

Update in Nonpulmonary Critical Care

Interventional Therapy for Coronary Artery Disease

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Increasing numbers of patients who have undergone percutaneous interventions for the management of coronary artery disease are admitted to intensive care units for the management of intercurrent noncoronary critical illness. This review discusses percutaneous coronary interventional procedures, their outcomes, their complications, and their implications for care of the critically ill.

CORONARY ANGIOPLASTY

Since the introduction of percutaneous coronary intervention in the 1970s, its use has increased dramatically. An estimated 650,000 patients underwent percutaneous coronary intervention in 1999 (1), and the American College of Cardiology and the American Heart Association guidelines now designate the quality of the evidence of benefit for high-risk patients as 1A. Balloon angioplasty allows for minimally invasive treatment of coronary artery disease but has limitations when used alone. These limitations include abrupt vessel closure (caused by vessel recoil or persistent intimal dissection) in up to 5% of patients and restenosis requiring repeat angioplasty or coronary artery bypass surgery in up to 40% of patients (2). Adjunct therapies now being developed appear to improve on the outcomes expected from balloon angioplasty and allow treatment of more complex lesions.

CORONARY ARTERY STENTS

A major advancement in coronary angioplasty was the introduction of coronary stents in the early 1990s. It is now clear that the placement of metal scaffolding at the site of the lesion significantly reduces the rate of abrupt closure and restenosis. Most stents in use today are stainless steel and have a slotted tube design. Stents vary in the geometry of the metal struts, flexibility, and access to arterial side branches. The stent is mounted on a balloon angioplasty catheter. The coronary artery is accessed with a guide catheter, and a fine wire is advanced into the coronary artery across the lesion to be treated. The stent balloon catheter is advanced over the guidewire into the coronary artery, and the stent is positioned at the lesion using fluoroscopic guidance. The balloon is then inflated using a device outside of the body that is connected to the balloon catheter, resulting in expansion and deployment of the stent. Deployment of the stent results in compression and outward radial displacement of the

plaque, increased luminal diameter, and enhanced coronary blood flow (Figure 1).

The Stent Restenosis Study trial was one of the first large-scale clinical trials to demonstrate that stent placement significantly reduced restenosis rates (by 25–30%) and the need for repeat revascularization (by 30% at 6 months) compared with stent-enhanced angioplasty (3). This trial evaluated the use of the Palmaz-Schatz stent, a first-generation stent. Since then, there have been numerous advances in stent design, and later generation stents have been associated with restenosis rates of approximately 15% in selected patient populations.

The United States Food and Drug Administration initially approved stents for use in emergency situations when balloon angioplasty was complicated by severe dissection or abrupt vessel closure. Currently, however, coronary stents are used as first-line treatment in as many as 80% of percutaneous coronary interventions. The one lesion subset for which coronary stents have not been convincingly shown to improve on balloon angioplasty is diseased vessels with diameters of less than 2.5 mm (4). These lesions are often treated with balloon angioplasty alone.

DIRECTIONAL CORONARY ATHERECTOMY

Although coronary stents are the mainstay for treatment for obstructive coronary artery disease, several adjunctive devices and techniques are available for coronary intervention. Directional coronary atherectomy has been used since the late 1980s. Although balloon angioplasty and coronary stenting work primarily by displacing plaque outward, directional coronary atherectomy physically removes plaque from the arterial wall. At the distal end of a directional coronary atherectomy catheter is a metal housing mounted on a balloon with a window (Figure 2A). Inside the window is a metal cutter, and distal to the window is a nose-cone collection chamber. At the proximal end of the catheter (outside of the body) is a motor drive unit that rotates the cutter and the cutter advancer that allows the operator to advance and retract the cutter under fluoroscopic guidance. Cuts are made in several quadrants of the artery so as to effectively "debulk" the lesion. Directional coronary atherectomy has been shown to improve acute angiographic results and facilitate both balloon angioplasty and coronary stenting in select lesions. However, it has not been shown to reduce the need for repeat target lesion revascularization, a clinical measure of restenosis (5). Its greatest value is for use in lesions in which the physical removal of plaque at ostial or bifurcation lesions will allow successful balloon angioplasty and coronary stenting.

