ACC/AHA PRACTICE GUIDELINES

ACC/AHA Guidelines for Percutaneous Coronary Intervention (Revision of the 1993 PTCA Guidelines)

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Revise the 1993 Guidelines for Percutaneous Transluminal Coronary Angioplasty)

**Endorsed by the Society for Cardiac Angiography and Interventions**

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PREAMBLE

It is important that the medical profession play a significant role in critically evaluating the use of diagnostic procedures and therapies in the management and prevention of disease. Rigorous and expert analysis of the available data documenting relative benefits and risks of those procedures and therapies can produce helpful guidelines that improve the effectiveness of care, optimize patient outcomes, and favorably impact the overall cost of care by focusing resources on the most effective strategies.

The American College of Cardiology (ACC) and the American Heart Association (AHA) have jointly engaged in the preparation of such guidelines in the area of cardiovascular disease since 1980. This effort is directed by the ACC/AHA Task Force on Practice Guidelines, which is charged with developing and revising practice guidelines for important cardiovascular diseases and procedures. Experts in the subject under consideration are selected from involved organizations to examine subject-specific data and write guidelines. The process includes additional representatives from other medical practitioner and specialty groups where appropriate. Writing groups are specifically charged to perform a formal literature review, weigh the strength of evidence for or against a particular treatment or procedure, and include estimates of expected-health outcomes in areas where data exist. Patient-specific modifiers, comorbidities, and issues of patient preference that might influence the choice of particular tests or therapies are considered, along with frequency of follow-up and cost-effectiveness.

The ACC/AHA Task Force on Practice Guidelines makes every effort to avoid any actual or potential conflicts of interest that might arise as a result of an outside relationship or personal interest of a member of the writing panel. Specifically, all members of the writing panel are asked to provide disclosure statements of all such relationships that might be perceived as real or potential conflicts of interest. These statements are reviewed by the parent task force, reported orally to all members of the writing panel at the first meeting, and updated as changes occur.

These practice guidelines are intended to assist physicians and other healthcare providers in clinical decision making by describing a range of generally acceptable approaches for the diagnosis, management, or prevention of specific diseases or conditions. These guidelines attempt to define practices that meet the needs of most patients in most circumstances. The ultimate judgment regarding care of a particular patient must be made by the physician and patient in light of circumstances specific to that patient.
This committee includes cardiologists with and without involvement in interventional procedures, a cardiac surgeon, and an official representative from the Society for Cardiac Angiography and Interventions (SCA&I). This document was reviewed by three official reviewers nominated by ACC, three official reviewers nominated by AHA, the AHA Committee on Diagnostic and Interventional Cardiac Catheterization, the ACC Interventional Database Committee, the ACC Cath Lab Accreditation Working Group, the ACC Cardiac Catheterization Committee, the SCA&I, and 21 outside reviewers nominated by the Writing Committee. This document was approved for publication by the governing bodies of ACC and AHA and officially endorsed by the SCA&I. These guidelines will be considered current unless the Task Force revises them or withdraws them from distribution.

Raymond J. Gibbons, MD, FACC  
Chair, ACC/AHA Task Force on Practice Guidelines

I. INTRODUCTION

The ACC/AHA Task Force on Practice Guidelines was formed to gather information and make recommendations about appropriate use of technology for the diagnosis and treatment of patients with cardiovascular disease. Percutaneous coronary interventions (PCIs) are an important group of technologies in this regard. Although initially limited to balloon angioplasty and termed percutaneous transluminal coronary angioplasty (PTCA), PCI now includes other new techniques capable of relieving coronary narrowing. Accordingly, in this document, rotational atherectomy, directional atherectomy, extraction atherectomy, laser angioplasty, implantation of intracoronary stents and other catheter devices for treating coronary atherosclerosis are considered components of PCI. In this context PTCA will be used to refer to those studies using primarily balloon angioplasty while PCI will refer to the broader group of percutaneous techniques. These new technologies have impacted the effectiveness and safety profile initially established for balloon angioplasty. Moreover, important advances have occurred in the use of adjunctive medical therapies such as glycoprotein (GP) IIb/IIIa receptor blockers. In addition, since publication of the previous Guidelines in 1993, greater experience in the performance of PCI in patients with acute coronary syndromes and in community hospital settings has been gained. In view of these developments, further review and revision of the guidelines is warranted. This document reflects the opinion of the third ACC/AHA committee charged with revising the guidelines for PTCA to include the broader group of technologies now termed PCI.

Several issues relevant to the Committee’s process and the interpretation of the Guidelines have been noted previously and are worthy of restatement. First, PCI is a technique that has been continually refined and modified; hence continued, periodic Guideline revision is anticipated. Second, these Guidelines are to be viewed as broad recommendations to aid in the appropriate application of PCI. Under unique circumstances, exceptions may exist. These Guidelines are intended to complement, not replace, sound medical judgment and knowledge. They are intended for operators who possess the cognitive and technical skills for performing PCI and assume that facilities and resources required to properly perform PCI are available. As in the past, the indications are categorized as Class I, II, or III, based on a multifactorial assessment of risk as well as expected efficacy viewed in the context of current knowledge and the relative strength of this knowledge. Initially, this document describes the background information that forms the foundation for specific indications. Topics fundamental to coronary intervention are reviewed followed by separate discussions relating to unique technical and operational issues. Formal recommendations for the use of angioplasty are included in Section V. Indications are organized according to clinical presentation. This format is designed to enhance the usefulness of this document for the assessment and care of patients with coronary artery disease (CAD).

This document employs the ACC/AHA style classification as Class I, II, or III. These classes summarize the indications for PCI as follows:

Class I: Conditions for which there is evidence for and/or general agreement that the procedure or treatment is useful and effective.

Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.

Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIb: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful/effective, and in some cases may be harmful.

The weight of evidence in support of the recommendation for each listed indication is presented as follows:

Level of Evidence A: Data derived from multiple randomized clinical trials.

Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.

Level of Evidence C: Consensus opinion of experts.

II. GENERAL CONSIDERATIONS AND BACKGROUND

Coronary angioplasty was first introduced by Andreas Gruentzig in 1977 (1) as a nonsurgical method for coronary arterial revascularization. Fundamentally, the technique involved advancing a balloon tipped catheter to an area of coronary narrowing, inflating the balloon and then removing the catheter following deflation. Early reports demonstrated that balloon angioplasty could reduce the severity of
coronary stenosis and diminish or eliminate objective and subjective manifestations of ischemia (2–4). Although angioplasty was clearly feasible and effective, the scope of coronary disease to be treated was quite narrow. Also, since angioplasty could result in sudden arterial occlusion and subsequent myocardial infarction (MI), immediate access to coronary bypass surgery was essential (5). With experience and time, however, the cognitive and technical aspects as much as the equipment used to perform angioplasty became more refined. Observational reports of large numbers of patients confirmed that coronary angioplasty could be applied to broad groups of coronary patients with higher rates of success and lower rates of complications when compared to initial experiences (6,7). More than 500,000 PCI procedures are performed yearly in the U.S. (8), and it has been estimated that more than 1,000,000 procedures are performed annually worldwide.

The value of coronary angioplasty was further defined by comparing its results to those of alternative methods of treatment. Randomized clinical trials have assessed the outcomes of patients treated by a strategy of initial angioplasty to one of medical therapy alone or to coronary artery bypass surgery (9–14). The results of these trials have clarified the utility of angioplasty in terms of effectiveness, complications, and patient selection. The technique of coronary angioplasty has also been expanded by the development of devices that replace or serve as adjuncts to the balloon catheter. These “new devices” have been thoroughly evaluated and have had a critical impact in enhancing the immediate- and long-term efficacy and safety of coronary angioplasty. The following section of this report expands on this background and describes the practice of PCI as it is applied today.

New coronary devices have expanded the clinical and anatomical indications for revascularization initially limited by balloon catheter angioplasty. For example, stents reduce both the acute risk of major complications and late-term restenosis. The success of new coronary devices in meeting these goals is in part represented by the less frequent use of balloon angioplasty alone (<30%) and the high (>70%) penetration of coronary stenting in the current practice of interventional cardiology (Fig. 1). Atherectomy devices and stenting, associated with improved acute angiographic and clinical outcomes compared to balloon angioplasty, in specific subsets, continue to be applied to a wider patient domain that includes multivessel disease and complex coronary anatomy. However, strong evidence (level A data from multiple randomized clinical trials) is only available for stenting in selected patients undergoing single-vessel PCI.

