Care of the Patient and Management of Complications after Percutaneous Coronary Artery Interventions

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Certain aspects of patient management are common with conventional balloon angioplasty and newer coronary artery interventions. These aspects include the evaluation of chest pain or treatment of acute vessel closure shortly after the intervention, management of the vascular access site (especially if complications occur), prevention and treatment of contrast-induced renal dysfunction, and the use of anticoagulant or antiplatelet agents after the procedure. However, some aspects of management vary among techniques. Several different drug therapies are indicated after these procedures, but pharmacologic therapy for restenosis has been largely unsuccessful. Placement of an intracoronary stent decreases the frequency of restenosis and subsequent revascularization procedures, and functional testing may be of value in some patients after coronary artery interventions. It is important for the specialist in internal medicine to have a firm working knowledge of the various aspects of care that are required because their role in management is increasing.

Management during the First 48 Hours

Chest Pain

Up to 50% of patients experience mild chest discomfort immediately after a percutaneous coronary artery procedure (8, 9). A careful clinical assessment and 12-lead electrocardiography usually identify the few patients with serious complications. Electrocardiograms should be obtained before and immediately after the procedure and used for comparison with tracings obtained if symptoms occur. In general, an important ischemic event is identified by unequivocal ST-segment elevation or depression and can be distinguished from the relatively minor changes related to contrast media or residual ischemia from the procedure.

Of the possible causes of chest pain after the procedure, acute vessel closure is the most serious, occurring after 2% to 7% of all interventions (5, 10-12). Approximately half of acute closures after balloon angioplasty occur while the patient is still in the catheterization laboratory, and another 24% to 33% develop within 24 hours of the procedure (10, 11). Acute closure that occurs during the procedure is usually managed by prolonged balloon inflations or insertion of an intracoronary stent; this avoids emergency bypass surgery in more than 90% of cases (13, 14). Acute closure that occurs outside of the laboratory is often temporally associated with the discontinuation of heparin therapy or is the result of an undetected dissection; this type of acute closure is much more troublesome to manage and usually causes some myocardial necrosis (15). More than 90% of patients with acute closure have angina and electrocardiographic changes that evolve into the changes seen with acute myocardial infarction (16, 17). As during any infarction, heart rate, heart rhythm, and blood pressure should be stabilized and narcotics should be given to relieve pain.

In general, patients with "out-of-lab" acute closure are managed by repeated intervention (which is successful in 35% to 95% of cases), but some pa-
patients require emergency bypass surgery (18). In a few patients, the risk associated with surgery done to revascularize a small amount of myocardium may exceed that of a small infarction. The decision to proceed with repeated intervention or surgery, however, must be individualized and should take into account hemodynamic stability, the amount of jeopardized myocardium, the availability of the catheterization laboratory or surgeons, and the likelihood that repeated treatment will be successful. Thrombolytic therapy, administered either systemically or into the affected artery, can be considered for thrombosis but should be avoided if emergency surgery is being contemplated. Intraaortic balloon counterpulsation may reduce the magnitude of ischemia, augment systemic perfusion, and help to maintain patency of the artery (19). Coronary stents and new platelet inhibitors have favorably affected the incidence and treatment of acute closure and are discussed later in this paper.

Up to 10% of patients with acute closure may not develop electrocardiographic changes, especially if the intervention was performed in the circumflex coronary artery. In fact, less than 50% of patients have surface electrocardiographic changes during balloon inflation in the circumflex artery (20). Acute closure is also obscured when collaterals to the affected artery exist. After a successful intervention, collaterals may regress quickly but are recruited again if the vessel occludes. When this happens, chest pain and electrocardiographic changes may resolve; the artery appears to have spontaneously opened but actually has not. Acute closure contributes substantially to morbidity and mortality in coronary interventions; approximately half of myocardial infarctions and emergency bypass operations occur in patients with acute closure, and mortality rates increase fivefold in this group (10-12, 21). Clinical and angiographic factors that correlate with death after acute closure include female sex; large ischemic burden; left ventricular ejection fraction less than 30%; age greater than 70 years; proximal right coronary artery disease; and an acute presentation, such as unstable angina (18, 22-24).

Another cause of chest pain after intervention is coronary artery spasm. Vasoactive compounds released by platelets at the site of disrupted endothelium promote coronary spasm. The immediate therapy is nitroglycerin, given either sublingually or intravenously. Rapidly relieved ischemia is probably related to coronary spasm, which may occur as an isolated event or may occur several times after an intervention. Patients are often treated with calcium-channel blockers before the procedure to reduce the chance of spasm afterward. Ischemia that is not promptly relieved by nitroglycerin and repeated episodes of ischemia may be harbingers of acute vessel closure. Repeated episodes of ischemia after an intervention should be evaluated with angiography to ensure that the result remains satisfactory.