ROTATIONAL ATHERECTOMY

Rotational atherectomy is a newer modality for plaque removal. The tip of the rotational atherectomy catheter consists of a diamond-studded burr ranging in size from 1.25 to 2.5 mm in diameter (Figure 2B), attached to a shaft that rotates the burr at speeds between 150,000 and 200,000 rpm under the power of a compressed air turbine. The operator advances the burr over

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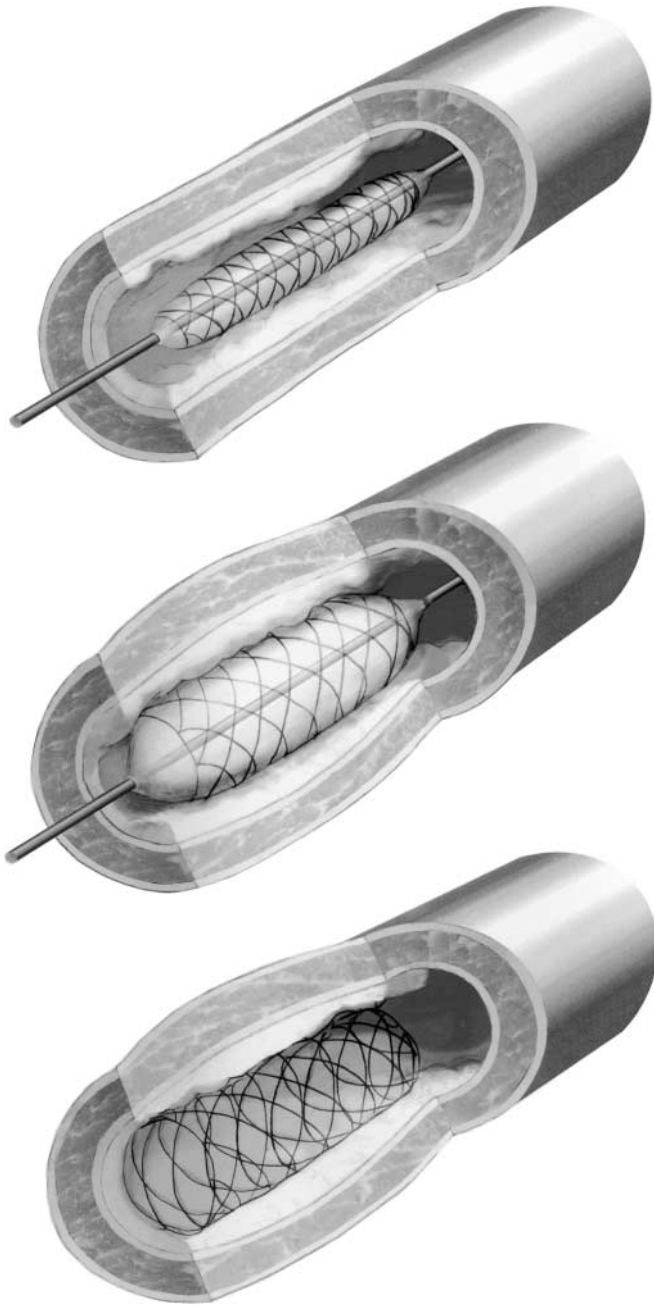


Figure 1. Mechanism of arterial lumen enlargement with coronary stenting.

a guide wire to the lesion and activates the rotation to burrow physically into the lesion. The plaque is pulverized into particles 20–50 μm in diameter, which pass through the coronary microcirculation and are removed by the reticuloendothelial system. Like directional coronary atherectomy, rotational atherectomy has not been shown to improve target lesion revascularization (6); however, it is an important tool to facilitate balloon angioplasty and coronary stenting. The best application of rotational atherectomy is in calcified lesions that make delivery of balloons and stents difficult. Like directional coronary atherectomy, rotational atherectomy plays an important role in the treatment of ostial and bifurcation lesions.

