

Management of Patients Undergoing Percutaneous Coronary Revascularization

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While performance of percutaneous coronary intervention (PCI) remains the domain of specialized cardiologists, patients undergoing PCI are cared for by noninvasive cardiologists, internists, and primary care physicians. Therefore, patient care is optimized when the entire patient care team understands procedural risks and complications as well as optimum patient management before, during, and after PCI.

Before PCI, patients with contrast dye allergies should be identified and pretreated with steroids and an H₁-blocker. Hydration should be initiated and maintained before and after the procedure to minimize the risks for contrast nephropathy. Periprocedure, patients should be monitored clinically for evidence of ischemia. In patients with significant groin, flank, abdominal, or

back pain, as well as those with decrease in hematocrit or unexplained hypotension, the diagnosis of groin or retroperitoneal hematoma should be considered and promptly evaluated. Groin tenderness, pulsatile mass, or bruit should prompt evaluation for possible femoral pseudoaneurysm or arteriovenous fistulae. After the procedure, all patients treated with coronary stents should receive aspirin plus clopidogrel. Patients who develop typical anginal symptoms between the 1st and 6th to 8th months after PCI are likely to have restenosis and can be evaluated by an imaging study or repeated catheterization.

Ann Intern Med. 2003;139:123-136.

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Coronary balloon angioplasty using the percutaneous approach was first performed by Andreas Gruentzig in 1977 (1). Since then, percutaneous coronary revascularization has been extended to include atherectomy, stenting, and other procedures, together now known as percutaneous coronary intervention (PCI). While performance of PCI itself remains the domain of specialized cardiologists, patients undergoing PCI are cared for by noninvasive cardiologists, internists, and primary care physicians. Therefore, patient care can be optimized if the patient care team understands procedural risks and complications as well as patient management before, during, and after the procedure.

As part of its mission, the American Heart Association Diagnostic and Interventional Catheterization Committee is charged with educating physicians on information relevant to PCI. Members of the committee have therefore prepared this document for physicians to serve as a review of the complications that can occur during PCI. Some issues regarding the diagnosis, prevention, and management of complications remain unsettled, and in certain cases the committee has intentionally opted to present what it considers reasonable strategies regarding these issues rather than specific recommendations. The Science Advisory Coordinating Committee of the American Heart Association approved this document for publication.

METHODS

We searched MEDLINE for articles published over the past 20 years, using the indexing terms *coronary angioplasty, stents, contrast nephropathy, stent thrombosis, vascular complications, pseudoaneurysm, arteriovenous fistula, vascular closure devices, and restenosis*. Additional data sources included consensus conference statements from the Ameri-

can College of Cardiology, American Heart Association, and Society for Cardiac Angiography and Interventions. Randomized and observational studies were systematically reviewed. We considered factors such as study design, number of patients studied, statistical significance of results, and relevance to contemporary clinical practice when deciding whether to incorporate these results into our conclusions and recommendations. Consensus conference statements regarding issues addressed in this document were incorporated into our recommendations when relevant.

PREPROCEDURAL CONSIDERATIONS

Allergic reactions to contrast dye and contrast nephropathy are important potential complications that must be considered in patients undergoing contrast angiographic procedures. Data on these complications are derived from studies of diagnostic cardiac catheterization and recent studies of PCI.

Allergic Reactions

Allergic reactions related to iodine-based contrast agents for angiographic imaging are classified as minor (hives, rash), moderate (urticaria, bronchoconstriction), or severe (anaphylactoid reaction [as opposed to anaphylactic reaction] with hemodynamic collapse). Anaphylactoid reactions to intravascular contrast are rare (2–6). However, in patients with a history of contrast reaction, the risk for repeated anaphylactoid reaction is generally reported to range from 17% to 35% (2, 7–9). Although previous adverse reactions to shellfish or seafood in general are believed to be associated with future anaphylactoid reaction to iodine-based contrast, no significant body of data supports this conjecture (3, 10, 11).

Pretreatment with corticosteroids appears to decrease

Table 1. Recommended Regimens for Pretreatment (Prevention) and Treatment of Anaphylactoid Reactions in Patients Undergoing Percutaneous Coronary Interventions*

Phase	Clinical Setting	Intervention
Pretreatment (prevention)	Known history of anaphylactoid reaction to contrast	Oral prednisone, 50 mg, 13, 7, and 1 h preprocedure, and oral diphenhydramine, 50 mg, 1 h preprocedure (3, 7), or oral prednisone, 60 mg, the night before and morning of the procedure, and oral diphenhydramine, 50 mg, the morning of the procedure (13)
Treatment	Urticaria or pruritus (3)	No treatment, or IV diphenhydramine, 25–50 mg If no response to therapy, epinephrine, 0.3 mL of 1:1000 solution SC, every 15 min up to 1 mL with or without IV cimetidine, 300 mg, or IV ranitidine, 50 mg, in 20 mL normal saline over 15 min
	Bronchospasm (3)	Oxygen by mask and oxymetry monitoring Depending on condition: Mild: Albuterol inhaler Moderate: Epinephrine, 0.3 mL of 1:1000 solution SC every 15 min up to 1 mL Severe: Epinephrine, 10- μ g IV boluses every min, then infusion of 1–4 μ g/min IV diphenhydramine, 50 mg IV hydrocortisone, 200–400 mg H ₂ -blocker (optional)
	Facial and laryngeal edema (3)	Airway protection/intubation + supplemental oxygen Epinephrine, 0.3 mL of 1:1000 solution SC every 15 min up to 1 mL, or 10- μ g IV boluses every min followed by infusion of 1–4 μ g/min
	Hypotension or shock (3)	Epinephrine, 10- μ g IV boluses every min, followed by infusion of 1–4 μ g/min Supplemental oxygen or intubation IV diphenhydramine, 50–100 mg IV hydrocortisone, 400 mg If unresponsive to therapy, dopamine, H ₂ -blocker, and advanced cardiac life support as indicated.