**Drugs To Reduce Thrombosis and Acute Closure**

Platelet inhibitors, including aspirin, ticlopidine, and abciximab (ReoPro, Centocor, BV Leiden, the Netherlands; distributed by Eli Lily and Co., Indianapolis, Indiana), are used to reduce acute closure from thrombosis during and after coronary interventions. Compared with placebo, aspirin reduces the risk for acute closure by half (absolute reduction, 10% to 5%) (25-29). Although fewer data on ticlopidine exist, this drug also seems to reduce the frequency of ischemic complications (29, 30). Because neither aspirin nor ticlopidine completely inhibits platelet function, more potent agents, such as abciximab (the Fab fragment of the chimeric human-murine monoclonal antibody [7E3] against platelet glycoprotein IIb/IIIa receptors), were developed. The EPIC (Evaluation of 7E3 for the Prevention of Ischemic Complications) trial focused on clinical and anatomic situations that placed patients at high risk for abrupt closure (31). Patients treated with abciximab in addition to heparin and aspirin had a 35% reduction in ischemic end points compared with those who received aspirin and heparin alone, but the rate of major bleeding complications increased. In subsequent studies, bleeding complications were reduced by decreasing the heparin dose without compromising the benefit of abciximab (32).

Thrombin inhibitors, such as heparin, are also used to prevent acute closure. Heparin dosing for interventional procedures was empirical until studies showed that 11% to 55% of patients did not receive adequate anticoagulation with 10,000 units (33-35). Heparin dosage is now monitored by measurement of activated clotting times, and the occurrence of abrupt closure has been shown to be inversely related to the level of anticoagulation (16, 36-39). The optimal duration of heparin therapy after a successful procedure is unknown. In one study (40), the rate of acute closure and ischemic complications decreased when patients received heparin for 18 to 24 hours after angioplasty to prolong the activated partial thromboplastin time more than three times the control value. In other studies of uncomplicated procedures, however, more bleeding occurred, hospitalizations were longer, and outcomes were not improved in patients who were treated with heparin for 12 to 24 hours (41, 42). Therefore, heparin treatment for 18 to 24 hours after an intervention is warranted in patients at high risk for acute closure, but no data support pro-
longed use in patients having uncomplicated procedures (11, 16, 22, 43).

Although effective in reducing the rate of ischemic complications, heparin has some limitations. The dose–response relation is nonlinear, which makes adjustments difficult; in addition, a cofactor, antithrombin III, is necessary for heparin to produce an effect. Heparin inhibits fibrin-bound thrombin less effectively than it does free thrombin, and it is neutralized by platelet factor IV, released by activated platelets (44). Hirudin, a new antithrombin agent, does not require a cofactor, readily inactivates fibrin-bound thrombin, and inhibits platelet-mediated thrombosis (45). Randomized studies comparing hirudin with heparin show that hirudin reduces the rate of early ischemic complications but not the rate of restenosis (46, 47). A nonpeptide analogue, hirulog, also seems promising (48, 49).

### Elevated Creatine Kinase Levels

Interventional procedures that are complicated by acute vessel closure or require emergency bypass surgery are frequently associated with elevated creatine kinase levels. According to recent reports, the incidence of Q-wave myocardial infarction after angioplasty is less than 1%; however, the incidence of non-Q-wave infarctions is uncertain, in part because the criteria used for diagnosis vary among studies (50, 51). The importance of elevated creatine kinase levels, which occur after 10% to 30% of apparently uncomplicated procedures, is currently being questioned (52–58). Patients who have elevated levels after angioplasty frequently have certain characteristics, including recent infarction, postinfarction angina, side-branch occlusion, intimal dissection, or vein graft procedures (54, 55). Although some small studies with limited follow-up suggest that elevated enzyme levels are “benign,” recent reports show a relation between elevated creatine kinase levels and death, myocardial infarction, and subsequent revascularization (57, 59). Other contemporary data suggest that only patients with fivefold increases in creatine kinase–MB fraction have a trend toward decreased rate of late survival (58). At this point, the meaning of elevated creatine kinase levels after uncomplicated procedures is unclear and warrants further study, but the common notion that small increases in enzyme levels are unimportant may be incorrect. Until this issue is clarified, routine monitoring of enzyme levels after all procedures is advised, and patients with substantial increases should be carefully followed.

### Vascular Access Complications

Vascular complications occur in 0.9% to 14% of patients; the different surveillance criteria among studies explains this large range (60–66). Vascular complications requiring surgical repair occur in 0.9% to 3.5% of procedures (60–66). Risk factors associated with vascular complications include periprocedural thrombolytic therapy, heparin use after sheath removal, anticoagulation with warfarin, age, long-term use of corticosteroids, peripheral vascular disease, and female sex (61, 63–68). Larger-diameter arterial sheaths required for some devices have been related to complications in some but not all studies (64, 66, 69).