The range of new, non-balloon revascularization technology approved by the Food and Drug Administration (FDA) for use in native or graft coronary arteries includes balloon expandable stents, atherectomy by the Transluminal Extraction Catheter (TEC), Directional Coronary Atherectomy (DCA), rotational atherectomy, angiojet thrombolysis catheter, and Excimer Laser Coronary Atherectomy (ELCA). A variety of devices is under investigation including new designs of balloon or self-expanding stents, mechanical thrombectomy devices, and local radiation devices intended to reduce restenosis. These guidelines will focus on the FDA-approved balloon related and non-balloon coronary revascularization devices.

III. OUTCOMES

The outcomes of coronary interventional procedures are measured in terms of success and complications and are related to the mechanisms of the employed devices, as well as the clinical and anatomic patient-related factors. Complications can be divided into two categories: 1) those common to all arterial catheterization procedures and 2) those related to the specific technology used for the coronary procedure. Specific definitions of success and complications exist, and where appropriate, the definitions used herein are consistent with the ACC-National Cardiovascular Data Registry™ Catheterization Laboratory Module Version 2.0
(15). With increased operator experience, new technology, and adjunctive pharmacotherapy, the overall success and complication rates of angioplasty have improved.

A. Definitions of PCI Success

The success of a PCI procedure may be defined by angiographic, procedural, and clinical criteria.

1. Angiographic Success. A successful PCI produces substantial enlargement of the lumen at the target site. The consensus definition prior to the widespread use of stents was the achievement of a minimum stenosis diameter reduction to <50% in the presence of grade 3 TIMI flow (assessed by angiography) (16). However, with the advent of advanced adjunct technology, including coronary stents, a minimum stenosis diameter reduction to <20% has been the clinical benchmark of an optimal angiographic result. Frequently, there is a disparity between the visual assessment and computer-aided quantitative stenosis measurement (17,18), and the determination of success may be problematic when success rates are self-reported.

2. Procedural Success. A successful PCI should achieve angiographic success without in-hospital major clinical complications (e.g., death, MI, emergency coronary artery bypass surgery) during hospitalization (2,16). Although the occurrence of emergency coronary artery bypass surgery and death are easily identified end points, the definition of procedure-related MI has been debated. The development of Q-waves in addition to a threshold value of CK elevation has been commonly used. However, the significance of enzyme elevations in the absence of Q-waves remains a subject of investigation and debate. Several reports have identified non–Q-wave MIs with CK-MB elevations 3 to 5 times the upper limit of normal as having clinical significance (19,20). Thus a significant increase in CK-MB without Q-waves is considered by most to qualify as an associated complication of PCI.

3. Clinical Success. In the short term, a clinically successful PCI includes anatomic and procedural success with relief of signs and/or symptoms of myocardial ischemia after the patient recovers from the procedure. The long-term clinical success requires that the short-term clinical success remains durable and that the patient has persistent relief of signs and symptoms of myocardial ischemia for more than 6 months after the procedure. Restenosis is the principal cause of lack of long-term clinical success when a short-term clinical success has been achieved. Restenosis is not considered a complication but rather an associated response to vascular injury. The frequency of clinically important restenosis may be judged by the frequency with which subsequent revascularization procedures are performed on target vessels after the index procedure. A very high rate of restenosis may suggest that the operator chooses an excess of lesions which are likely to restenose, such as long lesions or those involving small vessels.

B. Definitions of Procedural Complications

As outlined in the 1998 coronary interventional document (21), procedural complications are divided into six basic categories: death, MI, emergency coronary artery bypass graft (CABG) surgery, stroke, vascular access site complications, and contrast agent nephropathy. Key data elements and definitions to measure the clinical management and outcomes of patients undergoing diagnostic catheterization and/or PCI have been defined in the Clinical Data Standards document (22) and the ACC-National Cardiovascular Data Registry™ Catheterization Laboratory Module version 2.0 (15). These rigorous definitions for key adverse events are endorsed by this Writing Committee for inclusion in the present PCI Guidelines (Table 1).

Notably, the definition of MI has evolved over the past several years. It should be emphasized that the simple categorization of MI into two classes based on the development of new Q-waves alone is no longer sufficient as a classification scheme for measuring MI following PCI. Since the measurement of CK and CK-MB are widely available, myocardial necrosis may be measured with a high level of sensitivity and specificity, regardless of the clinical presentation and associated ECG findings. The use of CK-MB for measuring myocardial necrosis is preferable to a less sensitive and less specific CK determination. The mass determination of CK-MB is now commonly used at most hospitals, and elevations of this myocardial specific enzyme are reported in nanograms per deciliter. Cardiac troponin T and I have now been introduced as measurements of myocardial necrosis and have been proven to be more sensitive and specific than CK-MB. However, prognostic criteria after PCI based on troponin T and I have not yet been developed.

Since normal values may vary among hospitals and selected patient subsets, an index of the measured value is usually reported in terms of the value of the upper limit of normal (i.e., CK-MB index of 3 corresponds to an elevation of CK-MB to 3 times its upper limit of normal value). Thus, myocardial necrosis may be determined as an abnormally elevated CK-MB index (>1), based upon 2 or 3 serial determinations during the 18 to 24 h after coronary intervention and the abnormality may range from a low index (1 to 3 times normal) with non- or non-specific ECG findings, to a high index (>10 to 15 times normal) with significant ECG findings including the development of new Q-waves.

If serial determinations are performed after PCI, an abnormally high value (CK-MB >1 times normal) can be expected in 10 to 15% of balloon angioplasty procedures, 15 to 20% of stent procedures, 25 to 35% of atherectomy procedures, and >25% for any device used in saphenous vein grafts (SVGs) or long lesions with a high atherosclerotic burden, even in the absence of other signs and symptoms of MI. There is no accepted consensus on what level of CK-MB index (with or without clinical or electrocardiographic [ECG] findings) is indicative of a clinically
Table 1. Definitions of Procedural Complications (15)

