 mm in diameter.

Despite the impressive acute and long-term results observed in the STRESS and Benestent trials, widespread application remained limited by the 3% incidence of thrombosis and a significantly higher incidence of hemorrhagic complications and length of hospital stay associated with the draconian anticoagulation regimens employed as prophylaxis against thrombosis (11). In the early 1990s, Colombo and colleagues, using intravascular ultrasound (IVUS), demonstrated that the majority of stents were inadequately expanded despite excellent angiographic appearance (12). By employing routine high-pressure adjunctive dilatation, he and other European investigators showed that such “optimal stenting” reduced the incidence of stent thrombosis to less than 1% to 2% using only aspirin and a second platelet agent, ticlopidine, rather than prolonged warfarin therapy (13). Subsequently, two randomized trials—the German Intracoronary Stenting and Antithrombotic Regimen (ISAR) study (14) and the U.S. multicenter STent Anticoagulation Restenosis Study (STARS) (15)—definitively established the superiority of dual antiplatelet therapy (with aspirin and ticlopidine) over anticoagulation (with warfarin) for prevention of stent
thrombosis. Additional trials showed the efficacy of stenting in broader anatomic and clinical situations (beyond focal de novo native vessel lesions). With the more effective antiplatelet regimens and expanding indications (16–19), which included saphenous vein bypass grafts, chronic total occlusions, prior restenosis, and acute myocardial infarction (MI), as well as the introduction since 1997 of a wide range of newer stent designs with improved flexibility, visibility, and profile, stent placement is now used in approximately 80% of percutaneous revascularizations.

**STENT DESIGNS**

As of 2000, more than 30 stent types have been implanted in the human coronary circulation (Fig. 25.1). Stent types differ in their composition (e.g., stainless steel, tantalum, nitinol), architecture (e.g., slotted tube, coiled wire), and mode of implantation (e.g., self-expanding, balloon-expandable) (Table 25.1). In theory, the perfect coronary stent would be made of a relatively nonthrombogenic material and have sufficient flexibility in its unexpanded state to allow passage through guiding catheters and tortuous vessels. Despite its flexibility and low profile in the collapsed state, it should have an expanded configuration that provides uniform scaffolding of the vessel wall with low recoil and maximal radial strength. In addition, the stent should be sufficiently radioopaque to allow fluoroscopic visualization but not so opaque as to obscure important vascular details. All clinically tested coronary stents have been constructed from metallic alloys, including stainless steel, tantalum, nitinol, and cobalt/platinum. The largest experience has been with stainless steel. Although each stent design is unique, they can be divided into broad categories based on whether they are balloon-expandable or self-expanding, and subcategorized based on architecture (e.g., coil, tube, hybrid tube-coil).

**FIG. 25.1.**

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Ten contemporary stent designs evaluated in humans as of January 2000. **Left to right, top row:** Crown Stent, Minicrown Stent. **Second row:** CrossFlex LC Stent, BX Stent. **Third row:** Duet Stent, NIR Stent. **Fourth row:** Radius Stent, Wallstent. **Bottom row:** GFX stent, BeStent.

**Balloon-Expandable Stents**

Balloon-expandable stents are delivered into the coronary artery in their collapsed state, mounted on a delivery balloon. Once in the desired location, inflation of the delivery balloon expands the stent and imbeds it into the arterial wall. Within the balloon-expandable stent category, all stents can be assigned to one of three subgroups, based on construction: wire coils, slotted tubes, and modular designs.

**Wire Coils**

The Gianturco-Roubin FlexStent (Cook Cardiology, Indianapolis, IN) was the initial coil stent prototype. It was constructed by winding stainless steel wire into a serpiginous pattern of reversing loops and then folding that pattern onto a compliant balloon to create an interdigitating coil. Although this device was the first stent to receive FDA approval (in 1993), its mechanical deficiencies (e.g., low axial and radial strength and a tendency for plaque to prolapse through large gaps between adjacent loops) largely limited its use to acute or threatened vessel closure. To address these deficiencies, a second-generation Gianturco-Roubin II (GR-II) stent incorporated a longitudinal spine to enhance radial and axial strength. For ease of manufacture, the desired geometry was actually cut from a flat sheet, and small dots of gold solder were placed at each end of the stent to enhance radiographic visualization. Although this design retained the excellent flexibility and deliverability of the original, the GR-II was still troubled by plaque prolapse and excessive recoil after deployment (up to 30% of cross-sectional area); this must be compensated by intentional oversizing of the delivery balloon (ratio of balloon to artery diameter, about 1.2) (24),(25), which may lead to edge dissections or even vessel perforation.

**Slotted Tubes**

In the mid 1980s, Palmaz introduced the concept of an endovascular prosthesis whose wall was made of offset rows.
of rectangular slots, each of which was plastically deformed into a “diamond” during expansion. In their expanded state, these diamonds (like the trusses of a bridge) made the stent relatively resistant to recoil and compression. The initial Palmaz prototypes, however, were relatively rigid and difficult to deliver through angulated guiding catheters or tortuous vasculature. Schatz therefore modified the original Palmaz design by breaking the 15-mm rigid length into two 7-mm segments joined by a 1-mm central articulation. When bare-mounted on an angioplasty balloon by the operator, the Palmaz-Schatz stent proved susceptible to being stripped off the balloon, leading to systemic embolization if the target lesion could not be crossed. To overcome this problem, a protective 5F delivery sheath was introduced in 1990 (Palmaz-Schatz Coronary Stent Delivery System, Cordis Corporation, Miami, FL); this helped to prevent snagging of the stent on coronary irregularities during advancement and precluded embolization during withdrawal if advancement across the lesion proves unsuccessful. Although this was the design released in 1994 and used for the pivotal randomized trials of stenting, this relatively inflexible stent and its bulky (5F) delivery sheath required large-lumen (more than 0.084-inch) guiding catheters, was difficult to deliver in tortuous anatomy or to distal lesions, and provided suboptimal scaffolding at the articulation site.

In an effort to preserve the radial strength and wall coverage of the tubular design but improve flexibility in the collapsed state, a number of newer (second- and third-generation) slotted-tube stents were developed. These included the modified Palmaz-Schatz geometry of the Crown (Cordis), the MultiLink and Duet (Guidant Corporation, Santa Clara, CA), and the NIR (Medinol, Israel) stent. Each involves laser cutting of a unique multicellular pattern into a metallic tube, which increases the overall flexibility of the stent by distributing bending throughout the stent length without compromising radial strength or elastic recoil (see later discussion). The newer stents have also been marketed in a broader range of stent lengths (8 to 32 mm) and diameters (2.25 to 6.0 mm) to facilitate stenting of long lesions, small vessels, saphenous vein grafts, and distal lesions. With better balloon materials and techniques for crimping and retaining the stent on the delivery balloon, the concept of a protective sheath has proved unnecessary. All current slotted tube designs are “bare mounted” on a delivery balloon, with deflated profiles smaller than 0.040-in. (1 mm), comparable with the best angioplasty balloons of only a few years ago.

Modular Stents

Despite enhanced flexibility, even second-generation slotted-tube stents are sometimes difficult to deliver through tortuous and noncompliant vessels. In an effort to enhance flexibility and deliverability without sacrificing the excellent scaffolding of the slotted-tube stents, the modular or hybrid stents are constructed by flexibly joining multiple, short repeating modules to each other. The initial modular stent was the MicroStent (Arterial Vascular Engineering, Santa Rosa, CA), in which 4-mm-long stainless steel corrugated ring subunits were welded to each other. Although this first-generation MicroStent was extremely deliverable, it was limited by low surface coverage and radial strength. Subsequent designs incorporated an elliptorectangular strut profile and reduced the length of the individual modules to 3 mm (Micro II), 2 mm (GFX), and 1.5 mm (S670), with further reductions in crossing profile and increased surface area coverage.