Small decreases in hematocrit (5% to 6%) are common after coronary angioplasty and are not necessarily related to hemorrhage (70). Important bleeding complications at the access site are usually obvious, but some patients develop an occult leg hematoma or retroperitoneal bleeding. Signs and symptoms of retroperitoneal hematoma include suprapigual tenderness or fullness, severe back or lower quadrant pain, and femoral neuropathy (71). Sometimes, the only indications of retroperitoneal hematoma are progressive hypotension and a decreasing hematocrit (72). Computed tomography of the pelvis confirms the diagnosis. Blood loss with retroperitoneal hematoma can be severe (average transfusion requirement, 4.6 units), and most large series have reported some deaths (71). Retroperitoneal hematoma can usually be treated conservatively with transfusion alone, but surgery was necessary in 16% of patients in one large series (71).

When surgical repair is needed, it is usually for pseudoaneurysm or arteriovenous fistula; together, these conditions account for 58% to 88% of the vascular complications that require surgery (61–65). Both of these conditions are associated with puncture and cannulation of the superficial artery rather than the common femoral artery (73). A pseudoaneurysm may not appear until days after the procedure and may present as a painful or painless mass over the arterial puncture site or, if rupture occurs, as an expanding hematoma in the groin area. Ultrasonography-guided compression of a pseudoaneurysm is successful in 88% to 100% of patients who are not bleeding and do not require continued anticoagulation; if anticoagulation is continued, however, the success rate decreases to 29% to 54% (67, 74, 75). Surgery is necessary when rupture and bleeding occur or if compression does not abolish the pseudoaneurysm. Arteriovenous fistulas develop when the femoral artery and vein are cannulated and a communication develops. Fistulas are detected by the presence of a continuous murmur over the puncture site within days of the procedure; fistulas may also develop slowly over months (76). The symptoms are often trivial, but vascular insufficiency and high-output heart failure sometimes occur (76, 77). Approximately one third of arteriovenous fistulas can be closed by using prolonged compression,
but surgery is necessary in the remaining, clinically important fistulas (75).

Alternatives to manual compression for the control of bleeding at the time of sheath removal include mechanical or pneumatic compression devices (68, 78). These devices are safe and may reduce vascular complications (78). Another alternative is the percutaneous collagen plug, but initial enthusiasm for this device has been tempered by subsequent studies showing no reduction in the rate of vascular complications and a worrisome risk for arterial occlusion (79–83).

**Contrast-induced Nephropathy**

Contrast-induced nephropathy is the third leading cause of acute renal failure in hospitalized patients (84). The creatinine level slightly increases in all patients who have had a contrast study, and nephropathy is commonly defined as an increase of 88.4 μmol/L above baseline (85). Depending on the definition used and the baseline characteristics of the study sample, contrast-induced nephropathy occurs in 0% to 44% of patients after cardiac catheterization (86, 87). The incidence after coronary interventions is unknown but is probably the same or higher. Contrast-induced nephropathy is strongly related to preexisting renal dysfunction and is uncommon in normal kidneys (84, 86, 88). Diabetes mellitus is not an independent predictor of contrast-induced nephropathy in patients with normal creatinine levels but has an additive negative effect in patients with renal dysfunction (84, 86, 88, 89). Only the amount, not the type, of contrast affects the occurrence of contrast-induced nephropathy, especially in patients with impaired renal function (85, 90, 91). In patients with a baseline creatinine level greater than 177 μmol/L, the risk for contrast-induced nephropathy is 2% in patients who receive less than 125 mL of contrast compared with 19% in patients who receive more than 125 mL (90). Guidelines are available for administration of contrast in patients with renal insufficiency (92), but some situations require larger contrast loads. The risk for contrast-induced nephropathy is higher when a second dose of contrast is given within 72 hours (93). This is important because some patients have diagnostic catheterization followed by an intervention the next day. Patients undergoing more than one contrast study within 72 hours have an additional 40% risk for contrast-induced nephropathy (88).

Treatments to prevent contrast-induced nephropathy include intravenous hydration, mannitol, furosemide, calcium-channel blockers, low doses of dopamine, and adenosine antagonists (84, 94). Unfortunately, few randomized trials have evaluated these therapies. One recent trial compared intravenous hydration beginning 12 hours before and continuing for 12 hours after contrast administration with hydration plus mannitol or furosemide administered during the procedure; mannitol or furosemide had no advantage over hydration (95). If possible, therapy with nephrotoxic drugs (such as certain antibiotics, nonsteroidal anti-inflammatory agents, and cyclosporine) should be discontinued before contrast administration. An additional drug of concern is the oral hypoglycemic agent metformin. Metformin does not contribute to contrast-induced nephropathy, but when it is administered during worsening renal insufficiency or failure it may cause fatal lactic acidosis (96–98). Although the risk for this complication is low, metformin should be withheld for 48 hours before contrast administration (99). Contrast-induced nephropathy is usually nonoliguric and only rarely requires dialysis (84). Most patients who develop this condition have an uneventful clinical course, and their creatinine level returns to baseline within 2 to 7 days (84).