<table>
<thead>
<tr>
<th>Procedural Complications</th>
<th>Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Cause of Death</td>
<td>Patient died during this hospitalization.</td>
</tr>
<tr>
<td>Periprocedural MI</td>
<td>The NEW presence of an MI as documented by at least 1 of the following criteria:</td>
</tr>
</tbody>
</table>
|                          | 1. Evolutionary ST-segment elevations, development of new Q-waves in 2 or more contiguous ECG leads, or new or presumably new LBBB pattern on the ECG.  
|                          | 2. Biochemical evidence of myocardial necrosis; this can be manifested as 1) CK-MB ≥3 x the upper limit of normal or if CK-MB not available 2) total CK ≥3 x upper limit of normal. Because normal limits of certain blood tests may vary, please check with your lab for normal limits for CK-MB and total CK. |
| CABG During this Admission | If the patient had a CABG during this admission indicate the CABG status using the following categories: |
|                          | I. Elective: The procedure could be deferred without increase risk of compromised cardiac outcome. |
|                          | II. Urgent: All of the following conditions are met: |
|                          | A. Not elective  
|                          | B. Not emergency  
|                          | C. Procedure required during same hospitalization in order to minimize chance of further clinical deterioration. |
| III. Emergency: The patient’s clinical status includes any of the following: |
|                          | A. Ischemic dysfunction (any of the following): |
|                          | 1. Ongoing ischemia including rest angina despite maximal medical therapy (medical and/or IABP)  
|                          | 2. Acute evolving MI within 24 h before intervention  
|                          | 3. Pulmonary edema requiring intubation  
|                          | B. Mechanical dysfunction (either of the following): |
|                          | 1. Shock with circulatory support  
|                          | 2. Shock without circulatory support  
| CVA/Stroke                | Patient experienced a cerebrovascular accident (CVA) as documented by a loss of neurological function caused by an ischemic event with residual symptoms at least 24 h after onset. |
| Vascular Complications    | Blood loss at the site of arterial or venous access or due to perforation of a traversed artery or vein requiring transfusion and/or prolonging the hospital stay, and/or causing a drop in hemoglobin >3.0 gm/dl. Bleeding attributable to the vascular site could be retroperitoneal, a local hematoma >10 cm diameter or external.  
|                          | A. Occlusion | A total obstruction of the artery usually at the site of access requiring surgical repair. Occlusion is defined as total obstruction of the artery by thrombus, dissection or other mechanism, usually at the site of access, requiring surgical repair. Occlusion may be accompanied by absence of palpable pulse or Doppler signal and associated with signs and symptoms of an ischemic limb requiring surgical intervention. |
|                          | B. Dissection | A dissection occurred at the site of percutaneous entry. Dissection is defined as disruption of an arterial wall resulting in splitting and separation of the intimal (or subintimal) layers. |
|                          | C. Pseudoaneurysm | Pseudoaneurysm is defined as the occurrence of an aneurysmal dilation of the artery at the site of catheter entry demonstrated by arteriography or ultrasound. |
|                          | D. AV Fistula | AV fistula is defined as a connection between the access artery (e.g., femoral) and access vein (e.g., femoral) that is demonstrated by an imaging study (arteriography or ultrasound) and most often characterized by a continuous bruit. |
| Renal Failure             | After the lab visit—but before any subsequent lab visits only: |
|                          | A. Shock without circulatory support  
|                          | B. Shock with circulatory support  
|                          | C. Mechanical dysfunction (either of the following): |
|                          | 1. Shock with circulatory support  
|                          | 2. Shock without circulatory support  
|                          | D. Acute evolving MI within 24 h before intervention  
|                          | E. Ongoing ischemia including rest angina despite maximal medical therapy (medical and/or IABP)  
|                          | F. Acute evolving MI within 24 h before intervention  
|                          | G. Acute evolving MI within 24 h before intervention  
|                          | H. Acute evolving MI within 24 h before intervention  
|                          | I. Acute evolving MI within 24 h before intervention  
|                          | J. Acute evolving MI within 24 h before intervention  
|                          | K. Acute evolving MI within 24 h before intervention  
|                          | L. Acute evolving MI within 24 h before intervention  
|                          | M. Acute evolving MI within 24 h before intervention  
|                          | N. Acute evolving MI within 24 h before intervention  
|                          | O. Acute evolving MI within 24 h before intervention  
|                          | P. Acute evolving MI within 24 h before intervention  
|                          | Q. Acute evolving MI within 24 h before intervention  
|                          | R. Acute evolving MI within 24 h before intervention  
|                          | S. Acute evolving MI within 24 h before intervention  
|                          | T. Acute evolving MI within 24 h before intervention  
|                          | U. Acute evolving MI within 24 h before intervention  
|                          | V. Acute evolving MI within 24 h before intervention  
|                          | W. Acute evolving MI within 24 h before intervention  
|                          | X. Acute evolving MI within 24 h before intervention  
|                          | Y. Acute evolving MI within 24 h before intervention  
|                          | Z. Acute evolving MI within 24 h before intervention  

CABG = coronary artery bypass graft; CK = creatine kinase; CPR = cardiopulmonary resuscitation; ECG = electrocardiographic; IABP = intra-aortic balloon pump; LBBB = left bundle-branch block; MI = myocardial infarction.

important MI following the interventional procedure. The Writing Committee recommends that a CK-MB determination be performed on all patients who have signs or symptoms of suggestive MI following the procedure or in patients in whom there is angiographic evidence of abrupt vessel closure, important side branch occlusion, or new and persistent slow coronary flow. In patients in whom a clinically driven CK-MB determination is made, a CK-MB of >3 times the upper limit of normal would constitute a clinically significant MI. These relationships may be confounded by other factors, such as atherosclerosis.

C. Acute Outcome

Despite the extension of coronary intervention to higher-risk patients with comorbid disease and complex coronary anatomy, angiographic and procedural success have increased since the first National Heart Lung and Blood Institute (NHLBI) registries with an associated decrease in the major complications of Q-wave MI and emergency CABG (Table 2) (2,6,23,24). Improvements in balloon technology coupled with the increased use of non-balloon devices, particularly stents (which are effective in treating abrupt vessel closure) (25) and glycoprotein IIb/IIIa platelet receptor antagonists (26–28) have favorably influenced acute procedural outcome. This combined balloon/device/pharmacologic approach to coronary intervention in elective procedures has resulted in angiographic success rates of 96 to 99%, with Q-wave MI rates of 1 to 3%, emergency coronary artery bypass surgery rates of 0.2 to 3%, and unadjusted in-hospital mortality rates of 0.5 to 1.4% (29–
**Table 2. Unadjusted In-Hospital Outcome Trends Following Percutaneous Interventions**

<table>
<thead>
<tr>
<th>Registry</th>
<th>Years</th>
<th>Reference</th>
<th>N</th>
<th>Clinical Success, %</th>
<th>In-Hospital Mortality, %</th>
<th>Q-Wave MI, %</th>
<th>Emergency CABG, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>NHLBI (I)‡</td>
<td>1977–1981</td>
<td>(37)</td>
<td>3,079</td>
<td>61</td>
<td>1.2</td>
<td>Not reported</td>
<td>5.8</td>
</tr>
<tr>
<td>NHLBI (II)§</td>
<td>1985–1986</td>
<td>(37)</td>
<td>2,311</td>
<td>78</td>
<td>1.0</td>
<td>4.8</td>
<td>5.8</td>
</tr>
<tr>
<td>BARI Registry¶</td>
<td>1988–1991</td>
<td>(38)</td>
<td>1,189</td>
<td>Not reported</td>
<td>0.7</td>
<td>2.8</td>
<td>4.1</td>
</tr>
<tr>
<td>Northern New England¶</td>
<td>1990–1993</td>
<td>(39)</td>
<td>13,014</td>
<td>88.8</td>
<td>1.0</td>
<td>2.4</td>
<td>2.2</td>
</tr>
<tr>
<td>SC&amp;A&amp;I#</td>
<td>1990–1994</td>
<td>(40)</td>
<td>4,366</td>
<td>91.5</td>
<td>2.5</td>
<td>Not reported</td>
<td>3.4</td>
</tr>
<tr>
<td>NY State Database</td>
<td>1991–1994</td>
<td>(42,43)</td>
<td>62,670</td>
<td>Not reported</td>
<td>0.9</td>
<td>Not reported</td>
<td>3.4</td>
</tr>
<tr>
<td>Northern New England¶</td>
<td>1994–1995</td>
<td>(39)</td>
<td>7,248</td>
<td>89.2</td>
<td>1.1</td>
<td>2.1</td>
<td>2.3</td>
</tr>
<tr>
<td>NCN</td>
<td>1994–1997</td>
<td>(44)</td>
<td>76,904</td>
<td>Not reported</td>
<td>1.3</td>
<td>Not reported</td>
<td>1.7</td>
</tr>
<tr>
<td>Northern New England¶</td>
<td>1995–1997</td>
<td>(39)</td>
<td>14,490</td>
<td>91.5</td>
<td>1.2</td>
<td>2.0</td>
<td>1.3</td>
</tr>
<tr>
<td>NHLBI Dynamic Registry††</td>
<td>1997–1998</td>
<td>(23)</td>
<td>1,559</td>
<td>92</td>
<td>1.9</td>
<td>2.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

MI = myocardial infarction; CABG = coronary artery bypass graft. The N varied among registries; several reported patients* rather than procedures†; ‡NHLBI (I), Emergency CABG was defined as in-hospital CABG; $NHLBI (II), MI was defined as the presence of at least 2 of the 3 criteria: clinical symptoms, Q-waves on ECG (Minnesota Code), or elevated cardiac enzyme level (double the normal levels for CK or its MB fraction without Q-waves). Emergency CABG was defined as in-hospital CABG; ¶BARI, MI was defined as the appearance of ECG changes (new pathologic Q-waves) supported by abnormal CK-MB elevations; Northern New England, A new MI is defined as a clinical event, ECG changes and a creatine phosphokinase (CPK) rise to ≥2 × normal levels with positive isoenzymes. Emergency CABG is defined as surgery performed to treat acute closure, unstable angina, or congestive HF requiring IV nitroglycerin or ABP, or tamponade resulting from the intervention; #SC&A&I, A new MI is defined as any significant infarction (>3 × normal) rise in MB fraction; **NACI, MI is defined as Q-wave MI; ††MI was defined as ≥2 of the following: 1) typical chest pain >20 min not relieved by nitroglycerin, 2) serial ECG recordings showing changes from baseline or serially in ST-T and/or Q-waves in ≥2 contiguous leads, or 3) serum enzyme elevation of CK-MB >5% of total CK (total CK >2 × normal; LDH subtype 1 > LDH subtype 2). For expansion of study names, see the corresponding reference.