Self-Expanding Stents

The prototype self-expanding stent—the Wallstent (Boston Scientific, Minneapolis, MN)—is a direct descendent of the first coronary stent used in 1985. It is manufactured from 16 stainless steel wire strands that are woven together to form a mesh tube (Table 25.1; Fig. 25.1). The stent is positioned on the delivery system in its collapsed state, constrained by an outer membrane. Retraction of the membrane allows the stent to reassume its unconstrained (expanded) geometry, which can be reinforced by balloon dilatation within the stent, if necessary. In the original Wallstent design, a double-layer outer membrane rolled over itself during retraction but gave the delivery system a large diameter (5F); this has been replaced by a single-layer sliding membrane in current designs. In an effort to reduce thrombogenicity and the amount by which the stent shortens during delivery, 140,300,410 the braiding angle of the mesh wires has also been reduced by approximately 40° (the Less Shortening Wallstent). The present-generation Wallstent (the Magic Wallstent) incorporates a platinum core within the wires (to increase radioopacity), further modification of the braiding angles, and the ability to readvance the delivery sheath to recapture a partially deployed stent.

The Radius stent (Boston Scientific) is a self-expanding nitinol stent that makes use of the shape memory of the nickel-titanium alloy, nitinol. Once baked at high temperature in its expanded diameter, the superelasticity of this
material allows it to be compressed to small diameter and constrained by a membrane on the delivery catheter. The stent is placed within the target lesion and the membrane is withdrawn; the stent then springs back to its memory diameter. The advantage of this design over the Wallstent is the fact that minimal shortening takes place during expansion.

Self-expanding stents typically are selected to have an unconstrained diameter that is oversized by 0.50 to 1.0 mm relative to the diameter of the adjacent reference segment. This ensures contact with the vessel wall and increases the expansile force, but final optimization of stent expansion usually requires inflation of an angioplasty balloon within the stent. (The diameter of that balloon must never exceed the unconstrained stent diameter in air.) Although self-expanding stents are extremely flexible and can be delivered through tortuous vessels without risk of dislodgement, the difficulties relating to accurate sizing and precise placement necessitate a longer operator “learning curve” and render these stents unsuitable for the treatment of ostial lesions or involved side branches.

**FIG. 25.2.**

Early example of placement of a Gianturco-Roubin coil stent for threatened abrupt closure. A long lesion is present in the left anterior descending coronary artery (upper left), with a long dissection after angioplasty (upper right, open arrow). Placement of a coil stent (lower left) results in effacement of the dissection and elimination of the need for emergency bypass (lower right).

**INDICATIONS FOR STENTING**

**Acute or Threatened Closure**

Balloon expansion within an arterial stenosis causes luminal enlargement by overall vessel expansion and fracture of atheromatous plaque, but the combination of medial dissection and elastic recoil causes sufficient luminal compromise to culminate in abrupt vessel closure in roughly 5% of lesions treated by balloon angioplasty (see Chapter 23). One of the major benefits of stenting is the ability to definitively reverse abrupt closure due to dissection and recoil, and thus eliminate the need for high-risk emergency bypass surgery. A 518-patient multicenter registry of the Gianturco-Roubin FlexStent as a definitive treatment for acute or “threatened” vessel closure (local dissection, reduced antegrade flow, or clinical evidence of ongoing ischemia) was conducted from 1988 through 1991 (5) (Fig. 25.2). Although 95% of patients were successfully stented, 7.7% of patients with frank closure (and 2.7% of those with threatened closure) still required surgery, and there was an 8.7% incidence of stent thrombosis, particularly in smaller stents (2.5 mm or less).

Two small, randomized trials compared bailout stenting with prolonged inflations with perfusion balloons. In the Trial of Angioplasty and Stents in Canada (TASC II), patients with abrupt or threatened closure were randomly assigned to treatment with a perfusion balloon or stent placement (20). Even though about 25% of the patients assigned to balloon angioplasty crossed over to bailout stenting, the 6-month restenosis rate was significantly lower for stented lesions (22% vs. 50%). In the STENT-BY study, 100 patients were randomly assigned to prolonged balloon inflations or Palmaz-Schatz placement; they showed similar reductions in rate of target vessel revascularization at 6 months (24% vs. 65%) (21). Although bailout stenting is therefore a very effective technique (Fig. 25.3), the exponential growth in elective stenting during the past 5 years has left very few vessels that require bailout stenting, as the need for emergency bypass surgery to less than 0.5% between.

**FIG. 25.3.**

Stenting as definitive treatment for acute vessel closure. A high-grade stenosis is present in an angulated segment of the proximal right coronary artery (arrow). After balloon dilatation, a grade F dissection is seen (middle). After stent placement, normal flow is restored (right).

**Elective Stenting of Focal, De Novo Native Coronary Lesions**
This indication was used in two landmark studies-STRESS (11) and Benestent I (10)-to establish the ability of the Palmaz-Schatz coronary stent to significantly lower incidence of angiographic and clinical restenosis, compared with balloon angioplasty, in focal denovo lesions in 3- to 4-mm native coronary arteries (Table 25.2). These trials also confirmed that this benefit was a result of the ability of the stent to provide a larger acute lumen compared with balloon angioplasty. The strongest predictor of freedom from restenosis was a large posttreatment lumen diameter, and once posttreatment lumen diameter was incorporated into the statistical model of restenosis, there was not any independent effect attributable to the stent itself (22). Other randomized trials comparing stenting with balloon angioplasty (11) (10) have consistently demonstrated the superiority of stenting for focal, de novo lesions in 3- to 4-mm native coronary arteries.

The superior acute and long-term clinical outcomes reported in the STRESS and Benestent trials heightened the interest in evaluating stenting in other lesion subsets-chronic total occlusions, aortoostial location, and saphenous vein graft lesions-that respond poorly to conventional angioplasty due to marked elastic recoil, a predisposition to dissection, and high restenosis rates. Each of these “non-STRESS/Benestent” lesion categories is reviewed separately below.

**Saphenous Vein Graft Lesions**

The most common cause of recurrent ischemia after coronary artery bypass surgery is atheromatous degeneration within the body of the saphenous vein graft. Balloon angioplasty and atherectomy techniques have high rates of angiographic restenosis (40% to 50%) and long-term clinical failure (23–25), but early single-center registries suggested that stenting of saphenous vein graft lesions had lower rates of angiographic restenosis (17% to 25%) and repeat revascularization of the target site (26),(27). This finding was evaluated further in the randomized SAphenous VEin graft Disease (SAVED) trial (28), which compared Palmaz-Schatz stenting with balloon angioplasty for treatment of relatively focal, de novo lesions in 3.0- to 5.0-mm saphenous vein grafts. Stenting had greater technical success (residual stenosis less than 50% by QCA, 95% vs. 75%); greater procedural success (technical success in the absence of a major adverse event, 92% vs. 69%); and a lower incidence of adverse clinical events (death, MI, or subsequent revascularization, 26% vs. 38%). Although the angiographic restenosis rates were not statistically different (due to inadequate sample size), the incidence of major adverse events was significantly reduced in stented patients (26% vs. 38%).