**Angioplasty for Acute Myocardial Infarction**

Primary coronary angioplasty is an alternative to thrombolytic therapy for the treatment of acute myocardial infarction. Although debate about the exact role of primary angioplasty continues, the procedure compares favorably with thrombolytic therapy and may be advantageous in some circumstances (100–105). Patients treated with primary angioplasty are managed like any other patient with acute myocardial infarction. Drug therapy may be necessary to control arrhythmias or maintain acceptable hemodynamics. Intraaortic balloon pump counterpulsation may have a unique role in patients treated with primary angioplasty. Balloon counterpulsation reduces recurrent ischemia and the need for early repeated angioplasty but does not reduce rates of death or reinfarction (106, 107). Initial results with platelet IIb/IIIa receptor inhibitors in patients undergoing primary angioplasty are encouraging; these results include a reduction in the composite end point of death, reinfarction, and urgent intervention at 1 and 6 months (108).

On the basis of the triage information obtained from coronary angiography with primary angioplasty, low-risk patients may be candidates for early hospital discharge (109, 110). Patients with depressed left ventricular function after infarction should be treated with angiotensin-converting enzyme inhibitors (111). Restenosis remains a clinical problem after angioplasty performed for acute myocardial infarction, but its true incidence is not well characterized (112–115). The presence of an angiographically identifiable thrombus during elective angioplasty is associated with a higher risk for restenosis; because a thrombus is probably present in patients...
with acute myocardial infarction, higher rates of restenosis in this circumstance are not unexpected (116).

Radiation-Induced Skin Injury

Radiation exposure has increased as interventional procedures have become more complex, especially in patients having multiple procedures during a single hospitalization (117, 118). Each procedure involves a mean skin entrance dose of 32 mCi per kg of body weight (124 Rads) assuming an average fluoroscopy time of 19 minutes, but the duration of exposure may exceed 1 hour in complicated and difficult cases (119). Although mild erythema may develop several hours after radiation exposure, most radiation-related skin effects are not apparent until weeks after the procedure. Late findings include temporary or permanent epilation by 3 weeks, desquamation by 4 weeks, dermal atrophy and necrosis after 10 to 14 weeks, and telangiectasia after 1 year. Proper maintenance and monitoring of radiographic equipment and attention to details of image acquisition minimize exposure in most patients (119, 120). Most skin changes require no treatment, but it is important that their association with a previous procedure be recognized.

Table 1. Major Classes of Therapeutic Agents Tried for Restenosis*

<table>
<thead>
<tr>
<th>Class of Therapeutic Agents</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiplatelet agents</td>
<td>Aspirin, Dipyridamole, Ticlopidine, Glycoprotein IIb/IIIa inhibitors, Prostacyclin, Ketanserin, Antithrombins</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>Diltiazem, Nifedipine, Verapamil</td>
</tr>
<tr>
<td>Omega-3 fatty acids</td>
<td>Cilazapril, Enalapril, Fosinopril</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>Captopril, Lisinopril, Ramipril, Losartan, Valsartan, Telmisartan</td>
</tr>
<tr>
<td>Lipid-lowering drugs or treatment</td>
<td>Lovastatin, Pravastatin, Probufol, Low-density-lipoprotein apheresis</td>
</tr>
<tr>
<td>Radiation</td>
<td>Magnesium, Gene therapy</td>
</tr>
</tbody>
</table>

* Numbers in parentheses are reference numbers.

Management Considerations after the First 48 Hours

Restenosis

Restenosis is an important follow-up consideration that limits the long-term effectiveness of percutaneous coronary artery procedures. Restenosis results from elastic recoil of the artery, neointimal proliferation, and vascular remodeling (121). Although several definitions exist, restenosis is usually defined on angiography as a recurrent luminal narrowing exceeding 50% (122). On the basis of this definition, restenosis develops in 30% to 50% of patients after the intervention. However, anatomic definitions of restenosis correlate poorly with the need for repeated revascularization, and relatively few studies include both clinical end points and angiographic data. Up to 50% of patients with angiographically proven restenosis are asymptomatic, and only half require another revascularization procedure (122–128). Some data suggest that restenosis is not a binary, “all or none” outcome but rather that some narrowing occurs in all arteries after an intervention (129, 130). Attempts to predict restenosis on the basis of clinical or anatomic variables have been largely unsuccessful (131–133). The optimal management for patients with asymptomatic restenosis is uncertain; some data suggest that these patients have a greater chance of recurrent ischemic events, whereas other studies show a favorable long-term outcome (123, 125, 126, 128). Patients with asymptomatic restenosis may develop angina or remain asymptomatic, but acute myocardial infarction is uncommon (123, 125, 131, 134). Therefore, a watchful waiting approach is appropriate in asymptomatic patients after an intervention.