34). The integrated approach utilizing adjunct pharmacologic therapies and the enormous increase in the use of stents as a primary strategy have resulted in an improved procedural outcome of balloon angioplasty (35). Improved balloon/pharmacologic techniques may achieve results comparable to those obtained with stents with the ability to perform provisional (for suboptimal result) or bail-out (for acute or threatened vessel closure) stent deployment.

It should be noted, however, that the incidence of elevated creatine kinase has increased in the new device era (36). The significance of this finding, in the absence of a clinical event, is uncertain and the subject of ongoing debate. This issue is discussed in more detail in Section VI, C.1. Post-Procedure Evaluation of Ischemia.

**D. Long-Term Outcome and Restenosis**

Although improvements in technology, including stents and new pharmacologic therapy, have resulted in an improved acute outcome of the procedure, the impact of these changes on long-term (5 to 10 years) outcome may be less dramatic where factors such as advanced age, reduced left ventricular (LV) function, and complex multivessel disease in patients currently undergoing PCI may have a more important influence. In addition, available data on long-term outcome are mostly limited to patients undergoing PTCA. Ten-year follow-up of the initial cohort of patients treated with PTCA revealed an 89.5% survival rate (95% in patients with single-vessel disease, 81% in patients with multivessel disease) (45). In patients undergoing within the 1985–1986 NHLBI PTCA Registry (46), 5-year survival was 92.9% for patients with single-vessel disease, 88.5% for those with 2-vessel disease, and 86.5% for those with 3-vessel disease. In patients with multivessel disease undergoing PTCA in BARI (9), 5-year survival was 86.3%, and infract-free survival was 78.7%. Specifically, 5-year survival was 84.7% in patients with 3-vessel disease and 87.6% in patients with 2-vessel disease.

In addition to the presence of multivessel disease, other clinical factors adversely impact late mortality. In randomized patients with treated diabetes in BARI, the 5-year survival was 65.5%, and the cardiac mortality was 20.6% in comparison to 5.8% cardiac mortality in patients without treated diabetes (47), although among eligible but not randomized diabetic patients, the 5-year cardiac mortality was 7.5% (48). In the 1985–1986 NHLBI PTCA Registry, 4-year survival was significantly lower in women (89.2%) in comparison to men (93.4%) (49). In addition, although LV dysfunction was not associated with an increase in inhospital mortality or nonfatal MI in patients undergoing PTCA in the same registry, it was an independent predictor of a higher long-term mortality (50).

A major determinant of event-free survival following coronary intervention is the incidence of restenosis which had, until the development of stents, remained fairly constant, despite multiple pharmacologic and mechanical approaches to limit this process (Table 3). Depending on the definition, (i.e., whether clinical or angiographic restenosis or target lesion revascularization is measured), the incidence of restenosis following coronary intervention had been 30 to 40%, and higher in certain clinical and angiographic subsets (51).

The pathogenesis of the response to mechanical coronary injury is thought to relate to a combination of growth factor stimulation, smooth muscle cell migration and proliferation, organization of thrombus, platelet deposition, and elastic recoil (69,70). In addition, dynamic change in vessel size (or lack of compensatory enlargement) has been implicated (71). It has been suggested that attempts to reduce restenosis have failed, in part due to lack of recognition of the importance of this factor (72). Although numerous defini-
tions of restenosis have been proposed, >50% diameter stenosis at follow-up angiography has been most frequently used. However, it is now recognized that the response to arterial injury is a continuous rather than a dichotomous process, occurring to some degree in all patients (73). Therefore, cumulative frequency distributions of the continuous variables of minimal lumen diameter or percent diameter stenosis are now used to evaluate restenosis in large patient populations (74) (Fig. 2).

Although multiple clinical factors (diabetes, unstable angina, acute MI, prior restenosis) (75,76), angiographic factors (proximal left anterior descending artery, small vessel diameters, total occlusion, long lesion length, SVG) (77), and procedural factors (higher post-procedure percent diameter stenosis, smaller minimal lumen diameter, and smaller acute gain) (74) have been associated with an increased incidence of restenosis, the ability to integrate these factors and predict the risk of restenosis in individual patients following the procedure remains difficult. The most promising potential approaches to favorably impact the restenosis process relate to: 1) the ability to decrease elastic recoil and remodeling using intracoronary stents, and 2) to the ability to reduce intimal hyperplasia using catheter-based ionizing radiation. More than 6,300 patients have been studied in 12 randomized clinical trials to assess the efficacy of PTCA versus stents to reduce restenosis (Table 4).

The pivotal BENESTENT (32) and STRESS Trials (31) documented that stents significantly reduce angiographic restenosis in comparison to balloon angioplasty (BENESTENT: 22% vs. 32%; STRESS: 32% vs. 42%, respectively). These results have been corroborated in the BENESTENT II trial in which the angiographic restenosis rate was reduced by 45% (from 31 to 16% in patients treated with balloon angioplasty versus heparin-coated stents, respectively) (66).

In addition, randomized studies in patients with in-stent restenosis have shown that both intracoronary gamma and beta radiation significantly reduced the rate of subsequent angiographic and clinical restenosis by 30 to 50% (78–81). Late subacute thrombosis was observed in some of these series (82), but this syndrome has resolved with judicious use of stents and extended adjunct antiplatelet therapy with ticlopidine or clopidogrel. Also, in a preliminary study of patients undergoing successful balloon angioplasty, delivery of intracoronary beta radiation resulted in a restenosis rate of 15% (83). When technically feasible, in patients who experience restenosis, it is standard practice to perform repeat PCI. In this setting, stents are being used with the hope of decreasing the rate of subsequent restenosis, particularly when diffuse, represents a challenging problem. The efficacy of various treatment modalities for in-stent restenosis is under active investigation.

E. Predictors of Success/Complications

1. Anatomic Factors. Target lesion anatomic factors related to adverse outcomes have been widely examined. Lesion morphology and absolute stenosis severity were identified as the prominent predictors of immediate outcome during PTCA in the pre-stent era (93,94). Abrupt vessel closure, due primarily to thrombus or dissection, was reported in 3 to 8% of patients and was associated with certain lesion characteristics (95–97). The risk of PTCA in
the pre-stent era relative to anatomic subsets has been identified in previous NHLBI PTCA Registry data (6) and by the ACC/AHA Task Force (16,98). The lesion classification based on severity of characteristics proposed in the past (98–100) has been principally altered using the present PCI techniques which capitalize on the ability of stents to manage initial and subsequent complications of coronary interventions (101). As a result the Committee has revised the previous ACC/AHA lesion classification system to reflect low, moderate, and high risk (Table 5) in accordance with the PCI Clinical Data Standards from the ACC-National Cardiovascular Data Registry™ (15).

2. Clinical Factors. Coexistent clinical conditions can increase the complication rates for any given anatomic risk factor. For example, complications occurred in 15.4% of diabetic patients versus 5.8% of nondiabetic patients undergoing balloon angioplasty in a multicenter experience (94,97). Several studies have reported specific factors associated with increased risk of adverse outcome following balloon angioplasty. These factors include advanced age, female gender, unstable angina, congestive heart failure (CHF), diabetes, and multivessel CAD (9,93,94,102,103) (Table 6). The BARI trial found that patients with diabetes and multivessel CAD had an increased periprocedural risk of ischemic complications and increased 5-year mortality in comparison to patients without diabetes or in comparison to patients with diabetes undergoing bypass surgery using internal thoracic arterial grafts (9,38). Patients with impaired renal function, especially diabetics, are at increased risk for contrast nephropathy (104) and increased 30-day and 1-year mortality.