The lack of stents that could be expanded beyond 4 mm, however, limited the ability to treat many vein grafts. One option for treatment of large grafts was to use hand-crimped larger Palmaz-Schatz biliary stents (Cordis) which could be expanded up to 6 mm (50). With the development of longer stents and those that can be expanded beyond 4 mm (e.g., the Wallstent and the nine-cell NIR stent [Boston Scientific]), vein graft stenting has become easier, although there are still issues relating to “no reflow” and distal embolization (see Chapter 23). Finally, even though the incidence of repeat revascularization triggered by failure of the stented site is low (less than 20%), the incidence of clinical events approaches 50% by 5 years owing to progression of disease at nontarget sites within the treated graft, as well as attrition of other grafts and progression of native coronary disease (26).

**Restenosis After Previous Angioplasty**

Retreatment of lesions that have restenosed after previous angioplasty generally has a higher incidence of recurrent restenosis, even after correction for confounding factors such as diabetes mellitus or small reference vessel diameter that might have predisposed to the original restenosis (29). The subset of such patients undergoing treatment of restenotic lesions in the TASC I trial had a significantly lower incidence of repeat revascularization (4.5% vs. 25%) than those in the percutaneous transluminal coronary angioplasty (PTCA) cohort (30). Similarly, the Restenosis Stent Study (REST) randomly assigned 383 patients with prior restenosis to either balloon angioplasty or the Palmaz-Schatz stent and found reductions in angiographic restenosis (18% vs. 32%) and subsequent need for revascularization of the target vessel (10% vs. 27%) with stenting (19). Using aspirin and ticlopidine, Colombo reported an angiographic restenosis rate of 25% with a low (0.8%) incidence of subacute thrombosis in patients with prior restenosis (31).

**Chronic Total Occlusions**
Balloon angioplasty of chronically occluded coronary arteries is associated with a high incidence (approximately 50%) of restenosis, reocclusion, and recurrent symptoms, compared with treatment of subtotal stenoses (see Chapter 23). Three randomized trials have compared stenting with conventional balloon angioplasty alone for treatment of chronic total occlusions. In the Stenting in Chronic Coronary Occlusion (SICCO) trial, which compared balloon angioplasty with Palmaz-Schatz stenting for treatment of chronic total occlusion in native coronary arteries, a lower incidence of both angiographic restenosis (32% vs. 74%) and target vessel revascularization (22% vs. 42%) was found with stenting (21),(32). The Gruppo Italiano di Studio Stent Nelle Occlusioni Coronariche (GISSOC) trial also showed a lower incidence of restenosis (32% vs. 68%), reocclusion (8% vs. 34%), and target lesion revascularization (5% vs. 22%) in patients assigned to stenting (33). Likewise, in the Total Occlusion Study of Canada (TOSCA), angiographic restenosis and target vessel revascularization were reduced in patients treated with stents compared with conventional angioplasty (34).

Acute Myocardial Infarction

With the completion of several large registries and randomized trials of acute MI demonstrating better outcomes in patients treated with primary angioplasty rather than thrombolytic therapy, “mechanical reperfusion” has become the preferred treatment for acute MI in many institutions (see Chapter 23). Despite successful initial reperfusion, however, there is a 10% to 15% incidence of reocclusion and a 30% to 50% incidence of restenosis after primary angioplasty (35),(36). Although the presence of acute MI was initially considered to be a contraindication to stent placement (because of concerns that this prothrombotic milieu would be associated with an unacceptably high incidence of acute thrombosis), the use of stents to treat suboptimal results and as “upfront” therapy in the treatment of MI has now become widespread. Bauters and colleagues showed that stenting of the infarct-related artery is associated with reduction in the incidence reocclusion (1% vs. 14%) and restenosis (27% vs. 52%) compared with balloon angioplasty (37). Data from several small randomized trials have also suggested that stenting may offer acute and long-term benefits (primarily a reduction in repeat revascularizations) compared with balloon angioplasty alone (38–41) (35) (36).

It is less clear that routine stenting of infarct vessels improves already good acute outcomes. The large Stent Primary Angioplasty in Myocardial Infarction (Stent-PAMI) study (balloon angioplasty vs. heparin-coated Palmaz-Schatz stent) randomly assigned 900 patients with acute MI to either PTCA alone or stenting with the heparin-coated Palmaz-Schatz coronary stent. Although patients assigned to stenting had a lower incidence of recurrent ischemia with ST-segment elevation during hospitalization (1.2% vs. 3.5%), angiographic restenosis (12.8% vs. 21.9%), and target vessel revascularization by 6 months (16.3% vs. 20%) (42), they more commonly exhibited reduced posttreatment TIMI flow compared with balloon angioplasty. This question is being evaluated further in the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC), in which patients with acute MI are randomly assigned to stenting (vs. PTCA) and then to abciximab (vs. heparin alone).

Long Lesions

Lesion length is associated with an increased incidence of acute complications and restenosis after conventional balloon angioplasty, as well as directional and rotational atherectomy (43–45). Early randomized trials (e.g., STRESS, Benestent) excluded lesions longer than 15 mm because of the lack of availability of longer stents and the concern that placement of multiple overlapping stents would be associated with a high incidence of subacute thrombosis and restenosis. With the availability of longer stents, improvements in stenting technique, and use of antiplatelet therapy, stenting of longer lesions and diffusely diseased arteries has become a viable option. In the early multicenter registry, lesions treated with multiple Palmaz-Schatz coronary stents had a 65% rate of restenosis (46) and an 8.9% incidence of subacute thrombosis (47). Despite high-pressure dilatation and use of antiplatelet therapy in more than 7,000 patients enrolled in five recently completed stent trials, Cutlip and colleagues found that total stent length was independently associated with stent thrombosis, with an odds ratio of 1.2 for each additional 10 mm of stent placed (48).

The pivotal question remains whether stenting will have any impact on the high rates (more than 50%) of restenosis observed with balloon angioplasty or atheroablative techniques in such lesions. Single-center and registry data suggest an almost linear relation between stent length and restenosis even with contemporary stenting techniques (49). Although total stent length is associated with increased risk for clinical and angiographic restenosis, it is uncertain...
whether total stent number or the ratios of stent to lesion length also independently affect restenosis. In the multicenter randomized trial comparing the GR-II stent (Cook) to the Palmaz-Schatz stent, the stent-to-lesion ratio was significantly greater (2.5 vs. 1.9) for patients randomly assigned to the GR-II cohort despite similar baseline lesion lengths, which may have contributed to the higher incidence of restenosis (47% vs. 21%) with that device (50). Similarly, data from Albiero and colleagues suggest that high stent-to-lesion ratios are associated with high rates of restenosis (37% to 40%) in both discreet and long lesions (51). This has led some to advocate the use of “spot stenting,” whereby aggressive balloon angioplasty or rotational atherectomy is performed in diffusely diseased segments and short stents are placed only in areas of high residual plaque burden or residual stenosis exceeding 20% (52). With current devices, it seems that both lesion length and stent length exert an independent effect on subsequent restenosis (53).