Clinically significant restenosis is often treated by use of a second interventional procedure (135, 136). Although the success rate for repeated procedures is high, so is the likelihood of a second restenosis (137). Multiple repeated angioplasties eventually relieve symptoms in 64% of patients (137). Many drugs have been used in attempts to inhibit restenosis; favorable effects were found in some small studies, but no large randomized trial has identified an effective drug (25, 27, 30, 138–162) (Table 1). It was hoped that newer interventional devices might prevent restenosis. In initial studies, directional atherectomy did not reduce restenosis, but the stenosis reduction was no different than that achieved by balloon angioplasty (163, 164). This technique has evolved, and more plaque is now removed; this results in smaller residual stenoses. The potential for so-called optimal atherectomy as well as rotational atherectomy to reduce restenosis is now being tested (165). Recoil of the elastic elements within
an artery contributes to restenosis, and coronary stents reduce recoil. Randomized comparisons of stent implantation and balloon angioplasty showed that stents reduced rates of restenosis (32\% compared with 22\%) and were associated with lower rates of clinical events (166, 167). In the short time that stents have been available, their deployment technique and the drug therapy required after implantation have evolved. Pilot data from a trial that used a heparin-coated stent, high-pressure deployment, and ticlopidine show a restenosis rate as low as 6\% (168). If this finding is confirmed, stent implantation will be a major advance in the treatment of restenosis.

**Functional Studies after Coronary Artery Intervention**

Functional studies to evaluate patients for ischemia can be very useful after coronary artery interventions (134, 169–180). Restenosis typically presents with recurrent angina about 3 months after the procedure (134, 169, 122, 181, 182). Recurrent symptoms within the first month suggest the possibility of technical problems, such as a dissection flap not initially visible or marked elastic recoil. If restenosis occurs, symptoms usually develop by 6 to 9 months after the procedure; new symptoms after this time are more likely to be related to progression of other coronary lesions (169). After successful angioplasty, exercise duration and double product increase, and angina and ST-segment depression occur less frequently. However, routine treadmill testing immediately after angioplasty is not a good predictor of restenosis or subsequent clinical events; in one study, the test was associated with a slightly increased risk for myocardial infarction (134, 170, 171, 173) (Table 2). Furthermore, in patients who did not have an intervening clinical event, exercise treadmill testing done 6 months after angioplasty missed nearly 60\% of patients with angiographic restenosis (172).

Thallium imaging shows improved perfusion after a successful intervention (180, 183–186). In most patients, reversible defects resolve or improve substantially within days after the procedure; in up to one third of patients, however, improvement is delayed for several months (184, 186). As shown by stress testing with either exercise or dipyridamole, approximately 75\% of patients who have perfusion defects soon after balloon angioplasty subsequently develop restenosis (187–191) (Table 3). Given our present understanding of restenosis, these early abnormalities may relate to considerable elastic recoil of the stenosis (191).

Exercise radionuclide ventriculography shows improvements in left ventricular ejection fraction and regional-wall motion early and late after coronary angioplasty, but not in all patients who have a successful procedure (192–195). This finding may simply be the result of the imaging angles used in some patients. In patients with multivessel disease, however, improvements in ejection fraction after treatment of one stenosis may be negated by the effects of untreated disease. Despite these limitations, exercise radionuclide ventriculography performed soon after an intervention is somewhat predictive of restenosis (196, 197).

Stress echocardiography has recently been used

**Table 2. Results of Exercise Testing after Coronary Angioplasty**

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Patient Population</th>
<th>Patients</th>
<th>Overall Rate of Angiographic Restenosis</th>
<th>Test</th>
<th>Angiographic Restenosis†</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bengtson et al., 1990(177)</td>
<td>Successful PTCA after myocardial infarction without event at 6 months</td>
<td>209</td>
<td>48</td>
<td>Bruce protocol ETT at 6 months</td>
<td></td>
<td>33</td>
<td>83</td>
<td>65</td>
<td>57</td>
</tr>
<tr>
<td>Hecht et al., 1991(179)</td>
<td>Recurrent angina, abnormal ETT result, or complex PTCA</td>
<td>116</td>
<td>60</td>
<td>Bruce protocol ETT at 6 months</td>
<td></td>
<td>52</td>
<td>64</td>
<td>68</td>
<td>48</td>
</tr>
<tr>
<td>Hillegass et al., 1992(170)</td>
<td>No patients had events during 6-month follow-up</td>
<td>334</td>
<td>28</td>
<td>Bruce protocol ETT after discharge</td>
<td></td>
<td>39</td>
<td>65</td>
<td>31</td>
<td>73</td>
</tr>
<tr>
<td>Hillegass et al., 1992(172)</td>
<td>No patients had events during 6-month follow-up</td>
<td>513</td>
<td>28</td>
<td>Bruce protocol ETT at 6 months</td>
<td></td>
<td>58</td>
<td>64</td>
<td>39</td>
<td>79</td>
</tr>
<tr>
<td>Hecht et al., 1993(180)</td>
<td>Recurrent angina, abnormal ETT result, or complex PTCA</td>
<td>80</td>
<td>75</td>
<td>Supine bicycle stress test</td>
<td></td>
<td>55</td>
<td>79</td>
<td>89</td>
<td>37</td>
</tr>
<tr>
<td>Roth et al., 1994(174)</td>
<td>Consecutive patients after PTCA with readable electrocardiogram</td>
<td>78</td>
<td>28</td>
<td>Modified Bruce protocol ETT at 1, 3, and 6 months</td>
<td></td>
<td>50</td>
<td>66</td>
<td>37</td>
<td>77</td>
</tr>
<tr>
<td>Desmet et al., 1995(173)</td>
<td>Asymptomatic patients 6 months after PTCA</td>
<td>191</td>
<td>9</td>
<td>Supine bicycle stress test</td>
<td></td>
<td>29</td>
<td>89</td>
<td>20</td>
<td>93</td>
</tr>
</tbody>
</table>