* Most recommendations were adapted from Goss JE et al. (3). Numbers in parentheses are reference numbers. IV = intravenous; SC = subcutaneously.

the incidence of adverse reactions (6, 7, 12). In one large series of patients who had previous anaphylactoid reactions to iodine contrast and received prednisone and diphenhydramine (Benadryl, Pfizer, New York, New York) before repeated contrast administration (7), the incidence of anaphylactoid reaction was 11%. Hypotension occurred in only 3 of 415 treated patients (0.7%) (7). Additional routine treatment with the H₂-blocker cimetidine does not appear to have any benefit in patients with previous allergic reactions (7).

On the basis of limited data, patients with known previous anaphylactoid reactions to contrast dye should be pretreated with steroids and an H₁-blocker. One previously studied regimen is oral prednisone, 50 mg, administered 13 hours, 7 hours, and 1 hour before the procedure, plus diphenhydramine, 50 mg, administered 1 hour before the procedure (3, 7). We recommend an alternate and more practical regimen: prednisone, 60 mg, the night before and the morning of the procedure, plus an oral H₁-blocker (such as diphenhydramine), 50 mg, the morning of the procedure (13). The Society for Cardiac Angiography and Interventions has issued recommendations for treatment of patients who develop anaphylactoid reactions (3). These recommendations are summarized in **Table 1**.

Contrast-Induced Nephropathy

Deterioration of renal function may occur as a result of both direct and indirect effects of the iodine-based contrast agents used during PCI (14, 15). The observed incidence of contrast nephropathy in studies varies widely and depends on the study design, patient population studied, and definition of contrast nephropathy used. Most recent

studies have defined contrast nephropathy as an increase in serum creatinine concentration of 25% or an absolute increase of 44 μ mol/L (0.5 mg/dL). In recent studies of patients undergoing coronary procedures, the incidence of contrast nephropathy in high-risk patients (those with an elevated creatinine concentration at baseline) who received “standard therapy” (usually pre- and periprocedure hydration) ranged from 11% to 41% (16–21). Contrast nephropathy usually first manifests as an elevation in creatinine concentration 24 to 48 hours after the procedure that peaks 3 to 5 days after the procedure (14, 15). Contrast nephropathy requiring dialysis is extremely rare (<1%) in the general population of patients undergoing PCI (22), although an incidence of 9% was observed in one small series of patients with preexisting renal insufficiency (serum creatinine level, 177 to 698 μ mol/L [2.0 to 7.9 mg/dL]) (23). Patient-related factors associated with an increased risk for contrast nephropathy include diabetes; preexisting renal insufficiency; and, possibly, reduced intravascular volume status (4, 14, 22, 24). Many but not all studies have found a relationship between the amount of contrast used and the risk for contrast nephropathy (14, 21–23, 25–27). Analysis of data from the largest series of patients undergoing PCI found a statistically significant relationship between contrast dose and risk for contrast nephropathy, although the odds ratio for developing contrast nephropathy with higher doses of contrast was only 1.008 (22).

Available data from studies of diagnostic cardiac catheterization suggest that pre- and postprocedure hydration decreases the incidence of contrast-induced renal failure

(20, 28–30). Administration of various pharmacologic agents during the periprocedural period, including furosemide, mannitol, dopamine, aminophylline, and atrial natriuretic peptide, has not been shown to be of benefit in patients undergoing diagnostic cardiac catheterization or percutaneous intervention; in some cases, these agents adversely affected renal function (20, 21, 24, 30–32). Low-osmolar contrast agents are associated with less contrast nephropathy than high-osmolar agents in patients with preexisting renal insufficiency (33). In one recent study, use of the iso-osmolar agent iodixanol (Visipaque, Amersham Health, Buckinghamshire, United Kingdom) led to less contrast nephropathy than did a low osmolar agent (16).

Modestly sized studies have examined whether administration of acetylcysteine before and after exposure to contrast agents can decrease the incidence of contrast nephropathy during various imaging procedures (including PCI) in patients with baseline renal insufficiency (17, 19, 34–37). The most common dosing regimen was 600 mg orally twice per day on the day before and the day of the study. Most but not all of these studies have demonstrated some benefit with acetylcysteine administration. It should be noted, however, that the benefit was limited to predefined changes in serum creatinine concentration and that no benefits in harder end points, such as need for dialysis, were demonstrated.

On the basis of available data, pre- and post-PCI hydration is recommended, at least in patients with baseline renal insufficiency (0.45% saline at 1 mL/kg of body weight per hour for 12 hours preprocedure and 12 hours postprocedure). Diuretics should not be administered before the procedure. Acetylcysteine treatment can be considered in patients who are at high risk for contrast nephropathy.