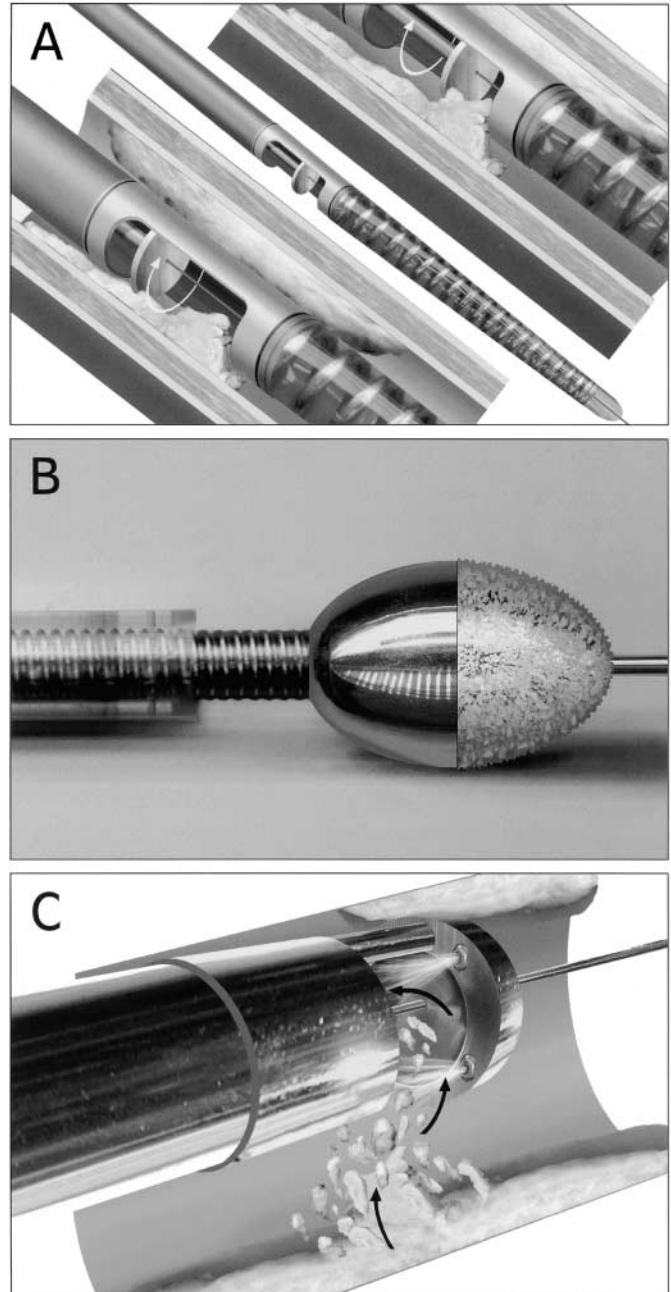


Figure 2. Adjunctive devices for coronary angioplasty. (A) Directional coronary atherectomy. (B) Rotational atherectomy. (C) Rheolytic thrombectomy.

RHEOLYTIC THROMBECTOMY

The percutaneous treatment of lesions that have significant thrombus burden is challenging. Several studies have shown that patients with intracoronary thrombus burden have higher periprocedural complication rates (7), often relating to the distal embolization of thrombus during balloon angioplasty or coronary stenting. Rheolytic thrombectomy has become a useful tool for the removal of coronary thrombi before coronary stenting. The rheolytic thrombectomy catheter works by forcing saline out of the distal tip of the catheter at high flow rates into a proximal lumen of the catheter. The high saline flow rates allow

for suction of thrombus into the proximal lumen by the Venturi effect (Figure 2C). Although rheolytic thrombectomy has not been shown to reduce restenosis, it is extremely effective in clearing thrombus and facilitating balloon angioplasty or coronary stenting (8). It is of particular value in the treatment of acute myocardial infarction, subacute stent thrombosis, and lesions in degenerated saphenous vein grafts.

DISTAL PROTECTION DEVICES

Distal protection devices are now used to prevent embolization of particulate matter during percutaneous coronary intervention. Currently, the GuardWire (Medtronic-AVE, Santa Rosa, CA) is approved for percutaneous coronary intervention on saphenous vein grafts. This device occludes the vein graft with a balloon during intervention and allows for removal of particulate matter from the graft by means of an aspiration catheter. In the Saphenous Vein Graft Angioplasty Free of Embolization Randomized (SAFER) trial, use of the GuardWire during saphenous vein graft intervention resulted in 53% fewer periprocedural ischemic complications than during vein graft intervention without distal protection (9). Other devices, including intraluminal filters, are presently being evaluated for vein graft and native coronary artery interventions.