Increased risk for severe compromise in LV function or fatal outcome may occur with a complication of a vessel that also supplies collateral flow to viable myocardium. Certain variables were used to prospectively identify patients at risk for significant cardiovascular compromise during PTCA (105,106). These resulted in a composite 4-variable scoring system, prospectively validated to be both sensitive and specific in predicting cardiovascular collapse for failed PTCA and includes: 1) percentage of myocardium at risk (e.g., >50% viable myocardium at risk and LV ejection fraction of <25%), 2) pre-angioplasty percent diameter
stenosis, 3) multivessel CAD, and 4) diffuse disease in the dilated segment (107) or a high myocardial jeopardy score (108). Patients with higher pre-procedural jeopardy scores were shown to have a greater likelihood of cardiovascular collapse when abrupt vessel closure occurred during PTCA (105). The clinical risk factors associated with in-hospital adverse events have been further evaluated with additional experience during the PCI era and summarized based on odds ratio 2.0 or results of multivariate analysis (Table 6).

3. Risk of Death. In the majority of patients undergoing elective PCI, death as a result of PCI is directly related to the occurrence of coronary artery occlusion and is most frequently associated with pronounced LV failure (105,106) (Table 6). The clinical and angiographic variables associated with increased mortality include advanced age, female gender, diabetes, prior MI, multivessel disease, left main or equivalent coronary disease, a large area of myocardium at risk, pre-existing impairment of LV or renal function, and collateral vessels supplying significant areas of myocardium that originate distal to the segment to be dilated (Table 6) (9,93,95,97,102–105,107–110).

4. Women. In comparison to men, women undergoing PCI are older and have a higher incidence of hypertension,
diabetes mellitus, hypercholesterolemia, and comorbid disease (49,111–114). Women also have more unstable angina and a higher functional class of stable angina (Canadian Cardiovascular Society Class III and IV) for a given extent of disease (115). Yet, despite the higher-risk profile in women, the extent of epicardial coronary disease is similar (or less) in comparison to men. In addition, although women presenting for revascularization have less multivessel disease and better LV systolic function, the incidence of CHF is higher in women than in men. The reason for this gender paradox is unclear, but it has been postulated that women have more diastolic dysfunction, perhaps based on older age and hypertension, in comparison to men (116).

Early reports of patients undergoing PTCA revealed a lower procedural success rate in women (112); however, more recent studies have noted similar angiographic outcome and incidence of MI and emergency coronary artery bypass surgery in women and men (49). Although reports have been inconsistent, in several large-scale registries, in-hospital mortality is significantly higher in women, and an independent effect of gender on acute mortality following PTCA persists after adjustments for the baseline higher-risk profile in women (49,117). The reason for the increase in mortality is unknown, but small vessel size and hypertensive heart disease in women have been thought to play a role. Although a few studies have noted that gender is not an independent predictor of mortality when body surface area (a surrogate for vessel size) is accounted for (111), the impact of body size on outcome has not been thoroughly evaluated. The higher incidence of vascular complications, coronary dissection, and perforation in women undergoing coronary intervention has been attributed to the smaller vasculature in women in comparison to men. In addition, diagnostic intravascular ultrasound (IVUS) studies have not
detected any gender-specific differences in plaque morphology or luminal dimensions once differences in body surface area were corrected, suggesting that differences in vessel size account for some of the apparent early and late outcome differences previously noted in women (118). It has also been postulated that the volume shifts and periods of transient ischemia during coronary angioplasty are less well tolerated by the hypertrophied ventricle in women, and CHF has shown to be an independent predictor of mortality in both women and men undergoing coronary angioplasty (119).

An improved outcome has been reported in women undergoing both coronary balloon and new device angioplasty, despite the fact that the women (similar to men) are older and with more complex disease than women treated previously. In fact, in the 1993–1994 NHLBI PTCA Registry (open to women only), procedural success was higher and major complications lower in comparison to women treated in the 1985–1986 registry (24). Additionally, patients undergoing balloon angioplasty in BARI, in-hospital mortality, MI, emergency coronary artery bypass surgery rates, and 5-year mortality were similar in women and men, although women had a higher incidence of periprocedural CHF and pulmonary edema (120).

In a registry of 373 consecutive patients undergoing directional coronary atherectomy (DCA), although early and late outcomes were similar, the lower procedural success observed in women (73% vs. 83%, p = 0.011) was again attributed to their smaller vessel caliber (121). Therefore, although women presenting for coronary revascularization have a higher-risk profile, currently the acute and long-term outcomes are similar to those in men. Much of the increase in adverse outcome seen in women can be accounted for by comorbidities, although gender imparts a small independent effect. Finally, it is important to note that in women undergoing coronary intervention, the acute outcome has improved and the long-term outcome remains excellent. Therefore, coronary intervention should be considered for women in need of revascularization with the anticipation of a favorable outcome (Table 7).

5. The Elderly Patient. Age >75 years is one of the major clinical variables associated with increased risk of complications (125). In the elderly population, the morphologic and clinical variables are compounded by advanced years with the very elderly having the highest risk of adverse outcomes (126). In octogenarians, although feasibility has been established for most interventional procedures, the risk of both percutaneous and nonpercutaneous revascularization is increased (127,128). Octogenarians undergoing percutaneous intervention have a higher incidence of prior MI, lower LV ejection fraction, and more frequent CHF (129). In the stent era, procedural success rates and short-term outcomes are comparable to those for nonoctogenarians (130). Thus, with rare exception (primary PCI for cardiogenic shock for patients >75 years), a separate category has not been created in these Guidelines for the elderly. However, their higher incidence of comorbidities should be taken into account when considering the need for PCI.

6. Diabetes Mellitus. In the TIMI-IIb study of MI, patients with diabetes mellitus had significantly higher 6-week (11.6% vs. 4.7%), 1-year (18.0% vs. 6.7%), and 3-year (21.6% vs. 9.6%) mortality rates compared to nondiabetic patients (131). Patients with diabetes with a first MI who were randomly assigned to the early invasive strategy fared worse than those managed conservatively (42-day mortality: death or MI, or death alone 14.8% vs. 4.2%; p < 0.001) (132). Early catheterization and intervention strategy after thrombolysis was of little benefit in these patients with diabetes. Routine catheterization and angioplasty in this patient subgroup should be based on clinical need and ischemic risk stratification.

Stenting decreases the need for target revascularization procedures in diabetic patients compared with balloon angioplasty. The efficacy of stenting with glycoprotein IIb/IIIa inhibitors was assessed in the diabetic population compared to those without diabetes in a substudy of the EPISTENT trial (133). One hundred seventy-three diabetic patients were randomized to stent/placebo combination, 162 patients to stent/abciximab combination, and 156 patients to balloon angioplasty/abciximab combination. For the composite end point of death, MI, or target-vessel revascularization, the rates were as follows: 25%, 23%, and 13% for the stent/placebo, balloon/abciximab, and stent/abciximab groups (p = 0.005). Irrespective of revascularization strategy abciximab significantly reduced 6-month death and MI rate in patients with diabetes for all strategies. Likewise, 6-month target-vessel revascularization was reduced in the stent/abciximab group approach. One-year mortality for diabetics was 4.1% for the stent/placebo group and 1.2% for the stent/abciximab group. Although this difference was not significant, the combination of stenting and abciximab among diabetics resulted in a significant reduction in 6-month rates of death and target-vessel
revascularization compared to stent/placebo or balloon angioplasty/abciximab therapy (133). The BARI trial, in which stents and abciximab were not used, showed that survival was better for patients with treated diabetes undergoing CABG surgery with an arterial conduit than for those undergoing angioplasty. A discussion about the selection of diabetic patients for surgical revascularization or PCI may be found in Section III. Outcomes, F. Comparison With Bypass Surgery.

7. Coronary Angioplasty After CABG Surgery. Although speculated to be at higher risk, patients having PCI of native vessels after prior coronary bypass surgery have, in recent years, nearly equivalent interventional outcomes and complication rates compared to patients having similar interventions without prior surgery. For PCI of SVG, studies indicate that the rate of successful angioplasty exceeds 90%, death ≤2%, and Q-wave MI ≤2.5% (Table 8). The incidence of non–Q-wave MI may be higher than that associated with native coronary arteries (134–136).

In consideration of PCI for SVG, the age of the SVG and duration and severity of myocardial ischemia should be taken into consideration. Use of GP IIb/IIIa blockers has not been shown to improve results of angioplasty in vein grafts. The native vessels should be treated with PCI if feasible. Patients with older and/or severely diseased SVGs may benefit from elective repeat CABG surgery rather than PCI (137,138).