Contrast-Induced Renal Failure and Lactic Acidosis

Lactic acidosis is a rare complication of contrast-induced acute renal failure that can occur in patients taking the oral hypoglycemic agent metformin (Glucophage, Bristol-Myers Products, New York, New York). Almost all reported cases have occurred in patients with preexisting renal insufficiency (38–41). Current product labeling precautions state that metformin should be discontinued at the time of or before an angiographic procedure, withheld for 48 hours after the procedure, and reinstated only after renal function has been reevaluated and found to be normal (42). We suggest that metformin should be discontinued on the day of the procedure in patients with normal renal function and 48 hours before elective PCI procedures, when possible, in patients with preexisting renal insufficiency at increased risk for contrast nephropathy.

Pretreatment with Antiplatelet Agents before PCI

Studies performed in the era of balloon angioplasty alone (that is, without coronary stenting) demonstrated consistently lower adverse event rates in patients who received pretreatment with aspirin plus dipyridamole or aspi-

rin alone than in those who did not (43–46). On the basis of these studies, it is recommended (and standard practice) that clinicians ensure that patients undergoing PCI have received aspirin treatment. The optimal dose and timing of aspirin administration have not been established; a dose of 80 to 325 mg, given at least 2 hours before PCI when possible, is recommended (47, 48).

Ticlopidine (Ticlid, Roche Pharmaceuticals, Nutley, New Jersey) and clopidogrel (Plavix, Bristol-Myers Products, New York, New York) are thienopyridines that irreversibly inhibit adenosine diphosphate-mediated platelet aggregation (49). Several retrospective analyses found that patients who had been pretreated with a thienopyridine before coronary stent implantation had fewer major adverse cardiac events, primarily enzymatically defined MI (50–52). In the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) study, in which patients with non-ST-segment elevation acute coronary syndrome were treated with either aspirin plus placebo or aspirin plus clopidogrel, 2658 of the 12 562 patients enrolled underwent PCI. Analyses of these study patients, referred to as the PCI-CURE study, revealed that those who had received aspirin plus clopidogrel before PCI had fewer major adverse cardiac events than those who had received aspirin plus placebo (4.5% vs. 6.4%; $P = 0.03$) (53). Some but not all of this difference was due to a reduction in PCI-related complications (54).

In the Clopidogrel for the Reduction of Events During Observation (CREDO) trial, patients undergoing PCI received pretreatment with a 300-mg loading dose of clopidogrel (administered ≥ 3 hours before PCI) or placebo. There was no statistically significant reduction in major adverse cardiac events at 28-day follow-up, although it was observed that fewer adverse events occurred in the prespecified subgroup of patients who received the loading dose of clopidogrel at least 6 hours before PCI (55). Taken together, these studies suggest, although do not definitively prove, that pretreatment with a thienopyridine, at least if it is administered a minimum of 6 hours before PCI, is associated with a lower incidence of adverse events. Clopidogrel therapy, however, is associated with an increased risk for bleeding complications, particularly in patients who undergo coronary artery bypass grafting (CABG) within 5 to 7 days of receiving the drug (56, 57). Pretreatment with clopidogrel (administered ≥ 6 hours before PCI) can be cautiously recommended in patients undergoing planned PCI. However, we do not routinely recommend such pretreatment in patients who have not yet undergone diagnostic cardiac catheterization and in whom coronary artery bypass surgery would be performed within 5 to 7 days if warranted based on findings at the time of cardiac catheterization.

The glycoprotein IIb/IIIa inhibitors are potent antiplatelet agents that act by inhibiting platelet aggregation. Administration of these agents before or at the time of PCI has been shown to decrease the risk for ischemic compli-

cations, particularly MI, during the procedure and in the early periprocedural period in patients with acute coronary syndromes, as well as in those undergoing elective PCI (58–63). A detailed discussion of the relative merits of glycoprotein IIb/IIIa treatment is beyond the scope of this review. We refer the reader to the American College of Cardiology/American Heart Association Guideline Update for the Management of Patients with Unstable Angina and Non–ST-Segment Elevation Myocardial Infarction (64), which recommends administration of glycoprotein IIb/IIIa inhibitors to patients who have non–ST-segment elevation acute coronary syndromes and high-risk features or those in whom a management strategy of cardiac catheterization and PCI (if indicated) is planned.

PERIPROCEDURAL CONSIDERATIONS

Myocardial Infarction

Myocardial infarction can occur during PCI because of coronary dissection, abrupt vessel closure, thrombotic occlusion of the epicardial vessel, distal embolization of thrombus or atheromatous material to the microcirculation, side branch occlusion, coronary spasm, or a combination of events (65–67). The incidence of MI detected during PCI is related to the clinical presentation (for example, acute coronary syndromes vs. stable angina); the intensity of creatine kinase (CK), CK-MB, or troponin monitoring after the procedure; the definition of the degree of enzyme elevation that constitutes an MI; and the revascularization procedures used (for example, atherectomy). The incidence of MI, defined primarily as CK-MB concentrations elevated to more than two to three times the upper limit of normal, generally ranges between 5% and 30% (48, 68). Rates of 5% to 10% are representative of most large interventional trials (69) (Table 2). A majority of these enzyme-defined infarctions are clinically “silent” (that is, without angina, arrhythmia, or hypotension) (48, 66, 79, 80).