ACUTE COMPLICATIONS OF PERCUTANEOUS CORONARY INTERVENTION

Percutaneous coronary intervention procedures are generally safe, with an estimated immediate complication rate of 1–10%, depending on the series. The most frequent complication after percutaneous coronary intervention is periprocedural creatine kinase, myocardial-bound elevation, or myocardial infarction. Most such events are asymptomatic and do not result in a decrement of left ventricular function, the most powerful predictor of survival after myocardial infarction. The threshold above which a postintervention creatine kinase, myocardial-bound elevation is considered harmful remains a controversial issue.

Vascular complications after percutaneous coronary interventions occur in 1–5% of procedures (10) and should be considered in the differential diagnosis of any patient with a significant drop in hematocrit after percutaneous coronary intervention or an abnormal exam at the access site. At the end of a percutaneous coronary intervention, the vascular access sheaths are typically removed manually once the level of systemic anticoagulation drops below an acceptable level. Hemostasis is then achieved by manual compression at the arteriotomy site or by the use of one of several mechanical compression devices. Alternatively, one of several vascular closure devices can be used to suture or plug the arteriotomy immediately after percutaneous coronary intervention, obviating the need for manual compression and prolonged bed rest.

The most common vascular complication after percutaneous coronary intervention is local hematoma, usually caused by ineffective compression or difficulty in achieving adequate hemostasis in patients who are obese or have unfavorable anatomy. Significant bleeding requiring blood transfusion occurs in approximately 1% of patients. Large hematomas are treated with prolonged compression, either manually or with a mechanical external compression device. In the majority of cases, however, these hematomas resolve without major discomfort or inconvenience to the patient.

Retroperitoneal hemorrhage, a potentially life-threatening vascular complication, usually occurs when the arteriotomy is above the level of the inguinal ligament. Adequate compression of high arteriotomy sites is not possible because of the lack of

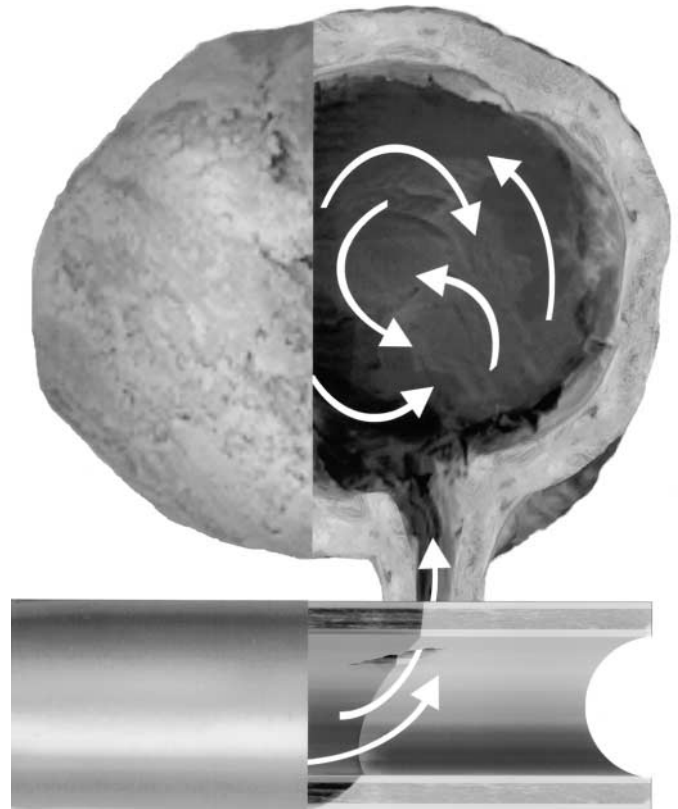


Figure 3. Arterial pseudoaneurysm.

pelvic skeletal structures against which to compress the artery. These patients typically present with hypotension and back or flank pain within the first hour after completion of the procedure. Emergency computed tomography scanning, consultation with a vascular surgeon, and transfusion of packed red blood cells and other blood products are crucial for the successful management of retroperitoneal hematoma.

Pseudoaneurysm of the femoral artery occurs after less than 1% of percutaneous coronary interventions. A collection of blood forms outside of the arteriotomy and directly communicates with the artery. Circulating blood exits the arteriotomy site and is contained within a sac composed of thrombus (Figure 3). Patients with significant pseudoaneurysm present with pain or a large pulsatile mass in the groin, an audible bruit on auscultation, and often neuropathic pain in the affected extremity caused by compression of the femoral nerve. The diagnosis is confirmed using vascular ultrasound. Therapeutic modalities include ultrasound-guided compression to seal the neck of the pseudoaneurysm that communicates with the artery, thrombin injection, or surgical closure.