In some circumstances, PCI of a protected left main coronary artery stenosis with a patent and functional left anterior descending or left circumflex coronary conduit can be considered. Percutaneous coronary interventions should be recognized as a palliative procedure with the potential to delay the ultimate application of repeat CABG surgery.

8. Specific Technical Considerations. Certain outcomes of PCI may be specifically related to the technology utilized for coronary recanalization. The occurrence of periprocedural CPK-MB elevation 3 times the upper limit of normal appears to occur more frequently following use of ablative technology such as rotational or directional atherectomy (20,34,58,140,146). Antecedent unstable angina appears to be a clinical predictor of slow flow and periprocedural infarction following ablative technologies (147), and direct platelet activation has been demonstrated to occur with both directional and rotational atherectomy (148). In support of the premise that platelets play a pathophysiologic role in periprocedural MI are observations that the presence and magnitude of CK-MB elevation following ablative technologies can be reduced to levels observed following balloon angioplasty by the administration of prophylactic platelet GP IIb/IIIa receptor blockade (149,150).

Coronary perforation may occur more commonly following the use of ablative technologies, including rotational, directional or extraction atherectomy, and excimer laser coronary angioplasty. However, the incidence of perforation has been reported variably to be 0.10 to 1.14% with balloon angioplasty; 0.25 to 0.70% with directional coronary atherectomy; 0.0 to 1.3% with rotational atherectomy; 1.3 to 2.1% with extraction atherectomy; and, 1.9 to 2.0% following excimer laser coronary angioplasty (151,152). Coronary perforation complicates PCI more frequently in the elderly and in women. While 20% of perforations may be secondary to the coronary guidewire, most are related to the specific technology used. Perforation is usually (80 to 90%) evident at the time of the interventional procedure and should be a primary consideration in the differential diagnosis for cardiac tamponade manifest within 24 h of the procedure. Perforations may be classified based on angiographic appearance as Type I—extraluminal crater without extravasation; Type II—pericardial and myocardial blush without contrast jet extravasation; and Type III—extravasation through a frank (>1 mm) perforation (151). In the absence of extravasation (Type III), the majority of perforations may be effectively managed without urgent surgical intervention. Type III perforations have been successfully managed nonoperatively with pericardiocentesis, reversal of anticoagulation, and either prolonged perfusion balloon inflation at the site of perforation or deployment of a covered stent. If these approaches are not successful, perforations caused by directional atherectomy catheters usually require surgical repair (Table 9).

9. Issues of Hemodynamic Support in High-Risk Angioplasty. Controversy exists about the ability to predict hemodynamic compromise during coronary angioplasty. Hemodynamic compromise, defined as a decrease in systolic blood pressure to an absolute level <90 mm Hg during balloon inflation, was often associated with LV ejection fraction <35%, >50% of myocardium at risk, and PTCA performed on the last remaining vessel (95,107).

Early feasibility studies of high-risk PTCA using percutaneous cardiopulmonary support (CPS) indicated that although initial likelihood of success was high, vascular morbidity was also high with an incidence of 43%

### Table 8. Probability of Success, Complications, and Restenosis After Balloon Angioplasty or Stenting in Patients Following Coronary Bypass Surgery

<table>
<thead>
<tr>
<th>Conduit Site</th>
<th>Success Rate</th>
<th>Death Rate</th>
<th>MI Rate</th>
<th>Restenosis Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saphenous vein graft</td>
<td>&gt;92%</td>
<td>&lt;2%</td>
<td>15%</td>
<td>20–35%</td>
</tr>
<tr>
<td>Internal mammary</td>
<td>75%</td>
<td>&lt;2%</td>
<td>15%</td>
<td>25%</td>
</tr>
<tr>
<td>Left main</td>
<td>95%</td>
<td>&lt;2%</td>
<td>10%</td>
<td>25%</td>
</tr>
</tbody>
</table>

"*3 times normal CK-MB on serial determinations following intervention; frestenosis measured as target-vessel revascularization."
(153,154). However, no study has published data to validate commonly employed high-risk categorization.

Elective high-risk PCI can be performed safely without intra-aortic balloon pump (IABP) or CPS in most circumstances. Emergency high-risk PCI such as direct PCI for acute MI can usually be performed without IABP or CPS. CPS for high-risk PCI should be reserved only for patients at the extreme end of the spectrum of hemodynamic compromise, such as those patients with extremely depressed LV function and patients in cardiogenic shock. However, it should be noted that in patients with borderline hemodynamics, ongoing ischemia, or cardiogenic shock, insertion of an intra-aortic balloon just prior to coronary instrumentation has been associated with improved outcomes (155,156). Furthermore, it is reasonable to obtain vascular access in the contralateral femoral artery prior to the procedure in patients in whom the risk of hemodynamic compromise is high, thereby facilitating intra-aortic balloon insertion, if necessary.

For high-risk patients, clinical and anatomic variables influencing complications and outcome should be assessed before the performance of PCI to determine procedural risk, the risk of abrupt vessel closure, and potential for cardiovascular collapse. In patients having a higher-risk profile, consideration of alternative therapies, particularly coronary bypass surgery, formalized surgical standby, or periprocedural hemodynamic support should be addressed before proceeding with PCI.

F. Comparison With Bypass Surgery

The major advantage of PCI is its relative ease of use, avoiding general anesthesia, thoracotomy, extracorporeal circulation, CNS complications, and prolonged convalescence. Repeat PCI can be performed more easily than repeat bypass surgery, and revascularization can be achieved more quickly in emergency situations. The disadvantages of PCI are early restenosis and the inability to relieve many totally occluded arteries and/or those vessels with extensive atherosclerotic disease.

Coronary artery bypass surgery has the advantages of greater durability (graft patency rates exceeding 90% at 10 years with arterial conduits) (157) and more complete revascularization irrespective of the morphology of the obstructing atherosclerotic lesion. Generally speaking, the greater the extent of coronary atherosclerosis and its diffuseness, the more compelling the choice of coronary artery bypass surgery, particularly if LV function is depressed. Patients with lesser extent of disease and localized lesions are good candidates for endovascular approaches.

PTCA and coronary artery bypass surgery have been compared in many nonrandomized and randomized studies. The most accurate comparisons of outcomes are best made from prospective randomized trials of patients suitable for either treatment. Although results of these trials provide useful information for selection of therapy in several patient subgroups, prior studies of PTCA may not reflect outcome of current PCI practice, which includes frequent use of stents and antiplatelet drugs. Similarly, many previous studies of CABG may not reflect outcome of current surgical practice in which arterial conduits are used whenever practicable. Beating heart bypass operations are also employed for selected patients with single-vessel disease with reduced morbidity (158). In addition, patients are selected for PCI (with or without stenting) because of certain lesion characteristics, and these anatomical criteria are not required for CABG.

Randomized trials also must be interpreted carefully. It is unethical to withhold subsequent PCI or CABG from patients solely because they fail an earlier treatment; thus, comparative prospective studies can only compare initial strategies of revascularization. This critically important point is frequently overlooked by those who claim that a randomized study proves equally good outcome of one method of revascularization over the other. Indeed, it would seem highly unlikely that any randomized trial of PCI and CABG could demonstrate a survival advantage of an initial revascularization method as long as frequent crossover to alternate and/or new therapies is allowed.

Despite these limitations, some generalizations can be made from comparative trials of PTCA and CABG. First, for most patients with single-vessel disease, late survival is similar with either revascularization strategy, and this might be expected given the generally good prognosis of most patients with single-vessel disease managed medically (159–161). Two prospective clinical trials have evaluated PTCA and CABG for revascularization of isolated disease of the left anterior descending coronary artery. Investigators in the Medicine, Angioplasty or Surgery Study (MASS) used a combined end point of cardiac death, MI, or refractory angina requiring repeat revascularization by surgery; at 3 years of follow-up, this combined end point occurred in 24% of PTCA patients, in 17% of medical patients, and in 3% of surgical patients (162). Importantly, there was no difference in overall survival in the three groups. In the Lausanne trial of 134 patients with isolated left anterior descending artery disease treated by either PTCA (68 patients) or bypass with an internal mammary artery, survival was similar in the two groups, and 94% of PTCA patients and 95% of CABG patients were free of limiting symptoms (163). However, patients in the PTCA group took more antianginal drugs than surgical patients, and at median follow-up of 2.5 years, 86% of CABG-treated versus 43% of PTCA-treated patients were free from late events (p < 0.01); this difference was primarily due to restenosis (32%) requiring subsequent CABG (16%) or PTCA (15%). It should be emphasized that neither of the two aforementioned trials included stenting, a technique which would be expected to reduce rates of early restenosis by as much as 50% in appropriately selected lesions (86,164,165).