Small Vessels

Small (less than 3.0 mm) vessels were formally excluded from the early randomized stent trials (8), although a significant number of vessels in both the STRESS and Benestent trials were actually smaller than 3.0 mm by quantitative coronary angiography (most between 2.75 and 3.0 mm). Most trials have suggested a higher incidence of subacute thrombosis and restenosis for stenting in vessels smaller than 3 mm compared with larger vessels. Despite this higher risk, there are emerging data from subgroup analyses of the randomized “stent versus PTCA” trials to suggest that stenting of vessels smaller than 3.0 mm may be associated with better clinical and angiographic outcome compared with balloon angioplasty (Table 25.4) (10,11,54–56). It must be cautioned, however, that good trials comparing stenting with balloon angioplasty in small vessels are lacking, and that the current stent systems for vessels 2.5 mm and smaller are based on the abrupt closure indication rather than elective stenting in these vessels. Finally, there is the unproven hope that stents specifically designed for smaller vessels, such as the MiniCrown (Cordis), may result in benefit from lower metal coverage with correspondingly lower restenosis rates.

Aortoostial Lesions

True aortoostial lesions extend proximal to the coronary ostia into the walls of the aorta, where abundant elastic fibers contribute to elastic recoil and poor outcome (57). By resisting recoil, stents may provide significantly larger lumens and lower the risk of restenosis in this lesion subset. Although randomized trials comparing stenting with balloon angioplasty or atherectomy techniques as a treatment for aortoostial lesions have not been performed, Rocha-Singh (58) reported a restenosis rate of 27.8%, and Rechavia (59) a repeat revascularization rate of only 9% after stent placement. Accurate stent placement and expansion in the ostium is often technically challenging, however, because the lesion must be covered completely without excessive protrusion of the stent into the aortic lumen. This is aided by the use of an angiographic projection that shows the coronary ostium and wall of the aorta in profile, by the use of a radioopaque stent, and by first debulking the lesion with rotational atherectomy (see Chapter 24). These techniques have allowed successful treatment of left main as well as ostial right coronary lesions (60–63), although the risk of restenosis of an “unprotected” left main lesion manifesting as sudden cardiac death is a concern (see Chapter 23).

Bifurcation Lesions

Lesions involving the bifurcation of a coronary artery and a major side branch are associated with increased procedural complications and poor long-term outcome owing to recoil and plaque shifting at the origin of the side branch (64). Dauerman and colleagues (65) demonstrated that atherectomy debulking of such lesions (see Chapter 24) reduces the need for subsequent revascularization, but optimal performance may be technically demanding. Other investigators have explored a number of approaches to stenting of bifurcation lesions (Fig. 25.4). If the parent vessel is large and the side branch is relatively small, a stent can simply be deployed across the side branch, and the compromised side branch can be “rescued” by balloon dilatation out through the wall of the stent, using a low-profile balloon positioned half in the parent vessel and half in the jailed side branch.
Various techniques for stenting bifurcation stenoses. A: A typical bifurcation lesion with involvement of both the main vessel and the side branch. B: Stenting of the main vessel (1) with side branch rescue by dilatation through the stent struts (2). C: T-stent technique with initial placement of a stent in the side branch (1) followed by a second stent (2) in the parent vessel. Note the nonstented gap (*) caused by a side branch angle less than 90°. D: Kissing stents with simultaneous placement of two stents that then run side-by-side in the main vessel proximal to the bifurcation. E: Reverse T-stenting with placement of the main vessel stent and rescue as per B, but with placement of a second stent (2) into the side branch through the dilated cell of the parent vessel stent. F: Culotte stenting, in which the stent is placed in one vessel first (1), the side branch is dilated (as per B), and a second stent is placed into the side branch (as per E) but extending well into the proximal vessel (2). The procedure is completed (3) by dilating back into the main vessel through the side of the second stent (or with a kissing balloon inflation). None of these techniques is completely reliable, and their complexity and high restenosis rates lead us to favor debulking approaches for most such lesions (see Chapter 24).

When both the parent vessel and the side branch are large (more than 2.5 mm) and involved in the bifurcation lesion, optimal treatment may require stenting of both. With the “T stent” technique, a stent is deployed at the ostium of the side branch, followed by a second stent in the parent vessel. Unless the angle of origin of the side branch is 90°, however, the operator is faced with the dilemma of whether it is better to leave a portion of the ostial side branch lesion unstented, or risk having part of the stent protrude into the parent vessel (making subsequent advancement of the parent vessel stent difficult or impossible). The “culotte” technique involves placement of a stent into the side branch with extension into the proximal aspect of the parent vessel. A wire is then passed through the side of this stent and into the distal parent vessel. After balloon dilatation, a second stent is passed into the distal vessel through the side of the first stent, so that the proximal ends of the first and second stents overlap in the proximal vessel. Ideally, this and other bifurcation stent approaches should be finished by “kissing balloon” inflations-simultaneous inflation of balloons in the main and branch vessel-to optimize both lumens (66). Other approaches to stenting of bifurcation lesions include placement of “kissing” stents, whereby stents are simultaneously deployed in the parent vessel and side branch, allowing the operator to shift the “carina” or bifurcation more proximally in the vessel. All of these techniques are technically difficult and may result in significant difficulty in accessing the parent vessel or side branch because of overlapping metallic elements. Future purpose-specific bifurcation stents such as the Bifurcate Stent (AVE, Santa Rosa, CA) or the Jostent Bifurcation stent (Jomed International, Helsingborg) may facilitate treatment of this problematic subset and provide more durable long-term results (66a).

**FIG. 25.5.**

Unusual applications of stenting. A: Stenting of a severe muscle bridge. Upper panels show the left anterior descending (LAD) coronary artery in diastole and compressed in systole. Hemodynamic significance was established by thallium scintigraphy and Doppler flow wire. In the lower panels, systolic compression has been eliminated by placement of a 3.5 × 32 mm NIR stent within the bridged segment. B: Stenting as treatment for refractory coronary vasospasm. A young woman developed intermittent chest pain associated with reversible T-wave inversions in the precordial leads despite calcium blockers and nitroglycerin. Top: Angiography demonstrated a high-grade stenosis in the proximal LAD (left), which improved after intracoronary nitroglycerin administration (right). Top, inset: Intravascular ultrasound revealed moderate, eccentric soft plaque. Angiography and intravascular ultrasound after placement of a Crown stent.

**Intramyocardial Bridging and Refractory Coronary Vasospasm**

Systolic compression of a coronary artery that courses within the myocardium is a common observation during coronary angiography and occasionally causes myocardial ischemia (see Chapter 13). Using the Doppler flow wire, Klues and colleagues (67) demonstrated that severe myocardial bridging is characterized by abrupt acceleration of diastolic flow velocity, followed by a mid-diastolic plateau, and retrograde systolic flow. In 12 patients, these alterations in coronary flow were completely normalized and all patients symptomatically improved after stent placement (Fig. 25.5A). Stent placement has also been used successfully to treat coronary vasospasm refractory to vasodilators (68) (Fig. 25.5B).

**Multivessel Stenting**
In the past decade, six multicenter, randomized trials compared outcomes after multivessel balloon angioplasty and coronary artery bypass grafting (See Chapter 23) and failed to demonstrate a significant difference in mortality among patients randomly assigned to either mode of revascularization. All of these trials, however, showed a significantly higher incidence of recurrent angina and need for repeat revascularization within the first year after multivessel angioplasty. After multivessel stenting, approximately a 1-year event-free survival rate of 80% has been reported (69–71), and the randomized ARTS trial has confirmed a reduction of roughly 50% in the incidence of excess repeat revascularization procedures, compared with initial surgical treatment, when multivessel stenting is used instead of conventional balloon angioplasty.