Arteriovenous (AV) fistula after cardiac catheterization procedures is another complication of percutaneous coronary intervention. After inadvertently traversing the femoral vein, the sheath is inserted into the artery. A significant AV fistula should be suspected in any postintervention patient with a palpable thrill in the femoral artery and a continuous murmur detected in the artery on auscultation. Many small AV fistulas are insignificant or resolve without intervention; however, patients with large AV fistulas or patients requiring long-term anticoagulation may require surgical closure of the fistula to prevent complications such as high-output heart failure.

Patients undergoing percutaneous coronary intervention are occasionally exposed to substantial quantities of radio-contrast dye, which puts them at risk for contrast nephropathy. Patients who develop contrast nephropathy may be oliguric and generally will have an elevated serum creatinine level within 48 hours after the procedure. The patients at highest risk for contrast nephropathy are those with pre-existing renal dysfunction, those with diabetes, those who are older, and those who are volume depleted (11). The best preventive strategy for this complication is vigorous intravenous fluid hydration before and after procedure. N-acetylcysteine, 600 mg twice a day before the procedure, is effective for preventing renal dysfunction in patients undergoing computed tomography scanning and on this basis is expected to be helpful in the setting of coronary imaging (12). Fenoldopam, a dopaminergic receptor agonist, is also being evaluated in clinical trials for the prevention of contrast nephropathy in patients undergoing cardiac catheterization and intervention.

THE FIRST 30 DAYS: SUBACUTE STENT THROMBOSIS

Subacute stent thrombosis presents with chest pain, hypotension, and electrocardiographic changes consistent with myocardial injury. Subacute stent thrombosis is caused by thrombotic occlusion of the stent and usually occurs within 30 days of stent placement. Stent deployment is followed by migration of endothelial cells over the metal scaffolding in a process that ultimately covers the endoluminal surface of the stent. The contact of blood elements with bare metal can lead to platelet activation and aggregation and thrombosis of the stent. The risk factors for subacute stent thrombosis are well defined and include stents with small diameters (less than 2.5 mm), long stents, and multiple stents (13). With adequate antiplatelet therapy, the incidence of stent thrombosis is low (0.5–0.9%); however, the consequences of this complication are severe, with the incidence of death approaching 20% and the occurrence of transmural myocardial infarction approaching 40% (13).

THE FIRST 8 MONTHS: RESTENOSIS

Although coronary stenting has significantly reduced the rate of restenosis compared with that after balloon angioplasty, the restenosis rate remains at approximately 20% in all patients undergoing coronary stent placement. Restenosis rates are higher with small stent diameters, long stent lengths, multiple stents, and patients with diabetes (14). Restenosis is the gradual formation of a neointima composed of smooth muscle cells and macrophages within the stent. Once the narrowing caused by thickening of the neointima approaches a critical level, patients generally develop recurrent symptoms. It is rare for in-stent restenosis to present as an acute coronary syndrome; the peak period for clinical presentation is between 6 and 8 months after stent placement. In-stent restenosis rarely presents after 8 months after stent placement.

The current treatment for patients with in-stent restenosis is intracoronary brachytherapy. Coronary brachytherapy has been shown to reduce recurrent angiographic restenosis by 50–60% and to reduce the incidence of death, myocardial infarction, or repeat revascularization at 6 to 8 months by 31–36% (15, 16). Currently, there is no effective therapy for the prevention of restenosis. However, early studies of stents coated with the antiproliferative agent rapamycin have shown significant reductions in restenosis rates. In the recently published Randomized, Double-Blind Study with the Sirolimus-Eluting BX Velocity Balloon Expandable Stent in the Treatment of Patients with De Novo Native Coronary Artery Lesions (RAVEL) trial, 238 patients were randomized to coronary stenting with a bare coronary

stent or with a rapamycin-eluting coronary stent. The target lesion revascularization rate at 6 months was 26% in patients receiving a bare stent compared with 0% in patients receiving a rapamycin-eluting stent ($p < 0.001$) (17). Although these results are encouraging, the long-term safety of these stents has not been definitively proven. The Multicenter, Randomized, Double-Blind Study of the SIRoImUS-Coated BX Velocity Balloon-Expandable Stent in the Treatment of Patients with De Novo Native Coronary Artery Lesions (SIRIUS) trial, a 1,100-patient trial that will be reported soon, will provide further data regarding the safety of these stents. Other drug coatings being evaluated include paclitaxel and antisense DNA. Early data are also encouraging for the use of drug-eluting stents for the treatment of in-stent restenosis.