In a similar manner, the 3-year follow-up of the Argen-
Table 10. Summary of Randomized Trials of PTCA and CABG for Multivessel Disease

<table>
<thead>
<tr>
<th>Trial</th>
<th>Year</th>
<th>Reference</th>
<th>Location</th>
<th>N</th>
<th>Follow-Up (yrs)</th>
<th>Endpoint</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>BARI</td>
<td>1997</td>
<td>(9)</td>
<td>North America multicenter</td>
<td>1,829</td>
<td>5</td>
<td>Primary endpoint death</td>
<td>Overall survival similar with PTCA and CABG, but late survival of diabetic patients better with CABG when internal mammary grafts used</td>
</tr>
<tr>
<td>CABRI</td>
<td>1995</td>
<td>(167)</td>
<td>Europe multicenter</td>
<td>1,054</td>
<td>1</td>
<td>Mortality, symptom status</td>
<td>Complete revascularization with PTCA was not required</td>
</tr>
<tr>
<td>RITA</td>
<td>1993</td>
<td>(10)</td>
<td>U.K. multicenter</td>
<td>1,011</td>
<td>2.5</td>
<td>Death or MI</td>
<td>45% of patients had SVD</td>
</tr>
<tr>
<td>EAST</td>
<td>1994</td>
<td>(11)</td>
<td>Emory University</td>
<td>392</td>
<td>3</td>
<td>Death, Q-wave, MI, or large ischemic defect on thallium</td>
<td>Repeat revascularization in 54% of PTCA group compared to 13% of patients having CABG</td>
</tr>
<tr>
<td>GABI</td>
<td>1994</td>
<td>(12)</td>
<td>Germany multicenter</td>
<td>359</td>
<td>1</td>
<td>Freedom from angina</td>
<td>IMA used in only 37% of CABG patients; over 80% of patients had 2-vessel disease</td>
</tr>
<tr>
<td>Toulouse</td>
<td>1997</td>
<td>(168)</td>
<td>France</td>
<td>152</td>
<td>2.8</td>
<td>Freedom from angina 1 year after revascularization</td>
<td>Similar survival with PTCA and CABG at 5 years, but better event-free survival with CABG</td>
</tr>
<tr>
<td>ERACI</td>
<td>1996</td>
<td>(164)</td>
<td>Argentina</td>
<td>127</td>
<td>3.8</td>
<td>Event-free survival (MI, angina, and repeat revascularization)</td>
<td>Similar in-hospital and 1-yr survival and freedom from MI; less angina and fewer repeat procedures after CABG</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass graft; IMA = internal mammary artery; MI = myocardial infarction; PTCA = percutaneous transluminal coronary angioplasty; SVD = single-vessel disease. For expansion of study names, see the corresponding reference.

time randomized trial of PTCA versus CABG multivessel disease (ERACI study) (164) demonstrated that in patients randomized to angioplasty or bypass surgery, the 1-, 3-, and 5-year follow-up results indicated that freedom from combined cardiac events was significantly greater for bypass surgery than for angioplasty group (77% vs. 47%; p < 0.001). However, there were no differences in overall and cardiac mortality or in the frequency of MI between the two groups. Patients who had bypass surgery were more frequently free of angina (79% vs. 57%) and had fewer additional reinterventions (6.3% vs. 37%) than in patients who had angioplasty. This study indicated that freedom from combined cardiac events at 3-year follow-up was greater in bypass patients than those who had angioplasty and that the angioplasty group had a higher incidence of recurrence of angina and need for repeat procedures. Cumulative cost at 3 years was greater for surgery than for the angioplasty group.

In the ARTS trial, the first trial to compare stenting with surgery, there was no significant difference in mortality between PCI and surgical groups at one year. The main difference compared to previous PTCA and CABG trials was an approximate 50% reduction in the need for repeat revascularization in a group randomized to PCI with stent placement (166).

Direct comparison of initial strategies of PCI or CABG in patients with multivessel coronary disease is possible only by randomized trials because of selection criteria of patients for PCI. There have been 5 large (>300 patients) randomized trials of PTCA versus CABG and 2 smaller studies; characteristics of the studies are summarized in Table 10 (9–12,164,167,168). These trials demonstrate that in appropriately selected patients with multivessel coronary disease, an initial strategy of standard PTCA yields similar overall outcomes (e.g., death, MI) compared to initial revascularization with coronary artery bypass. In BARI, the only trial with the largest patient enrollment to look at survival alone, 5-year survival was 86.3% for those assigned to PTCA versus 89.3% for those assigned to CABG (p = 0.19), and 5-year survivals free from Q-wave MI were 78.7% and 80.4%, respectively. However, after 5 years of follow-up, 54% of those assigned to PTCA had undergone additional revascularization procedures compared to 8% of the patients assigned to CABG (9). Indications for PCI for various patient subsets are presented in Section V. Indications.

An important exception to the conclusion of the relative safety of PCI in multivessel disease is the subgroup of patients with treated diabetes mellitus. Among treated diabetic patients in BARI assigned to PTCA, 5-year survival was 65.5% compared to 80.6% for patients having CABG (p = 0.003); the improved outcome with CABG was due to reduced cardiac mortality (5.8% vs. 20.6%, p = 0.0003), which was confined to those receiving at least 1 internal mammary artery graft (9). Better survival of diabetic patients with multivessel disease treated initially with CABG has been observed in a large retrospective study from Emory (169) and may be due to the apparent additive effects of diabetes mellitus and instrumentation of an artery on development of new stenotic lesions (170). As compelling as these reports may be, it is of interest that treated diabetic patients enrolled in the BARI Registry did not show a similar advantage for CABG over PCI, suggesting that physician judgment in the selection of diabetic patients for PCI may be an important factor (38,48).

Moreover, direct comparison between outcomes of PCI and CABG among the diabetic population has not been made using platelet receptor antagonists with PCI. In this setting, PCI may be more competitive with CABG. The EPISTENT trial demonstrated significant reductions of...
major cardiac events at 30 days and at 6 months in the abciximab groups undergoing stenting compared to those with stenting and placebo (133). Randomized trials of PTCA and CABG provide additional information on symptom relief, quality of life, and costs of the two revascularization methods. Both revascularization techniques relieve angina. However, to achieve similar clinical outcomes, patients treated with PTCA are more likely to require further interventions than patients having surgery. Analysis of quality-of-life data from BARI suggests that functional status including activities of daily living improved less in patients assigned to PTCA than in those assigned to CABG (p < 0.05), although patients with initial PTCA returned to work five weeks sooner than did patients undergoing operation (p < 0.001) (171).

G. Comparison With Medicine

There has been a considerable effort made to evaluate the relative effectiveness of bypass surgery as compared to PCI for coronary artery revascularization. In contrast to this, very little effort has been directed toward comparing medical therapy with PCI for the management of stable and unstable angina. 3 Randomized trials are currently available comparing PCI with the medical management of angina (172–174). The ACME investigators randomized 212 patients with single-vessel disease, stable angina pectoris, and ischemia on treadmill testing to PTCA or medical therapy. This trial demonstrated superior control of symptoms and better exercise capacity in patients managed with PTCA as compared to medical therapy. Death and MI were frequent and similar in both groups. The Veterans Administration ACME trial investigators long-term results in an additional 101 randomized patients with double-vessel disease not previously reported (175) indicated that patients randomized to medical therapy or PTCA had similar improvement in exercise duration, freedom from angina, and improvement in quality of life at the time of 6-month follow-up. Thus, these patients with double-vessel angioplasty did not demonstrate superior control of their symptoms as compared to medical therapy as was experienced by the ACME patients with single-vessel disease. This small study suggests that PTCA is less effective in controlling symptoms in patients with double-vessel and stable angina as compared to single-vessel disease.