Most enzyme-defined MIs are due to small elevations in CK or CK-MB levels (less than three times the upper limit of normal). Controversy surrounds the clinical significance of small or modest CK-MB elevations (two to three times the upper limit of normal) and their relationship to adverse outcomes. Some authorities have contended that even these modest elevations in CK-MB levels are correlated with a greater incidence of future adverse cardiac events (68, 72, 81–86). More recently, however, it has been reported that only CK-MB elevations greater than five to eight times the upper limit of normal are correlated with worse long-term outcome (69, 87–89).

In many patients, elevations of CK levels after PCI may indicate more extensive or severe coronary artery disease. This may at least partially explain the worse long-term prognosis observed in such patients, particularly those with only modestly elevated enzyme levels (90). Although troponin I and T levels are frequently used to assess myo-

cardial damage in patients with acute coronary syndromes, the relationship, if any, between elevations of these markers and future adverse events after PCI has not yet been established.

An electrocardiogram should be obtained in all patients before and immediately after PCI, and again if anginal symptoms occur (48, 68). Serial CK and CK-MB measurements (6 to 8 and 16 to 24 hours after the procedure) should be obtained in patients with suspected ischemia during PCI (48, 67, 68). Patients with notably elevated CK-MB levels (at least five to eight times the upper limit of normal) after PCI should be regarded as having had an MI and should be treated as such (48, 68). In these patients, 1 or more days of additional monitoring, post-MI pharmacotherapy, and a more cautious resumption of daily activities may be warranted, depending on the clinical scenario (91).

As discussed previously, numerous studies have shown that administration of a platelet glycoprotein IIb/IIIa inhibitor during and for an additional 12 to 24 hours after PCI can decrease procedure-related adverse events, primarily enzymatically defined MI. The most recent studies have demonstrated a reduction of approximately 37% to 52% in adverse events (60, 61). In patients receiving glycoprotein IIb/IIIa inhibitor therapy, continued heparin administration after PCI does not decrease the incidence of adverse ischemic events but only increases bleeding complications (48, 59, 92–100). Therefore, anticoagulation with heparin should not be continued (or reinitiated) after most successful PCIs. Thrombocytopenia, usually defined as a decrease in platelet count to below 100 000 cells/cm², has been associated with use of glycoprotein IIb/IIIa inhibitors in 1% to 4% of patients, depending on the study design, definitions, and agent used. Monitoring of platelet counts during glycoprotein IIb/IIIa therapy is recommended. Platelet counts should be obtained initially 4 to 6 hours after glycoprotein IIb/IIIa initiation and again the following morning.

Emergency Coronary Bypass Surgery and Death

Recent data demonstrate that the need for emergency CABG has decreased since the introduction of coronary stents (48, 101–109) and that CABG rates are currently less than 1%. Death is similarly rare. Most recent registries and clinical trials report mortality rates of less than 1%, although these data are derived from selected populations and the incidence of death associated with PCI may be slightly higher in the general population (110). Factors associated with increased mortality rates during PCI include advanced age, female sex, diabetes, previous MI, multivessel disease, left main or equivalent coronary disease, a large area of myocardium at risk, preexisting left ventricular function, and preexisting renal insufficiency (47, 48). Although emergency CABG and death are rare, patients and family members should be made aware of the risks during discussion of PCI.

Table 2. Incidence of Reported Myocardial Infarction in Large (>1000 Patients) Multicenter Randomized Studies Involving Percutaneous Coronary Interventions and Routine Measurement of Creatine Kinase or Creatine Kinase–MB Levels*