* ETT = exercise tolerance test; PTCA = percutaneous transluminal coronary angioplasty.
† Values were derived from study data only for patients who had follow-up angiography.
to identify restenosis and predict prognosis after coronary interventions (180, 198, 199) (Table 4). The ability of stress echocardiography to detect restenosis varies depending on the patient population studied. In patients with recurrent angina or abnormal exercise test results, stress echocardiography detects restenosis with sensitivities ranging from 75% to 87% and specificities of 90% to 95% (180, 198). In a study of unselected patients, however, sensitivity and specificity were much lower (38% and 79%, respectively) (199). Although the clinical utility of stress echocardiography for detecting restenosis in unselected patients may be limited, it is helpful in identifying persons who are more likely to require future revascularization (200).

Recommendations for Functional Testing and Follow-up

In patients with single-vessel disease and classic angina, symptoms are usually relieved with improvements in exercise performance and myocardial perfusion after intervention. Although functional testing can document these changes, such patients are generally quick to report recurrent angina; this symptom alone may be all that is necessary to suggest restenosis. Because angiography is usually performed in this circumstance, the expense of functional testing is often unnecessary. However, if it is unclear that the symptoms are the result of myocardial ischemia, a functional test can be helpful before angiography is done.

Patients with multivessel disease are complex and thus require more attentive follow-up. Catheter-based interventions are used frequently in this setting, with success rates exceeding 90% and acceptable complication rates (201–204). Results from randomized trials comparing multivessel angioplasty with bypass surgery are remarkably consistent. Angioplasty is associated with lower initial cost, shorter hospitalization, less morbidity, and similar 1-year mortality rate compared with bypass surgery, but it provides complete revascularization less often, requires more repeated procedures, and produces a worse outcome in diabetic patients (205–212). Complete revascularization occurs in only 32% to 59% of patients having angioplasty, and such outcomes

Table 3. Results of Exercise Thallium Imaging after Coronary Angioplasty*

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Patient Population</th>
<th>Patients</th>
<th>Overall Rate of Angiographic Restenosis</th>
<th>Test</th>
<th>Angiographic Restenosis</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wijns et al., 1985 (187)</td>
<td>4 weeks after successful PTCA, angiography at 6–8 months after PTCA</td>
<td>99</td>
<td>39</td>
<td>Planar thallium imaging; bicycle ETT</td>
<td>74</td>
<td>83</td>
<td>74</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>Schroeder et al., 1989 (176)</td>
<td>Asymptomatic patients, 6 months after PTCA</td>
<td>111</td>
<td>12</td>
<td>Planar thallium imaging; bicycle ETT</td>
<td>86</td>
<td>93</td>
<td>63</td>
<td>98</td>
<td></td>
</tr>
<tr>
<td>Rennick et al., 1996 (174)</td>
<td>Unselected patients with 6-month follow-up angiography</td>
<td>84</td>
<td>31</td>
<td>Planar thallium imaging; bicycle ETT</td>
<td>73</td>
<td>76</td>
<td>58</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Hardoff et al., 1990 (131)</td>
<td>Unselected patients having repeated angiography at 6 months; 52% had chest pain</td>
<td>71</td>
<td>32</td>
<td>Planar thallium imaging; bicycle ETT</td>
<td>75</td>
<td>67</td>
<td>52</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>Hecht et al., 1991 (179)</td>
<td>6 months after PTCA; 55% had recurrent angina</td>
<td>116</td>
<td>60</td>
<td>Planar thallium imaging; Bruce protocol ETT</td>
<td>93</td>
<td>77</td>
<td>85</td>
<td>88</td>
<td></td>
</tr>
</tbody>
</table>

* ETT = exercise tolerance test; PTCA = percutaneous transluminal coronary angioplasty; SPECT = single-photon emission computed tomography.

† Values were derived from study data only for patients who had follow-up angiography.