COMPARISONS AMONG STENTS

Approval of the first-generation (Gianturco-Roubin and Palmaz-Schatz) stents was based on the knowledge that they reduced the incidence of emergency surgery for abrupt closure and the rate of restenosis after elective stenting of favorable lesions (see earlier discussion). Once the improved second-generation stent designs were ready for testing (1995–1998), the success of the early stents meant that operators were no longer willing to compare a new stent against balloon angioplasty in a randomized trial. To meet the FDA's requirement for a randomized pivotal trial, a new “stent versus stent” design was developed to show that a new stent was “equivalent” to the gold-standard Palmaz-Schatz design. A number of such randomized studies-ASCENT (MultiLink), NIRVANA (NIR), SMART (MicroStent II), EXTRA (XT), WINS (Wallstent), PAS (Paragon), SCORES (Radius), and BEST (BeStent)-were performed to compare newer investigational stents with the Palmaz-Schatz coronary stent, using an “equivalency” design (Table 25.5) (71–75). Only the GR-II stent (whose stent recoil, undersizing, and excessive stent length appear to have contributed to higher restenosis rates) failed to show equivalency, but none of the new stents showed significantly better performance than the Palmaz-Schatz stent. In part, this was a result of the inclusion of only lesion types that were stentable with the original Palmaz-Schatz stent. The most technically challenging patient and lesion subsets (e.g., severe calcification and tortuosity), which form such a large part of stent placement in today's practice, were excluded. This explains why the second-generation stents have completely replaced the Palmaz-Schatz stent in clinical practice since the mid-1997 approval of the MultiLink. Although study-to-study differences in patient and lesion complexity factors preclude direct comparison of one new stent with another, the stent-versus-stent studies have provided a broad database about acceptable stent performance that can be used to develop objective performance characteristics for stent approval, akin to those now used to approve new heart valves.

COMPLICATIONS OF STENTING

Thrombotic and Hemorrhagic Complications

Surface charge, surface texture, and surface energy all contribute to the thrombogenic potential of metallic endovascular prostheses. Although all stents attract platelets, they then undergo passivation as proteinaceous material is deposited on metallic surfaces, thereby altering the resting potential of the alloy (76).

At 9 to 12 days after stent placement, a neo-intima composed of macrophages and Alpha-actin–negative spindle cells (77) forms over this initial coating and reduces the risk of stent thrombosis.

Early Experience

Based on animal work, the original stent regimen was a combination of antiplatelet agents (aspirin, dipyridamole, and low-molecular-weight dextran). However, the incidence of stent thrombosis was still 16% to 20% for the early Palmaz-Schatz and Wallstent data (3),(9). This prompted the addition of uninterrupted anticoagulation (a transition from intravenous heparin to warfarin therapy sufficient to prolong the prothrombin time to 16 to 18 seconds, for 4 to 8 weeks) in the multicenter Palmaz-Schatz registry and subsequent early randomized trials. Although this regimen reduced the incidence of stent thrombosis to 3%, results were less satisfactory in bailout indication, stenting of small vessels, residual thrombus or dissection after stent placement, presence of inflow or outflow obstruction, incomplete stent expansion, and subtherapeutic anticoagulation (4,5,78–80). And the combination of aggressive antiplatelet and anticoagulation therapies increased the duration of hospitalization (8 vs. 3 days) and increased the incidence of hemorrhagic complications (14% vs. 3%) compared with balloon angioplasty (10),(11).
Contemporary Experience

A major breakthrough in understanding the pathogenesis of stent thrombosis by Colombo was the demonstration that most stents (approximately 80%) with an excellent angiographic appearance after low-pressure deployment were seen to be incompletely expanded by IVUS (13) (see Chapter 19). Only after high-pressure (18 to 20 atm) dilatation within the stent were full stent expansion and full apposition of struts to the vessel wall observed. Using this strategy of ultrasound-guided high-pressure dilatation, it appeared that antiplatelet therapy alone (with aspirin and ticlopidine) was sufficient to reduce stent thrombosis to less than 1%. This was confirmed in a large, multicenter French registry (81) and in a series of randomized trials (Table 25.6) (14,15,82–84) that demonstrated reduction in subacute thrombosis to 0.6% after optimal stent expansion followed by aspirin and ticlopidine for 4 weeks. In addition, the timing of subacute thrombosis was shortened, from a median of 6 days with coumadin-containing regimens, to 1 to 2 days (84a). The incidence of groin complications, which had fallen with better sheath removal strategies even before the switch away from coumadin (see Chapter 4) was not reduced further, but the length of stay fell to approximately 2 days with aspirin and ticlopidine therapy.

Ticlopidine, however, has a delayed onset of action (up to 3 days), causes rash and gastric upset in many patients, and is associated with neutropenia in about 1.5% of patients and life-threatening thrombotic thrombocytopenia purpura in a small minority of patients (85). These shortcomings have led many investigators to substitute a related platelet adenosine diphosphate–receptor antagonist (clopidogrel) for ticlopidine. The theoretic advantages of clopidogrel include the ability to achieve a high level of platelet inhibition after an oral loading dose, the absence of a significantly higher incidence of bone marrow suppression compared with aspirin alone, a low incidence of gastrointestinal and dermatologic side effects, and the convenience of once-a-day dosing (86). Moussa and colleagues found no significant difference in the incidence of stent thrombosis or major adverse cardiac events in patients treated with ticlopidine or clopidogrel after stenting (87). However, the incidence of side effects was significantly lower in patients treated with clopidogrel (5.3% vs. 10.6%). Randomized trials comparing outcome in patients treated with ticlopidine versus clopidogrel have failed to show a significant difference between these two agents, and most centers have switched to the better tolerated clopidogrel (88).

One circumstance has remained constant is that stent thrombosis, when it occurs, causes dire clinical consequences. In the STRESS trial, subacute thrombosis was associated with a 20% mortality rate; all patients had a major complication (either death, Q-wave MI, or emergency bypass surgery) (89). In the contemporary era, the 7,170-patient Cardiovascular Data Analysis Center database shows that 78% of patients with stent thrombosis experienced an acute MI, with a 30-day mortality rate of 15% and a 6-month rate of 19% (48). When thrombosis does occur, recanalization of the occluded stent was possible in 90% of patients by emergency balloon angioplasty or rheolytic thrombectomy (see Chapter 24), often in conjunction with administration of a platelet glycoprotein IIb/IIIa receptor antagonist (90). In patients who are at high risk because of either patient-related factors (e.g., hypercoagulable state, thrombocytosis) or lesion-related factors (e.g., long stents, bifurcation lesions [Fig. 25.6], residual dissection, small vessels, reduced final lumen diameter, slow flow), the addition of an intravenous platelet glycoprotein IIb/IIIa receptor antagonist is strongly recommended. In the future, the use of coatings with antithrombotic or antiplatelet activity may further reduce the incidence of stent thrombosis. In four studies, the use of the heparin-coated Palmaz-Schatz coronary stent (Cordis) was associated with a low incidence (0% to 0.8%) of stent thrombosis (18,55,91,92). Further studies must be performed to determine whether these benefits will also be seen when this device is placed for more challenging lesion subsets, such as small vessels or long lesions.

FIG. 25.6.

Stent thrombosis 10 days after “T-stenting” the bifurcation of the left circumflex and its obtuse marginal branch (top, left). The lesion is crossed with a hydrophilic guidewire and an infusion catheter to establish extent of thrombus and exclude passage under stent struts (top, center). The Possis Angiojet is positioned distal to the bifurcation (top, right). After aspiration with the Angiojet, antegrade flow is restored and filling defects are no longer apparent (bottom, left). However, flow is decreased in the atrioventricular groove portion of the bifurcation (arrow). Kissing balloon angioplasty is performed (bottom, middle), restoring normal flow in both branches (bottom, right).