Study (Reference)	Study Design	MI Definition	Follow-up Period	MI Incidence, %
ASCENT (70)	Multilink stent vs. Palmaz–Schatz stent	Increase in CK level to at least twice the ULN or new pathologic Q waves	30 d	3.7 vs. 5.0
Bittl et al. (71)†	Heparin vs. bivalirudin during balloon angioplasty	Increase in CK level to at least twice the ULN or Q-wave evolution	7 d	4.2 vs. 3.3
CAPTURE (58)	Placebo vs. abciximab in patients with refractory unstable angina undergoing PCI 18–24 h after randomization	Increase in CK or CK-MB level to at least three times the ULN in two separate blood samples and to 50% over the previous value, or new pathologic Q waves	30 d‡	8.2 vs. 4.1
CAVEAT (72)	Balloon angioplasty vs. DCA	Increase in CK-MB level to at least three times the ULN or increase in CK level to at least twice the ULN or new pathologic Q waves	30 d	6.8 vs. 15.2
CLASSICS (73)	Aspirin + ticlopidine vs. aspirin + clopidogrel (75 mg/d) vs. aspirin + clopidogrel (300 mg load then 75 mg/d) after coronary stenting	Increase in CK or CK-MB levels to at least three times the ULN or troponin T level >0.2 µg/L	28 d	0.3 vs. 0.3 vs. 0.7
CREDO (55)	Clopidogrel vs. placebo before and after coronary stenting	New significant Q waves in at least two leads or CK-MB levels at least two to three times the ULN	28 d	5.8 vs. 6.6
EPIC (74)	Placebo vs. c7E3 Fab bolus vs. c7E3 Fab bolus and infusion	Increase in CK-MB level to at least three times the ULN or new pathologic Q waves (different enzymatic criteria existed for those with elevated CK-MB levels at baseline)	30 d	8.6 vs. 6.2 vs. 5.7
EPILOG (59)	Abciximab vs. placebo in balloon angioplasty	Increase in CK or CK-MB levels to at least three times the ULN, or new Q waves	30 d	8.7 vs. 3.7 vs. 3.8
EPISTENT (60)	Stent + placebo vs. balloon angioplasty + abciximab vs. stent + abciximab	Increase in CK-MB level to at least three times the ULN	30 d	9.6 vs. 5.3 vs. 4.5
ESPRIT (61)	Placebo vs. eptifibatide during coronary stenting	Increase in CK-MB level to at least three times the ULN in two separate blood draws	48 h	9.0 vs. 5.4
IMPACT-II (75)	Placebo vs. eptifibatide in patients undergoing balloon angioplasty	Increase in CK-MB level to at least three times the ULN or new pathologic Q waves	30 d	~8.3 vs. 6.8
PCI-CURE (53)	Clopidogrel vs. placebo in patients with acute coronary syndrome	Presence of two of three criteria: ischemic symptoms, increase in CK-MB level to at least three times the ULN, and ECG changes consistent with MI	30 d	Including CVD death: 2.9 vs. 4.4 Excluding CVD death: 2.1 vs. 3.8
REPLACE-2 (76)	Bivalirudin vs. heparin and glycoprotein IIb/IIIa inhibitor	New significant Q waves in at least two leads or CK-MB level at least two to three times the ULN	30 d	6.2 vs. 7.0
RESTORE (77)	Placebo vs. tirofiban during balloon angioplasty or DCA	Increase in CK or CK-MB level to at least three times the ULN	30 d	5.7 vs. 4.2
STARS (78)	Aspirin alone vs. aspirin + warfarin vs. aspirin + ticlopidine after coronary stenting	CK level at least twice the ULN when CK-MB level was also elevated or new pathologic Q waves were present	“Procedure-related” (time not specified)	2.9 vs. 4.2 vs. 4.2
TARGET (52)	Tirofiban vs. abciximab during coronary stenting	CK-MB level at least three times the ULN in two separate blood samples or pathologic Q waves	30 d	6.9 vs. 5.4

* ASCENT = ACS MultiLink Stent Clinical Equivalence in De Novo Lesions Trial; CAPTURE = c7E3 Fab Antiplatelet Therapy in Unstable Refractory Angina; CAVEAT = Coronary Angioplasty Versus Excisional Atherectomy Trial; CK = creatine kinase; CLASSICS = Clopidogrel Aspirin Stent International Cooperative Study; CREDO = Clopidogrel for the Reduction of Events During Observation; CVD = cardiovascular disease; DCA = directional coronary atherectomy; ECG = electrocardiographic; EPIC = Evaluation of Platelet IIb/IIIa Inhibition for Prevention of Ischemic Complication; EPILOG = Evaluation of PTCA To Improve Long-term Outcome with abciximab GPIIb/IIIa Receptor Blockade; EPISTENT = Evaluation of Platelet IIb/IIIa Inhibitor for Stenting Trial; ESPRIT = European/Australasian Stroke Prevention in Reversible Ischaemia Trial; IMPACT-II = Integrilin to Minimise Platelet Aggregation and Coronary Thrombosis-II; MI = myocardial infarction; PCI = percutaneous coronary intervention; PCI-CURE = Percutaneous Coronary Intervention–Clopidogrel in Unstable angina to prevent Recurrent Events; REPLACE-2 = Randomized Evaluation in PCI Linking Angiomax to Reduced Clinical Events-2; RESTORE = Randomized Efficacy Study of Tirofiban for Outcomes and REstenosis; STARS = STent Anti-thrombotic Regimen Study; TARGET = Do Tirofiban and ReoPro Give Similar Efficacy Trial; ULN = upper limit of normal.

† Reanalyzed, final results from the Bivalirudin Angioplasty Study.

‡ Includes myocardial infarctions in the 18–24 hours before PCI.

§ Many additional definitions of MI were also used.

Vascular Complications

Major bleeding complications have been variously defined in different studies but generally include some combination of end points, such as overt bleeding with a decrease in hemoglobin level of at least 30 to 50 g/L (3 to 5

g/dL), need for blood transfusion, or retroperitoneal bleeding (52, 60, 61, 73). In current clinical practice, as evidenced by results of recent interventional trials, rates of major bleeding complications are low (0.7% to 1.7%) (52, 60, 61, 73). Insertion of vascular sheaths may produce

groin or retroperitoneal hematomas. Groin hematomas may present with localized pain, lower-extremity edema due to femoral vein compression, or lower-extremity neurologic symptoms due to compression of the femoral nerve. Palpation of localized swelling or tenderness in the area, or loss of sensory or motor function, is highly suggestive of hematoma. The diagnosis can be confirmed by ultrasonography or computed tomography.

Several studies have reported a low incidence of retroperitoneal hematomas (0.15% to 0.44%) (111). Nevertheless, retroperitoneal hematoma should be suspected in patients with unexplained hypotension and/or a marked decrease in hematocrit. Although patients with retroperitoneal bleeding may experience flank, abdominal, or back pain, the absence of these symptoms does not exclude this condition. The diagnosis is usually made by abdominopelvic computed tomography. Computed tomography should be strongly considered in patients with severe or continuing decreases in hematocrit; hypotension; or severe flank, abdominal, or back pain, particularly in cases of hemodynamic instability. Most retroperitoneal hematomas can be treated conservatively with discontinuation or reversal of anticoagulation and antiplatelet therapy and with blood transfusions alone when necessary; only 16% of patients require surgery (112). Indications for surgical intervention include persistent hypotension, decreasing hematocrit despite transfusion, or femoral neuropathy (due to nerve compression) (112, 113).