Table 4. Stress Echocardiography after Coronary Angioplasty*

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>Patient Population</th>
<th>Patients</th>
<th>Overall Rate of Angiographic Restenosis</th>
<th>Type of Stress</th>
<th>Angiographic Restenosis</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
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<tr>
<td>Hecht et al., 1981 (180)</td>
<td>Recurrent angina, abnormal ETT result, or complex PTCA</td>
<td>80</td>
<td>75</td>
<td>Supine bicycle</td>
<td>87</td>
<td>95</td>
<td>98</td>
<td>70</td>
<td></td>
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<tr>
<td>Pirelli et al., 1993 (198)</td>
<td>Asymptomatic patients with abnormal ETT result 3 months after PTCA</td>
<td>50</td>
<td>24</td>
<td>Dipyridamole</td>
<td>75</td>
<td>90</td>
<td>83</td>
<td>92</td>
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</tr>
<tr>
<td>Heinle et al., 1993 (199)</td>
<td>Unselected patients presenting for 5-month follow-up angiography as part of restenosis trial</td>
<td>103</td>
<td>44</td>
<td>Dobutamine</td>
<td>38</td>
<td>79</td>
<td>59</td>
<td>64</td>
<td></td>
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</table>

* ETT = exercise tolerance test; PTCA = percutaneous transluminal coronary angioplasty.
as myocardial infarction, the need for repeated revascularization, and survival correlate with the completeness of revascularization (213–215). Some studies, however, suggest that a satisfactory long-term outcome may not require complete revascularization by angioplasty (203, 216, 217).

Patients with multivessel disease improve considerably after intervention but, unlike patients with single-vessel disease, often do not become asymptomatic. Functional testing is especially helpful in this circumstance. Improvements in exercise variables, ST segments, and myocardial function or perfusion after the intervention can reestablish a baseline for comparison if new symptoms develop. The incidence of restenosis with multivessel procedures is higher than that seen with single-vessel angioplasty and largely depends on the number of stenoses treated. Multivariate analyses show that the best patient-related predictor of restenosis is the number of lesions dilated; the only lesion-specific predictor is the lumen diameter after the procedure (218, 219). Unfortunately, the results of functional testing in these patients are more difficult to interpret because of disease in other vessels. Although management after multivessel procedures is fundamentally similar to that after single-vessel angioplasty, certain factors identify high-risk patients and should influence subsequent management. High-risk clinical factors, such as advanced age, diabetes mellitus, and left ventricular dysfunction, all indicate a greater risk for future cardiac events after intervention.

Because such complications as pseudoaneurysm and arteriovenous fistula may not appear immediately, physicians should specifically look for them at the first follow-up examination (1 to 2 weeks after the procedure). If it is planned, repeated functional testing should be delayed until about 3 or 4 weeks after the intervention. This allows the femoral artery access site to heal completely, myocardial perfusion to return to normal, and exercise stamina to improve.

Long-Term Drug Therapy

Long-term pharmacologic management after coronary artery interventions should focus on secondary prevention of coronary events. The benefit of aspirin for reducing the occurrence of myocardial infarction, stroke, and death in patients with coronary disease is undisputed. After coronary angioplasty, the combined end point of myocardial infarction, stroke, and vascular death decreases by nearly 50% in patients treated with antiplatelet agents (220). Between 75 and 325 mg of aspirin daily is effective; higher doses provide no additional benefit. No other drug, either singly or combined with aspirin, is superior to aspirin therapy alone; thus, all patients should receive aspirin therapy indefinitely.

Although cholesterol-lowering drugs have not reduced the rate of restenosis or early clinical events (151–154), studies continue to show the value of such therapy for reducing the rate of coronary events and death in patients with coronary disease (221–225). For example, the Scandinavian Simvastatin Survival Study (225) showed a significant reduction in total coronary events and all causes of death after the first year, with continued improvements throughout the study. After approximately 5 years, one death was prevented for every 30 patients treated. The currently recommended goal for patients with established coronary disease (a group that includes all patients having interventions) is to reduce low-density lipoprotein cholesterol levels to 2.6 mmol/L or less (226). All patients undergoing coronary artery procedures should have their lipid status investigated and should be treated if necessary. Use of other medications, such as antianginal agents, is dictated by the clinical situation.

Specific Considerations after Intervention with Newer Devices

In the past 5 years, three different atherectomy catheters, the excimer laser, and two types of coronary artery stents have been approved for coronary intervention. Some newer devices are gaining popularity, whereas others have been relegated to select subgroups of patients. Although all interventions share some general management principles, newer devices involve some unique considerations.

Directional Atherectomy

Directional atherectomy removes atherosclerotic tissue from the coronary artery in a focal manner. This procedure uses a large catheter and thus is confined to vessels greater than 3 mm in diameter (usually those with bulky, eccentric stenoses). Early randomized trials comparing directional atherectomy with balloon angioplasty did not show a major clinical advantage of atherectomy over angioplasty (163, 164, 227). Preliminary results from subsequent trials are more encouraging about atherectomy but await final analysis (165, 228). Nevertheless, directional atherectomy is useful for stenoses at vessel bifurcations or ostial locations.