In-stent Restenosis
Despite overwhelming evidence that stenting reduces restenosis compared with conventional angioplasty alone, the exponential growth in stent usage has led to new challenges in the treatment of in-stent restenosis. Restenosis after stent placement is caused almost exclusively by smooth muscle hyperplasia (93), superimposed on a small amount of initial recoil. Although this proliferative response peaks at 8 weeks in dogs (94), serial angiographic and angioscopic studies in humans demonstrate that the greatest proliferation occurs between 1 and 6 months after placement, with only a small fraction of stents exhibiting further narrowing between 6 and 12 months (95–97). Thereafter, the proliferating smooth muscle cells are replaced by relatively inactive ground matrix and fibrosis. This transformation of the neointima from active proliferation to a quiescent, fibrotic matrix also explains the extremely low incidence (less than 2%) of late (more than 1 year) target site revascularization observed clinically (98).

Effect of “Optimal” Stenting Techniques

Although the risk of restenosis after stenting is clearly influenced by biologic factors such as diabetes mellitus and unalterable geometric factors such as small vessel size, there is a clear relationship between the immediate poststent lumen diameter and the freedom from subsequent restenosis. It is therefore up to the operator to achieve an optimal lumen at the time of stent deployment despite any lesion resistance and elastic recoil. The difficulty in achieving this goal is reflected in the findings of poststent IVUS, which can show poor expansion and apposition of stents that are apparently well deployed angiographically. Achieving an in-stent minimal cross-sectional area equal to at least 55% of the average (proximal/distal) reference cross-sectional area reduces the chance of subsequent restenosis by almost one half, compared with failure to do so (99). Other IVUS criteria have been proposed (see Chapter 19) based on large studies including the Angiography Versus Intravascular Ultrasound Directed Coronary Stent Placement (AVID) trial, the Strategy of ICUS Guided PTCA and Stenting (SIPS) trial, the Optimization with ICUS to Reduce Stent Restenosis (OPTICUS) trial, the Restenosis after IVUS-guided Stenting Trial (RESIST), and the Can Routine Ultrasound Influence Stent Expansion (CRUISE) substudy of the STARS trial. These studies have addressed whether routine use of IVUS guidance is associated with improvements in angiographic and clinical outcome after stenting (Table 25.7). In the RESIST, AVID, and CRUISE studies, IVUS-guided stenting was associated with slightly larger stent minimum lumen diameters or cross-sectional areas, but the clinical benefit has been less consistent. Given the added expense and time, formal recommendations regarding routine use of IVUS guidance for stenting cannot be made until the final long-term results from these studies are available and the criteria for optimal stenting are standardized.

One alternative is to perform physiologic assessments of stent deployment, measuring coronary flow reserve or the transstent pressure gradient at peak flow (see Chapter 18). Hanekamp and colleagues showed that a fractional flow reserve of 0.94 or more (measured with a pressure wire) was highly correlated with IVUS-derived parameters of optimal stenting (100). Preliminary observations with coronary flow reserve have also suggested that reduced coronary flow reserve (less than 2.5) after stenting may be associated with major adverse events at 6 months (101).

Despite these measures, 20% to 40% of stents fail to meet criteria for optimal expansion (102),(103). Factors contributing to this problem of inadequate stent expansion include balloon underexpansion and acute stent recoil. Although it was originally thought that stents eliminated elastic recoil, more recent data show 7% to 15% diameter recoil after deflation of the deployment or postdilating balloon (104),(105) (Fig. 25.7). To achieve the desired luminal diameter or area, the deployment or postdilating balloon must stretch the stent approximately 10% beyond the desired diameter (e.g., 3.3 mm for a final 3.0 mm result), which is one of the effects produced by inflating a semicompliant balloon to 14 to 16 atm. Contrary to early uncontrolled data, there is no evidence that such high-pressure stent expansion increases the incidence of subsequent restenosis (106), so current practice favors deployment at this pressure level.

FIG. 25.7.

Acute cross-section area (CSA) recoil for four different stents, as measured in normal porcine arteries using a 0.018-inch ultrasound imaging probe within the deployment balloon. (From Carrozza JP Jr, Hosley, SE, Cohen DJ, Baim DS. In-vivo assessment of stent expansion and recoil in normal porcine coronary arteries: Differential outcome by stent design. Circulation 1999;100:756, with permission).
In vessels with bulky eccentric or fibrocalcific plaques, balloon underexpansion may account for more than 20% of the discordance between expected and measured balloon cross-sectional area. In such lesions, vascular compliance may be improved by removing plaque from the lesion through pretreatment with high-speed rotational atherectomy (107) (see Chapter 24), thereby lowering the incidence of target vessel revascularization compared with stenting alone (Figs. 25.8 and 25.9). There is also preliminary evidence that debulking of large eccentric plaques with directional atherectomy before stenting reduces the amount of in-stent proliferation and lowers the incidence of angiographic restenosis (108),(109). These techniques are being evaluated in the randomized SPORT (using rotational atherectomy) and AMIGO (using directional atherectomy) trials.

**FIG. 25.8.**

Rota-stenting. A long, calcified stenosis is present in the left anterior descending coronary artery (top, left). After application of the rotational atherectomy burr (top, right), a smooth lumen with significant residual stenosis is present (bottom, left). After stent deployment, excellent expansion is observed (bottom, right). Without Rotablator pretreatment, stent passage and full stent expansion would each have been unlikely.

**FIG. 25.9.**

Rota-stenting for “protected” left main coronary artery lesion. Top: Severe stenosis in the distal left main, which supplies only the left anterior descending coronary artery, given a patent graft to the circumflex (not shown). Upper center: 1.75 mm Rotablator burr. Lower center: After rotational atherectomy, there is modest lumen improvement but enhanced lesion compliance. Bottom: After stent placement, excellent lumen dimension is established.

**Pharmacotherapy to Reduce In-stent Restenosis**

A number of agents-including heparin, angiopeptin, angiotensin-converting enzyme inhibitors, and antioxidants-have shown promise in reducing the exuberant proliferative response evoked by stenting in experimental models. However, there are few data available that support their efficacy in reducing the incidence of human in-stent restenosis. Although data from the EPIC trial suggested that the platelet glycoprotein IIb/IIIa receptor antagonist abciximab might be associated with a reduction in restenosis after balloon angioplasty, preliminary observations from the randomized ERASER trial showed no reduction in neointimal volume or restenosis after stenting with abciximab (110). In the larger EPISTENT trial, only diabetic patients who underwent stenting had a lower incidence of 6-month clinical restenosis events with abciximab (90). Given the difficulty in achieving high tissue concentrations of an agent administered systemically, local delivery may be required to place therapeutic levels of effective agents directly into the arterial wall. However, in neither the HIPS trial (using intraarterial heparin) nor the ITALICS (intraarterial antisense oligonucleotides against c-myc) study was active therapy associated with reductions in restenosis after stenting, compared with placebo (111),(112).