PHARMACOTHERAPY AFTER PERCUTANEOUS CORONARY INTERVENTION

All patients undergoing planned percutaneous coronary intervention—or diagnostic coronary angiography with high likelihood for requiring percutaneous coronary intervention—should be pretreated with 325 mg of aspirin. Most patients will also be loaded with an oral platelet adenosine diphosphate-receptor antagonist, either 300 mg of clopidogrel or 500 mg of ticlopidine, as prophylaxis for subacute stent thrombosis.

Three platelet glycoprotein IIb/IIIa receptor inhibitors are now routinely being used as adjunctive antiplatelet therapy during percutaneous coronary intervention: abciximab, eptifibatide, and tirofiban. These agents are administered as a bolus before the start of the percutaneous coronary intervention and are continued as an infusion for 12–18 hours after the intervention. Glycoprotein IIb/IIIa inhibitors have been shown to be effective in reducing periprocedural ischemic complications in several large-scale clinical trials of percutaneous coronary intervention (18, 19). On average, the incidence of death, myocardial infarction, or need for urgent revascularization is reduced by 30–40%. In the recently published Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial, abciximab use during primary angioplasty for ST-segment elevation myocardial infarction resulted in a significant reduction of subacute stent thrombosis within 30 days of the procedure (20).

In patients who develop significant bleeding complications after percutaneous coronary intervention, these agents should be discontinued immediately. Although abciximab can affect platelets for 5 to 7 days after administration, its effect can be reduced by platelet transfusions. Tirofiban and eptifibatide have half-lives of 1.8 and 2.5 hours, respectively, and their effects on platelet function are present for 4 to 6 hours after discontinuation. Given the large excesses of free tirofiban and eptifibatide after administration, platelet transfusions are not effective in reversing these agents. The decision to use these agents during percutaneous coronary intervention is guided by the perceived risk of periprocedural ischemic complications by the operator.

After percutaneous coronary intervention, all patients should be maintained on aspirin indefinitely. Patients should also be treated for 2 to 4 weeks with a platelet adenosine diphosphate-receptor antagonist to reduce the risk of subacute stent thrombosis. Ticlopidine and clopidogrel (in addition to aspirin) have both been shown to be significantly better at preventing subacute stent thrombosis than aspirin alone or aspirin with short-term anticoagulation with coumadin (21). Currently, 75 mg of clopidogrel for 30 days after stent placement along with aspirin is the preferred regimen for prevention of subacute stent thrombosis. Clopidogrel has the advantage of single-day dosing and a significantly lower incidence of potentially life-threatening leukopenia and thrombotic thrombocytopenic purpura than does ticlopidine.

For patients allergic to clopidogrel, however, ticlopidine administered 250 mg twice a day for 2 weeks in addition to aspirin is an acceptable alternative. For patients who are allergic to aspirin or both of the platelet adenosine diphosphate–receptor antagonists, it is important to consult a specialist in allergy so that the patient can undergo desensitization. The rate of subacute stent thrombosis for patients not treated with either agent is as high as 10% (22), whereas the rates of major bleeding are now less than 1.5%.

PRACTICAL ISSUES IN PERCUTANEOUS CORONARY INTERVENTION FOR THE INTENSIVIST

Intensivists often care for patients with multisystem organ dysfunction, including patients with myocardial ischemia and failure. In addition, it is likely that critical care specialists will be involved in the immediate postprocedure care of percutaneous coronary intervention patients or will care for patients with intercurrent illness who have recently undergone percutaneous coronary intervention. Therefore, it is important for critical care specialists to understand preprocedural and postprocedural issues pertaining to percutaneous intervention.