After the vascular sheath is removed from the femoral artery, a femoral pseudoaneurysm can form. A pseudoaneurysm is a communication between the femoral artery and the overlying fibromuscular tissue, resulting in a blood-filled cavity. The reported incidence of pseudoaneurysm ranges from 0.5% to 6.3% (111). Most series report an incidence of approximately 1%, but the true incidence can be significantly higher if careful imaging studies are performed on all patients (114, 115). Groin tenderness, a palpable pulsatile mass, and/or new bruit in the groin area should prompt examination by Doppler flow imaging. Smaller pseudoaneurysms are usually followed clinically. Most larger pseudoaneurysms can be treated with ultrasound-guided compression, ultrasound-guided thrombin injection, or surgical repair (116, 117). An emerging alternative therapy is percutaneous polytetrafluoroethylene-covered stent-graft deployment at the site of the pseudoaneurysm.

An arteriovenous (AV) fistula can result from sheath-mediated communication between the femoral artery and femoral vein. An AV fistula may be suggested by the presence of a systolic and diastolic bruit and confirmed by Doppler ultrasonography. Reported incidence of AV fistulae ranges from 0.2% to 2.1% (111, 118). Arteriovenous fistulae can be treated with conservative therapy (careful observation) in most patients or with ultrasound-guided compression, surgical repair, or percutaneous implantation of covered stents if necessary (116, 117).

The incidence of stroke in contemporary large series and randomized trials ranges from less than 0.1% to 0.38% (60, 61, 119–122). Approximately half of PCI-related strokes are hemorrhagic, and half are nonhemorrhagic. Factors associated with increased risk for stroke include older age, presence of diabetes, saphenous vein graft interventions, and placement of an intra-aortic balloon pump (placed either prophylactically or for intraprocedural complications) (60, 61, 119–122). In-hospital mortality rates are high in patients who have strokes (37.2% in one large series [120]). In patients with suspected periprocedural stroke, a computed tomography scan should be immediately obtained and cessation of any anticoagulant therapies should be discussed with the interventional cardiologist.

Many arterial access sites are “sealed” after the procedure with percutaneous vascular closure devices. These devices can percutaneously place one or more sutures in the femoral artery or deliver a procoagulant, such as collagen or collagen and thrombin, through a sheath to stimulate local hemostasis. Patients treated with such devices are usually able to sit up and ambulate within 2 hours of the PCI procedure. Physicians should be aware, however, that hemostasis success rates are less than 100% and that these devices are associated with a risk for vascular complications that is often similar to that seen with manual compression. These complications include pseudoaneurysm, bleeding and hematoma, infection, arterial stenosis or occlusion, and venous thrombosis. Most series report an incidence of major complications ranging from approximately 1% to 5% (123–133). Several reports in the surgical literature suggest that vascular closure devices are associated with a higher incidence of large pseudoaneurysms and pseudoaneurysms not amenable to ultrasound compression therapy, greater loss of blood and need for transfusions, higher incidence of arterial stenosis or occlusion, more extensive surgical repair, and higher incidence of groin infections compared with manual compression (123, 130, 134). Thus, the possibility of vascular complications should be considered at least as seriously in patients treated with vascular closure devices as in those treated with manual compression.

POSTPROCEDURAL CONSIDERATIONS

Stent Thrombosis and Postprocedure Thienopyridine Therapy

Stent thrombosis is a catastrophic complication, associated with 30-day mortality rates in recent series of 20.8% to 26% (135–137). Stent thrombosis most frequently occurs in the first days to weeks after stent implantation. Patients usually present with severe chest pain and often present with ST-segment elevation. With refinements in stent deployment techniques and integration of dual antiplatelet therapy (aspirin plus thienopyridine for 4 weeks after stent implantation), the incidence of stent thrombosis

is now approximately 1% (73, 78, 135, 138–142). Patients treated with bare-metal (non–drug-eluting) stents should receive 4 weeks of clopidogrel in addition to aspirin to prevent stent thrombosis. Because of concern that late stent thrombosis may develop in patients who are treated with drug-eluting stents, most recent trials have extended clopidogrel treatment to 3 to 6 months after PCI, in addition to aspirin therapy. We currently recommend at least 3 to 6 months of clopidogrel therapy after PCI in patients treated with drug-eluting stents. Because of the potential catastrophic effects of stent thrombosis, this regimen should not be interrupted for minor bleeding or elective invasive or surgical procedures, particularly during the first 4 weeks after the procedure. Patients who report substantial angina-like chest pain at rest in the days to weeks after stent implantation should be immediately hospitalized, receive anticoagulation, and undergo urgent cardiac catheterization.

Longer-Term Ischemic Event Reduction

As discussed previously, PCI-CURE was an observational study of patients in the CURE study who had clinically indicated PCI. In CURE, patients who presented with non–ST-segment elevation acute coronary syndrome were treated for 3 to 12 months with aspirin plus placebo or aspirin plus clopidogrel. In analyses of event rates from the time of PCI until the end of follow-up (an average of 8 months), those treated with clopidogrel had fewer adverse events (53, 54, 143). However, no statistically significant reduction in adverse event rates was seen between 30 days after PCI (the approximate traditional time at which clopidogrel would be discontinued after stent implantation) and the end of follow-up.