Patient management after directional atherectomy is similar to that after balloon angioplasty. The concern that the larger catheters necessary for directional atherectomy would increase complications around the access site has not been realized (229). However, longer periods of bedrest (18 to 24 hours) are usually advised after catheter removal. One trial found an increased incidence of elevated creatine kinase levels and myocardial infarction and
a small but significant increase in mortality rate after 1 year in patients treated with directional atherectomy (230). Whether this finding will be seen in ongoing trials that are using improved atherectomy techniques is uncertain.

**Rotational Atherectomy**

Rotational atherectomy ablates atherosclerotic plaque with an elliptical burr that is coated with diamond chips and rotates within the coronary artery at 160,000 to 180,000 revolutions per minute. It produces particulate material that is generally smaller than erythrocytes and ultimately passes through the capillary system. Its unique mode of action makes it particularly attractive for treating diffusely diseased segments or calcified lesions. Management after these procedures differs somewhat from management after balloon angioplasty. Transient vasospasm and bradycardia may occur during rotational atherectomy, requiring temporary pacing and intracoronary or intravenous nitroglycerin in some patients (231). If particulate debris accumulates too quickly in the capillaries, ischemia and ventricular dysfunction develop; in addition, electrocardiographic changes and hemodynamic instability may persist for several hours despite an open epicardial artery. In some patients, intraaortic balloon counterpulsation and vasopressor drug support may be necessary until the ischemic dysfunction clears. Restenosis occurs with similar or increased frequency after rotational atherectomy, but the lesions treated with this technique are often not suitable for other interventional techniques or even coronary bypass surgery (232).

**Transluminal Extraction Atherectomy**

The transluminal extraction catheter uses a rotating conical blade at the tip and a vacuum system to cut and extract atheroma and thrombus from the vessel. No large randomized trials have evaluated the effectiveness of this device, but it seems to have a specialized role in the treatment of degenerated vein grafts and native coronary arteries with extensive thrombus (233). Distal embolization of thrombotic material with subsequent myocardial infarction is an inherent risk in lesions treated with this device. Management of patients after this procedure is similar to that after treatment with other interventional devices, but such thrombotic lesions often require prolonged infusions of heparin. Complications at the vascular access site may occur more frequently than with other devices, in part because of the need for prolonged anticoagulation (64).

**Excimer Laser Angioplasty**

Atherosclerotic plaques may be ablated by excimer laser energy. Results from 3000 consecutive patients in the excimer laser registry show success rates of 90% in complex lesions and an acceptable complication rate (234). Other studies, however, have shown less favorable results: Abrupt closure occurred in 30% of patients, perforations occurred in 1.6% of patients, and restenosis rates were as high as 70% (235-237). Patient care after such procedures is similar to that after conventional balloon angioplasty.

**Coronary Stents**

Coronary stents were developed to combat abrupt vessel closure and restenosis, two major problems associated with balloon angioplasty. The Gianturco-Roubin stent has been approved and is effective for the treatment of acute or threatened vessel closure (14, 238). The Palmaz-Schatz stent reduces restenosis and the need for additional target-vessel revascularization procedures, and it has been approved for placement within native coronary arteries that have not been previously treated (166, 167).

Anticoagulant therapy is an important management consideration after placement of an intracoronary stent. The benefits of stent placement were initially overshadowed by subacute stent thrombosis, an event that is distinct from abrupt closure and restenosis. Unlike abrupt closure, which usually occurs within 24 hours after angioplasty (22), subacute stent thrombosis develops 2 to 14 days after stent placement (166, 167, 239). Furthermore, unlike restenosis, subacute stent thrombosis presents as an acute myocardial infarction rather than recurrent angina. Early series reported subacute stent thrombosis in 3% to 18% of patients despite intense anticoagulation regimens (including dextran, aspirin, dipyridamole, heparin, and warfarin), which, not surprisingly, were associated with an increased risk for bleeding and longer hospital stays (166, 239–241). We now know that subacute stent thrombosis is related more to incomplete stent deployment than to inadequate anticoagulation (242). Better deployment is achieved by use of high-pressure balloon inflations within the stent. By using this deployment technique and only antiplatelet agents, the risk for subacute thrombosis is 1% and important bleeding complications are eliminated (168, 242). The antiplatelet therapy now used after stent implantation is ticlopidine, 250 mg twice daily for 1 month, plus aspirin, 100 to 325 mg/d indefinitely (243). Because long-term ticlopidine therapy is associated with a 1% to 2% chance of neutropenia, leukocyte counts should be monitored. It must be emphasized that the use of antiplatelet agents alone after stent implantation is an "off-label" practice supported only by an increasing body of favorable patient experiences (244).
Conclusions

In the past 15 years, many advances in the percutaneous treatment of coronary artery disease have been made. Given the number of patients treated by using these techniques, it is important for the specialist in internal medicine to be aware of the care required after treatment. Future improvements in coronary artery interventions will probably focus on the reduction of procedural-related complications through the use of newer antiplatelet agents and improvements in therapies to reduce the recurrence of disease.

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