Life-threatening illnesses such as sepsis increase oxygen demand, which in turn can precipitate ischemia. Manifestations of ischemia include ST-segment depression on the electrocardiogram and minor cardiac enzyme elevation. In addition to treating the underlying cause of increased cardiac demand, optimal treatment includes heart rate control with β -adrenergic-receptor antagonists and blood pressure control with nitrates. It is generally preferable to avoid cardiac catheterization procedures during active infection. When medication-refractory myocardial ischemia limits recovery, percutaneous intervention should be considered if the expertise to provide a safe procedure is available. The wider recognition of cardiac ischemia limiting successful weaning from mechanical ventilation will make it possible to perform clinical trials to identify patients who can benefit from these procedures. Today the decision to perform invasive cardiac procedures in patients with ongoing life-threatening infection must be made after a careful risk–benefit analysis in consultation with cardiovascular and critical care specialists.

In addition to sepsis, patients in critical care units are subject to coagulopathies resulting from conditions such as hepatic failure or disseminated intravascular coagulation. Acute coronary syndromes in the setting of an acute bleeding disorder are uncommon. In the rare event that a patient with a bleeding disorder is in need of a percutaneous coronary intervention, most cardiologists would prefer that the international normalized ratio be less than 2.0 and that the platelet count be greater than 20,000, as the risk of bleeding complications is increased in these settings. Administration of fresh-frozen plasma and platelets may be necessary. In addition, arteriotomy closure devices may be of some value in the prevention of bleeding complications after coronary intervention. However, there are no clear guidelines for to management of anticoagulation in these patients if coronary intervention is necessary. In most situations, only intraprocedural heparin should be used without concomitant glycoprotein IIb/IIIa inhibitor, as this is reversible (1 mg protamine/50 U unfractionated heparin or 1 mg enoxaparin). Furthermore, most physicians opt to perform only balloon angioplasty to avoid the long-term antiplatelet therapy required after coronary stenting. Again, however, a careful risk–benefit analysis must be completed by the intensivist and cardiovascular specialist before undertaking such a procedure on a patient with an acute bleeding disorder.

Patients with critical illness are at particularly high risk for subacute stent thrombosis because of impaired gastrointestinal absorption of antiplatelet therapy and hypotensive episodes,

which can lead to reduced coronary blood flow within the stent and thrombosis. The cornerstone of therapy for suspected subacute stent thrombosis is the administration of effective antiplatelet agents (aspirin, an adenosine diphosphate–receptor antagonist, and a glycoprotein IIb/IIIa–receptor inhibitor), coronary angiography, and urgent percutaneous or surgical revascularization.

Patients in the intensive care unit often need specialized imaging procedures such as magnetic resonance imaging. Pacemakers and automated implantable cardiac defibrillators are absolute contraindications to undergoing magnetic resonance imaging. However, coronary stents are only weakly ferromagnetic, and most patients are advised to avoid magnetic resonance imaging for the first 30 days after stent implantation. Nevertheless, the risk of stent disruption is extremely low, and in some circumstances, magnetic resonance imaging within the first 30 days of coronary stenting may be justified.

Critically ill patients can require surgery, and the appropriate timing of noncardiac surgery after stent implantation is a common concern. It is recommended that surgery be delayed for 30 days after stent implantation to allow for adequate endothelialization of the stent and completion of antiplatelet therapy to reduce the risk of perioperative stent thrombosis. If surgery cannot be delayed for 30 days, the combination of aspirin and platelet adenosine diphosphate–receptor antagonist should be continued throughout the perioperative period. If the surgeon feels the risk of surgical bleeding precludes the continued use of these agents, yet the surgery is urgent, the patient must be made aware of the risk of perioperative stent thrombosis, which may approach 5–10% (22). When a patient requires coronary revascularization before an urgent surgical procedure, many interventional cardiologists will perform balloon angioplasty only and eliminate the risk of perioperative stent thrombosis at the expense of a less durable outcome compared with that from coronary stenting.

CONCLUSION

Rapid technologic advances in the percutaneous treatment of coronary artery disease are being made, and it is likely that many more patients will benefit from coronary intervention. One particularly promising technology is the development of drug-eluting stents. It is likely that as long-term success rates with percutaneous coronary intervention increase, more patients will undergo these procedures. Furthermore, as research continues to aid in the identification of nonobstructive plaques that may be prone to rupture (vulnerable plaques), it is likely that preventive intervention will be possible. A comprehensive understanding of coronary intervention by critical care physicians and a multidisciplinary approach, including cardiologists, are essential for the optimal care of cardiac patients with intercurrent noncardiac illness.

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