The CREDO study was specifically designed to assess the effects of pretreatment and longer-term (12-month) treatment with clopidogrel in patients undergoing PCI. At 1-year follow-up, the composite primary end point of death, MI, or stroke was reduced 26.9% by pretreatment and longer-term treatment with clopidogrel (8.5% vs. 11.5%; $P = 0.02$). Of importance, analysis of events occurring between day 29 and 1 year revealed that longer-term clopidogrel therapy was associated with a statistically significant 37.4% reduction in events (55). These data suggest that longer-term therapy (1 year or perhaps longer) with clopidogrel in addition to aspirin should be considered in many if not most patients undergoing PCI. We suggest that longer-term clopidogrel therapy should be strongly considered in patients with diffuse or multivessel coronary artery disease, atherosclerotic disease in other vascular beds, diabetes, chronic renal failure, and many previous acute coronary syndromes despite aspirin therapy. It should be noted that these recommendations are based on generally known principles. More informed recommendations will be possible only after subgroup analyses of the CREDO results.

Other Issues Specific to Stents

Although there is a theoretical risk that a stent, as a foreign body, could become infected in a patient who develops bacteremia, this does not appear to be a clinically significant issue. A recent literature review detected only four reported cases of infected stents, all of which occurred days to weeks after implantation (144). At this time, the presence of a coronary stent is not an indication for prophylaxis against endocarditis (145). Most coronary stents in current use are either nonferromagnetic or only weakly ferromagnetic; most consist of 316L stainless steel. Because these stents are considered to be compatible with magnetic resonance imaging procedures, their presence should not preclude MRI when it is clinically indicated (146–148).

Restenosis

Restenosis is the process by which a treated arterial narrowing recurs over time. The restenosis process is now believed to occur because of negative arterial remodeling (arterial “constriction”) and intimal hyperplasia, combined with other complex processes (149, 150). Factors associated with an increased risk for restenosis include diabetes; unstable or severe angina at the time of PCI; lesions in the left anterior descending artery or in a saphenous vein graft; total length of the lesion treated; chronically occluded arteries; previously treated lesions; and factors related to technical aspects of the procedure itself, most notably minimum luminal diameter immediately afterward (151–157).

The restenotic process occurs over the first 1 to 6 to 8 months after PCI (151, 152, 156). Most patients with symptomatic restenosis develop symptoms during a similar time frame (151, 152, 156, 158). The presenting symptom for most patients with restenosis is exertional angina (25% to 85%); fewer patients (11% to 41%) present with unstable angina, and presentation with acute MI is rare (1% to 6%) (151). Most patients who present between 1 and 6 to 8 months after PCI with recurrence of typical anginal chest pains are found to have restenosis (159).

Studies have demonstrated that implantation of coronary stents in native coronary arteries 3 mm or more in diameter is associated with an approximately 30% reduction in 6-month adverse event rates, primarily because of an approximately 50% reduction in the need for repeated revascularization (160). In addition, stents have been demonstrated to decrease restenosis rates in saphenous vein bypass grafts, in chronically occluded arteries, and in patients treated with primary angioplasty for acute MI (160–166).

Recent results from several trials of stents treated to contain and elute antiproliferative agents, such as sirolimus (Cordis, Miami Lakes, Florida) and paclitaxel (Boston Scientific, Natick, Massachusetts), have shown that implantation of these drug-eluting stents dramatically reduces the rates of restenosis compared with bare-metal stents. Most studies have generally reported single-digit restenosis rates (167–171), although not all agents studied have produced positive results (172). Many additional studies of drug-

Table 3. Incidence, Prevention, and Management of Adverse Events during the Pre-, Peri-, and Postprocedure Periods*

Adverse Event	Incidence	Comments
Preprocedure considerations		
Allergic reactions	Rare in general population 17%–35% in patients with previous reaction (if not premedicated)	Pretreat patients with history of allergic reaction to contrast with steroid and H ₁ -blocker.
Contrast nephropathy	14%–38% incidence of any detectable effect on kidney function Incidence of actual renal failure <1% in general population	Risks higher in patients with diabetes and patients with preexisting renal insufficiency. Hydrate patients before and after the procedure. Consider N-acetylcysteine in high-risk patients.
Lactic acidosis	Occurs rarely and almost exclusively in patients taking metformin who have dye-induced renal failure	Discontinue metformin the day of procedure in patients with normal renal function and, when possible, 48 hours before elective PCI in patients with preexisting renal insufficiency at increased risk for contrast nephropathy, and then for 2 d afterward. Reassess kidney function before restarting.
Periprocedural considerations		
MI	Enzymatically defined MI incidence, 5%–30%	Preprocedural antiplatelet therapy can reduce complications, particularly MI. Serial CK and CK-MB measurements (6–8 and 16–24 h postprocedure) should be obtained in patients with suspected ischemia during PCI. Patients with significant elevations in CK-MB levels may warrant additional monitoring and care and more cautious resumption of daily activities.
Emergency CABG	<1% in recent studies	Decreased incidence probably due to advances in field, including stents.
Mortality rate	<1% in recent studies	Decreased incidence probably due to advances in pharmacotherapy and technology.
Major bleeding	0.7%–1.7% incidence in most recent studies	Discontinue heparin therapy postprocedure.
Retroperitoneal hematoma	0.15%–0.44%	Suspect in patients with unexplained hypotension or decrease in hematocrit, or severe back or flank pain. Diagnosis confirmed by CT scan.
Pseudoaneurysm	Approximately 1%	Presence suggested by groin tenderness, a palpable pulsatile mass, or bruit. Diagnosis confirmed by ultrasonography.
AV fistula	0.2%–2.1%; current incidence probably is in the lower end of this range	Presence suggested by continuous bruit over groin area. Diagnosis confirmed by Doppler ultrasonography.
Postprocedural considerations		
Stent thrombosis	Approximately 1%	Treat patients with clopidogrel 4 weeks post-PCI (in addition to long-term aspirin therapy). Patients with severe anginal chest pain days to weeks after stent implantation should be admitted and should receive anticoagulation.
Restenosis	Clinical restenosis rates 10%–20% in recent studies of patients treated with bare stents, <10% in those treated with drug-eluting stents	“Routine” screening stress test not indicated in most patients. Restenosis symptoms recur 1–6 months post-PCI, most commonly exertional angina. Patients with suspected restenosis should undergo imaging study or repeated catheterization.