**Treatment of In-stent Restenosis**

Luminal narrowing within stents follows a Gaussian distribution (30). In patients without recurrent symptoms or provokable ischemia, mild to moderate degrees of in-stent restenosis (40% to 70% diameter stenosis) are associated with a favorable long-term prognosis and therefore can be treated with medical therapy alone (113). When in-stent restenosis results in recurrent coronary ischemia, however, treatment is indicated. The initial experience in treatment of in-stent restenosis involved balloon dilatation within the stent. The procedural success rate was almost 100%, and because the metallic struts were not reexposed to blood elements anticoagulation was not necessary (114), but the rate of recurrent restenosis exceeded 50% for dilatation of diffuse in-stent restenotic lesions (115),(116). One reason is that much of the hyperplastic material that has been compressed and extruded through the stent struts returns to the stent lumen within 30 minutes after the final balloon inflation (117). In an effort to improve on the suboptimal long-term results of diffuse in-stent restenosis, several groups have investigated the strategy of plaque removal from within the stent before balloon dilatation, using atheroablative techniques (see Chapter 24). Dauerman (118) and Sharma (119) reported a larger initial lumen and reduction in subsequent target vessel revascularization (from 46% to 26–28%) in lesions treated with rotational atherectomy compared with balloon angioplasty alone. Similar results have
also been reported after directional atherectomy (see Chapter 24) or excimer laser angioplasty (120–122). Although controlled, randomized clinical trials using less aggressive debulking and postplacement dilatation have not uniformly confirmed this benefit, the preponderance of evidence favors the concept that strategies incorporating tissue removal (rather than plaque compression alone) result in larger posttreatment lumen diameters and lower rates of target vessel revascularization.

Despite these reductions in repeat revascularizations observed with debulking of in-stent restenosis, almost 30% of these patients require additional interventions to treat this aggressive proliferative response. Because recurrent luminal narrowing after stenting is almost entirely the result of a smooth muscle cellular proliferative process, therapies such as radiation that are effective in the treatment of other benign proliferative disorders (e.g., Graves’ exophthalmos, keloid formation) are particularly attractive. Teirstein demonstrated a marked reduction in angiographic restenosis (17% vs. 54%), target lesion revascularization (12% vs. 45%), and major adverse cardiac events (19% vs. 62%) in patients treated by Gamma-irradiation with iodine 192 after stent placement (123). These dramatic benefits of Gamma-irradiation were confirmed in the larger, multicenter Gamma 1 study (124) and the Washington Radiation for In-Stent Restenosis Trial (WRIST) study. The long-term outcome of patients with in-stent restenosis was also favorably influenced by Beta-radiation with a 47% reduction in angiographic restenosis (46% to 24%), and a 34% reduction in target vessel revascularization (24% to 16%) in the active arm (124a). Although randomized trials of primary irradiation have not been completed, data from the Beta Energy Restenosis (BERT) trial using an encapsulated strontium 90/yttrium (source (Beta-Cath, Novoste Corporation, Norcross, GA) also suggested a reduction in late loss and restenosis (15%) after balloon angioplasty (125). The effect of primary irradiation on restenosis after initial angioplasty or stenting is currently being studied.

**Side Branch Occlusion**

In the early experience with the Palmaz-Schatz stent, Fischman et al. (126) and Iniguez et al. (127) reported a 5% incidence of acute branch occlusion when the stent was placed across a major (more than 1 mm) side branch. In all such cases, ostial stenoses greater than 50% had been present in the involved side branch. Although such side branch occlusion had a low morbidity in these series, it should be noted that stenting across large, diseased side branches was specifically avoided and that stent-induced occlusion of a large side branch clearly may result in significant myocardial ischemia. Because stenting may induce vasospasm in the involved side branch, administration of intracoronary nitroglycerin alone is sometimes adequate to restore normal flow. More commonly, side branch compromise results from the “snowplow” mechanism—shifting of plaque during stent deployment or high-pressure dilatation. If significant ischemia persists, a guidewire can be advanced out through a stent cell and into the effected side branch, to allow advancement of a low-profile angioplasty balloon catheter. The proximal end of the balloon catheter should always be kept in the parent vessel, to avoid the risk of entrapment in the side branch (128). The size of side branch dilatation may be limited by stent cell size (e.g., NIR, Palmaz-Schatz stents), and elastic recoil commonly observed at the origin of side branches may contribute to a high likelihood of repeat restenosis. If restenosis of a “jailed” side branch occurs, rotational atherectomy can safely be performed through the side of previously dilated stent cells to improve acute angiographic appearance (Fig. 25.10).

**FIG. 25.10.**

Rotational atherectomy of a restenotic branch “jailed” by an NIR stent in the left anterior descending coronary artery (top, left). A 2.15-mm Rotablator Burr is seen positioned just proximal to the stent (top, middle). After rotational atherectomy through the side of the stent, significant luminal enlargement is seen (top, right). Kissing balloon angioplasty (bottom, left) is performed, resulting in a large lumen in both the left anterior descending and diagonal arteries (bottom, right).

**Stent Embolization**

In the initial multicenter registry, in which the Palmaz-Schatz coronary stent was hand-mounted on a conventional angioplasty balloon and no sheath was used, stent embolization occurred in 2.5% of patients. There were no reported clinical sequelae (9), but clearly every effort should be made to avoid this complication. Sheathed delivery systems,
such as the Palmaz-Schatz Stent Delivery System (Cordis) or the Sheathed MultiLink System (Guidant), reduce the chance of embolization but may impede delivery owing to their large profiles. Present-generation bare stents have significantly higher crimp strength and unique attachment features (e.g., NIR on Sox system, Boston Scientific), retentive balloon coatings (e.g., Power Grip balloon, Cordis) or nesting of the stent into the balloon material, which improve stent retention. Nevertheless, virtually any stent may be dislodged from the balloon if it catches on the edge of the guiding catheter during forceful retraction after unsuccessful placement. If guidewire position has been maintained in the distal coronary artery, the delivery balloon or another low-profile balloon may be placed back through the stent, allowing it to be repositioned across the target lesion. If the stent cannot be repositioned, the balloon can be placed distal to the stent and inflated to trap the stent between the balloon and guiding catheter as they are withdrawn into the descending aorta and recovered into the sheath. If guidewire position has been lost and the unexpanded stent is located in a proximal portion of the coronary artery or has embolized into a peripheral artery, it may be removed by use of a variety of snare devices. Alternatively, a second stent may be expanded adjacent to the dislodged stent to trap it against the vessel wall and effectively exclude it from the lumen. If the stent cannot be removed or effectively “excluded” from the coronary lumen, strong consideration should be given to referring the patient for coronary artery bypass surgery.

Incomplete Expansion

Incomplete stent expansion may result from rupture of the delivery balloon or failure of the balloon to be expanded adequately in calcified or fibrotic vessels. The risk of incomplete expansion is significantly higher during “primary stenting,” when the operator deploys a stent without predilation or debulking. This practice is therefore best avoided in heavily calcified vessels or when deploying long stents. In such vessels, full stent expansion may be achieved at lower balloon pressures when the vessel is pretreated with rotational atherectomy.

When the delivery balloon ruptures before the stent is embedded adequately in the vessel wall, further expansion can be achieved by rapidly increasing pressure within the balloon using a power injector or a conventional manual inflation device. A new noncompliant balloon can then be placed within the stent to achieve full expansion. If the stent is markedly underexpanded at the end of the procedure, the administration of a platelet glycoprotein IIb/IIIa receptor antagonist may reduce the risk of stent thrombosis.