* AV = arteriovenous; CABG = coronary artery bypass grafting; CK = creatine kinase; CT = computed tomography; MI = myocardial infarction; PCI = percutaneous coronary intervention.

eluting stents are currently under way. These studies are examining different agents as well as the efficacy of drug-eluting stents in more complex lesions, for which restenosis rates tend to be higher.

In patients in whom restenosis is suspected on clinical grounds, stress testing is one diagnostic option. Exercise treadmill testing alone, however, is an insensitive test for restenosis (48, 173). One recent meta-analysis found a sensitivity of 46% and a specificity of 77% (174). Imaging studies have higher sensitivities and specificities and are thus the preferred modes of noninvasive evaluation of possible restenosis. In similar meta-analyses of nuclear imaging studies, the sensitivity was 87% and the specificity was

78%; echocardiographic imaging studies had a sensitivity of 63% and a specificity of 87% (174). As the incidence of restenosis declines, as it has over time, the positive predictive values for these tests decrease, although the negative predictive values increase above 90% (174). In patients with symptoms that substantially limit exertion, it may be more prudent as well as time- and cost-effective to proceed directly to coronary angiography (48). Patients who present with unstable symptoms should also preferentially be referred for cardiac catheterization.

Several series (175–178) have demonstrated that the prognosis of patients with asymptomatic or “silent” restenosis is generally favorable and that routine, periodic mon-

itoring of asymptomatic patients with stress testing after PCI is not beneficial, indicated, or recommended (48, 173, 179, 180). Recommendations about who may benefit from stress testing to detect possible restenosis were made in an era in which restenosis was much more common. Restenosis is likely to become even less common with the introduction of drug-eluting stents. Stress testing can be considered in patients who are considered to be high risk, including those with depressed left ventricular function, multivessel coronary artery disease, proximal left anterior descending lesion, history of sudden death, diabetes mellitus, and hazardous occupations (48, 173). **Table 3** describes the incidence, prevention, and management of adverse events during the pre-, peri- and postprocedure periods.

SUMMARY

Before PCI, patients with contrast dye allergies should be identified and pretreated with steroids and an H₁-blocker. Pre- and postprocedure hydration should be initiated and maintained to minimize the risks for contrast nephropathy. Appropriate preprocedural antiplatelet therapy should be evaluated on the basis of the clinical setting. Periprocedure, patients should be monitored clinically for evidence of ischemia. Those who manifest clinical or enzymatic evidence of MI warrant further care. In patients with significant groin, flank, abdominal, or back pain, as well as those with hypotension or unexplained decrease in hematocrit, the diagnosis of groin or retroperitoneal hematoma should be considered and promptly evaluated. Groin tenderness, pulsatile mass, or bruit should prompt evaluation for possible femoral pseudoaneurysm or AV fistula. After PCI, all patients treated with coronary stent implantation should receive aspirin plus clopidogrel. Patients who develop significant anginal chest pain at rest in the days to weeks after stent implantation and in whom stent thrombosis is suspected should be urgently hospitalized and receive anticoagulation; an interventional cardiologist should also be consulted. Patients who develop typical anginal symptoms between the 1st and 6th to 8th months after PCI are likely to have restenosis. Such patients can be evaluated by an imaging study or by repeated catheterization. Routine stress testing, however, is not generally indicated in asymptomatic patients after PCI. Finally, it should be remembered that PCI is only a palliative procedure and that patients require lifelong secondary prevention interventions, including lipid management, hypertension control, and lifestyle modification.

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Potential Financial Conflicts of Interest: *Consultancies:* G.N. Levine (Aventis, Schering-Plough, Merck, Pfizer, The Medicines Company), P.B. Berger (BMS/Sanofi, Aventis), T.A. Sanborn (Davax, Boston Scientific, Genvac, Ethicon); *Honoraria:* G.N. Levine (Aventis, Schering-Plough, Merck, Pfizer, The Medicines Company), P.B. Berger (BMS/Sanofi, Aventis); *Grants received:* P.B. Berger (BMS/Sanofi, Merck, Cordis Millennium), T.A. Sanborn (X-SITE Medical).

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