Perforation

Although the routine use of high-pressure postplacement dilatation improves stent expansion, the significant barotrauma imparted to the vessel may result in frank perforation (129). In a retrospective analysis, Ellis and colleagues documented a 0.1% incidence of perforation (130). Colombo showed that high-pressure dilatation of appropriately sized balloons (balloon-artery ratio, 1.1) is safe but that the use of markedly oversized balloons (ratio, 1.2) carries a risk of perforation and vessel rupture of 1.2% to 0% (13). Most small perforations can be sealed with prolonged balloon inflations and reversal of anticoagulation with protamine, unless a platelet glycoprotein IIb/IIIa receptor antagonist has been given. In the event of a large perforation, or when balloon dilatation is unsuccessful in sealing the leak, pericardial tamponade may ensue. The operator must be prepared to block the involved vessel with an angioplasty balloon, to perform emergency pericardiocentesis, and to obtain cardiac surgical consultation. In the future, deployment of a covered stent may provide reliable sealing and obviate the need for emergency surgery.

Infectious Endarteritis

Placement of a foreign body endovascular prosthesis carries a theoretic risk of bacterial endarteritis. In an experimental porcine model, after transient bacteremia, a significant number of recently placed coronary stents cultured positive for bacteria (131). In the early stenting experience, all patients received 48 hours of antibiotic prophylaxis during and after stent placement. Because the risk of suppurative endarteritis in stented coronary arteries is extremely rare, with only three documented cases in the literature (132–134), periprocedural antibiotic therapy is no longer recommended. However, if sterile technique has been breached, or if the patient requires an invasive procedure associated with transient bacteremia during the first 4 weeks after stenting, antibiotic prophylaxis should still be strongly considered.

Cost
In the present era of cost-consciousness, new technologies that affect not only clinical outcome but also resource utilization have come under intense scrutiny. There is no better example than coronary stenting, where the cost of a single stent (approximately $1,200) may exceed that of an angioplasty balloon by a factor of 4. In two early, single-center observational studies, stenting was associated with significantly higher initial hospital costs than other modalities of catheter-based revascularization. Cohen and colleagues (135) compared the costs of stenting and balloon angioplasty for patients treated in the STRESS trial and found that the initial hospital costs of Palmaz-Schatz stenting exceeded those of balloon angioplasty by $2,200 (based on a stent price of $1,400). Despite significant cost savings from the reduction in subsequent hospitalizations and repeat revascularizations, the overall cost of stenting still exceeded that of PTCA by $800 at 1 year. This excess cost may have fallen somewhat with the adoption of optimal stenting techniques, the replacement of warfarin-based regimens with antiplatelet therapy, and the concomitant reductions in length of stay and vascular complications. In the randomized Benestent II trial (in which optimal stenting techniques and dual antiplatelet therapy were used), stenting was still associated with a greater overall cost ($1,020 higher) than balloon angioplasty at 1 year (55), but it was still cost-effective (with an acceptable cost-effectiveness ratio of $23,600 per quality-adjusted life-year gained) due to the reduction in the need for subsequent procedures (136).

FUTURE TECHNOLOGY

Coated Stents

Metallic stents are inherently thrombogenic and also provoke an exuberant hyperplastic response within the first year after deployment. Given these limitations, modifications to the metallic surface to reduce its thrombogenicity and alter the long-term arterial response to injury would be desirable. Most stent coatings are polymers, which can be divided into biodegradable and nonbiodegradable groups (137). Biodegradable polymers such as polyurethane, polyethylene terephthalate, and polyorganophosphazene (138–141) were investigated but were found to provoke intense inflammatory reactions. An example of a nonbiodegradable coating that has been used clinically is Biogold, a 30-nm-thick hydrocarbon layer applied by gas exchange to the Wallstent (138). Other nonbiodegradable coatings that are presently under investigation include phosphorylcholine (DivYsio stent, Biocompatibles, Ltd., Surrey, U.K.), amorphous hydrogenated silicon carbide (Tensum and Tenax stents, Biotronik, Berlin, Germany) (137), diamond-like carbon, and pyrolitic carbon (Carbostent, Sorin BioMedica, Italy) (137a).

Drug-eluting Stents

In the future, stent coatings may also serve as reservoirs for the local delivery of active antiplatelet, antithrombotic, and antiproliferative agents. The largest experience to date with a coated stent has been with the heparin-coated Palmaz-Schatz coronary stent, in which heparin molecules are covalently bound by end-point attachment to a polymerized surface. The stent does not elute heparin, but it allows heparin to function as an “in situ” catalyst for activation of antithrombin III. Low rates of thrombosis have been observed in the four large studies using this device (18,55,91,92), without any demonstrable antiproliferative effect.

The other approach is to use biodegradable polymers to slowly release pharmacologically active agents. Animal studies have demonstrated that drugs such as forskolin (142) and dexamethasone (143), when embedded into a polymer matrix, can be incorporated into the arterial wall at concentrations several orders of magnitude higher than serum levels. Although the notion of a “therapeutic stent” is attractive, significant hurdles remain, such as identifying appropriate therapeutic agents and noninflammatory polymers, as well as defining optimal delivery kinetics and dosage. Finally, stents may be seeded with cells that secrete biologically active proteins (144).

Radioactive Stents

Fischell and colleagues (145) showed that stent wires impregnated with a Beta emitter (phosphorus 32) inhibited subsequent growth and migration of cultured smooth muscle cells. The concept of a radioactive stent offers several theoretic advantages over other methods of endovascular brachytherapy, but clinical trials with the $^{32}\text{P}$ Beta-emitting Isostent, in which a Palmaz-Schatz coronary stent is impregnated with $^{90}\text{Sr}$ (half-life, 14 days) (Cordis), have shown
mixed results. At low doses (1 μCi of total radiation), there was no significant reduction in restenosis (146). At higher doses (0.75 to 6.0 μCi), hyperplasia within the stent seemed to be reduced but significant luminal narrowing at the edges of the stents—termed “candy wrapper restenosis”—still occurred (147). Whether this problem can be overcome by increasing the dosage at the edge of the stent or by avoiding balloon injury to this vulnerable area remains to be seen.

Covered Stents

The difficulty in coating stents with noninflammatory polymers has led to the investigation of stents covered completely by artificial or natural material. Stefanidis described a technique for sewing thin segments of autologous veins or arteries to a metallic stent (148). The initial clinical experience with these autologous stents in thrombus-containing lesions and degenerated saphenous vein grafts has been encouraging, but the long-term outcome compared with uncovered stents has not been studied prospectively (149),(150). A more practical approach has been the use of stents covered by synthetic material. The Jostent (Jomed) Coronary Stent Graft is layer of polytetrafluoroethylene (PTFE) “sandwiched” between two layers of slotted-tube stent (Fig. 25.11). This covered stent has a relatively low crimped profile and may be an ideal choice for sealing perforations, excluding coronary aneurysms, and decreasing distal embolization when stents are placed in friable lesions. Although initial clinical results suggest that the PTFE-covered portions of the stent are largely free of hyperplasia, pharmacologic regimens to prevent thrombosis and avoidance of restenosis at the uncovered edges are ongoing issues (151).

FIG. 25.11.

Covered stent. The Jomed Jostent consists of a polytetrafluoroethylene membrane trapped between an inner and an outer Jostent. Such devices are potentially useful in treating vessel perforations, aneurysms, or occluding coronary sinus fistulas.

CONCLUSIONS

More than 30 years after Charles Dotter first proposed the concept of an endovascular prosthesis, coronary stenting has emerged as the dominant technology for catheter-based coronary revascularization. The availability of stents with excellent deliverability and scaffolding, the demonstration that stenting improves acute and long-term outcome in a wide variety of lesion types, and the development of effective and better-tolerated regimens to prevent stent thrombosis have facilitated the application of stenting to almost every lesion subset. In the future, stents also have the potential to provide regional arterial delivery of bioactive drugs or radiation to help prevent both thrombosis and subsequent restenosis.