The RITA-2 investigators randomized 1,018 stable patients with stable angina to PTCA or conservative (medical) therapy (173). Patients who had inadequate control of their symptoms with optimal medical therapy were allowed to cross-over to myocardial revascularization. The combined end point of the trial was all cause mortality and nonfatal MI. The 504 PTCA and 514 medical patients were followed for a mean of 2.7 years. Death and definite MI occurred in 32 of the PTCA patients (6.3%) and in 17 of the medical patients (3.3%), p = 0.02. Of the 18 deaths (11 PTCA and 7 medical) only 8 were due to heart disease. Twenty-three percent of the medical patients required a revascularization procedure during follow-up. Angina improved in both groups, but there was a 16.5% absolute excess of grade 2 or worse angina in the medical group at 3 months following randomization (p < 0.001). The PTCA patients also had greater improvement in their exercise duration as compared to the medical patients (p < 0.001). During follow-up 40 patients randomized to PTCA required CABG surgery (7.9%) as compared to 30 of the medical patients (5.8%). Thus, RITA-2 demonstrated that PTCA results in better control of symptoms of ischemia and improves exercise capacity as compared to medical therapy, but is associated with a higher combined end point of death and periprocedural MI. It is important to remember that although the patients in this trial were asymptomatic or had only mild angina, 62% of them had multivessel CAD and 34% had significant disease in the proximal segment of the left anterior descending coronary artery (176). Thus, most of these patients had severe anatomic CAD.

The Asymptomatic Cardiac Ischemia Pilot (ACIP) study provides additional information comparing medical therapy with PTCA or CABG revascularization in patients with documented CAD and asymptomatic ischemia by both stress testing and ambulatory ECG monitoring (176). This trial randomized 558 patients suitable for revascularization by PTCA or CABG to 3 treatment strategies: angina-guided drug therapy (n = 183), angina plus ischemia-guided drug therapy (n = 183), and revascularization by PTCA or CABG surgery (n = 192). Of the 192 patients that were randomized to revascularization, 102 were selected for PTCA and 90 for CABG. At 2 years of follow-up, death or MI had occurred in 4.7% of the revascularization patients as compared to 8.8% of the ischemia-guided group and 12.1% of the angina-guided group (p < 0.01). Because a large portion of the patients underwent CABG surgery instead of PTCA in order to achieve complete revascularization, it is not appropriate to directly compare these results with RITA-2. Nonetheless, the ACIP study suggests that outcomes of revascularization with CABG surgery and PTCA are very favorable compared to medical therapy in patients with asymptomatic ischemia with or without mild angina. It should be emphasized that aggressive lipid-lowering therapy was not widely employed in the medical treatment arm of ACIP.

AVERT (174) randomly assigned 341 patients with stable CAD, normal LV function, and Class I and/or II angina to PTCA or medical therapy with 80 mg daily atorvastatin (mean LDL = 77 mg/dl). At 18 months follow-up, 13% of the medically treated group had ischemic events as compared to 21% of the PTCA group (p = 0.048). Angina relief was greater in those treated with PTCA. Although not statistically different when adjusted for interim analysis, these data suggest that in low-risk patients with stable CAD, aggressive lipid-lowering therapy can be as effective as PTCA in reducing ischemic events.

Based on the limited data available from randomized trials comparing medical therapy with PTCA, it seems...
prudent to consider medical therapy for the initial management of most patients with Canadian Cardiovascular Society Classification Class I and II and reserve PTCA and CABG for those patients with more severe symptoms and ischemia. The symptomatic individual patient who wishes to remain physically active, regardless of age, will more often require PCI although one trial (RITA-2) (94,173) suggests that this option may be associated with an increased initial risk. The results of the ACIP trial indicate that higher-risk patients with asymptomatic ischemia and significant CAD who undergo complete revascularization with CABG or PTCA may have a better outcome as compared to those with medical management. This finding had not been previously demonstrated by trials comparing medical management with surgical revascularization (16,98) (Table 11). In contrast, the results of AVERT indicate revascularization provides no benefit when compared to aggressive lipiodlowering therapy in low-risk patients. Clinical Outcomes Utilization Revascularization and Aggressive Drug Evaluation (COURAGE) trial, a 3,250 patient-based trial, will compare intensive medical therapy with revascularization over 5 to 7 years. It is anticipated that this trial will answer many questions, in addition to quality-of-life assessment and economic cost analysis (177–179). Patients with unstable angina and non-ST-segment elevation MI have been randomized to medical therapy or PCI in the FRISC II and TACTICS TIMI 18 trials. These trials utilizing stenting as the primary therapy have favored the invasive approach. They are discussed under Section V. B.

IV. INSTITUTIONAL AND OPERATOR COMPETENCY

A. Quality Assurance

A mechanism for valid peer review must be established and ongoing at each institution performing PCI. Interventional cardiology procedures are associated with complications that in general are inversely related to operator and institutional volume (43,180–183). The mechanism for institutional review should provide an opportunity for interventionalists as well as physicians who do not perform angioplasty, but are knowledgeable about it, to review overall results of the program on a regular basis. The responsible supervising authority should monitor the following issues as outlined in Table 12.

The institutional credentialing committee should document that an interventionalist wishing to start practice meets the established training criteria, including those of the ACC Task Force on Training in Cardiac Catheterization and Interventional Cardiology (21,185,186). The ACC Training Statement (186) for coronary invasive training requires a 3-year comprehensive cardiac program with 12 months of training in diagnostic catheterization during which the trainee performs 300 diagnostic catheterizations with 200 of those being the primary operator. The interventional training requires a fourth year of fellowship during which the trainee should perform more than 250 interventional procedures, but not more than 600/year (186). To be eligible for the American Board of Internal Medicine (ABIM) certifying examination in interventional cardiology, a trainee must be actively involved in at least 250 interventional procedures during a 4th year of interventional cardiology fellowship. Only one trainee may receive credit for the intervention on a given patient. Until 2003, the practicing interventionalist can qualify for the examination by active involvement in interventional cardiology, including the performance of at least 150 interventions over the prior 2 year period (187). Credentials committees should evaluate the physicians’ outcomes to be certain that volume and results meet the current standards or benchmarks for successful management (21). These benchmarks refer to
d procedural rates of unadjusted mortality (0.9%) and emergency coronary artery bypass surgery (=3.0%). It should be noted that these benchmarks are derived from PTCA performed in New York State on all procedures including those for complicated acute MI and that they were gathered before the use of stents and platelet GP IIb/IIIa inhibitors. Thus, the standard for benchmark complication rates will be subject to future revision as newer data emerge. It is important that institutions assist with these efforts by participating in active database efforts to track clinical and procedural information for individual operators and their institutions. In the future, certification by the ABIM in Interventional Cardiology should be required.

This Writing Committee agrees with the ACC Task Force recommendations for the Assessment and Maintenance of Proficiency in Coronary Interventional Procedures (21). Institutions performing PCI should meet the following standards as outlined in Tables 13 and 14 (21,184,186).

B. Operator and Institutional Volume

The proliferation of small angioplasty or small surgical programs to support such angioplasty programs is strongly discouraged. Several studies have identified procedural volume as a determining factor for frequency of complications with PCI (43,182,183,188–191). Kimmel, using data from the Society of Cardiac Angiography and Interventions (SCA&I), found that an inverse relationship existed between the number of angioplasty procedures performed at a hospital and the rate of major complications (181). These results were risk-stratified and independent of the patient-risk profile. Significantly fewer complications occurred in laboratories performing ≥400 angioplasty procedures per year. Conversely, low-volume hospitals were associated with higher rates of emergency coronary artery bypass surgery and death (182). Improved outcomes were identified with a threshold volume of 75 Medicare angioplasties per physician and 200 Medicare angioplasty procedures per hospital. Using a 35 to 50% ratio of Medicare patients, the threshold value was 150 to 200 angioplasty procedures cardiologist and 400 to 600 angioplasty procedures/institution (40). Other studies have also supported the relationship of complications to procedural volume (43,180,183). Although
<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Reference</th>
<th>N</th>
<th>Patient Population</th>
<th>Follow-Up</th>
<th>Results</th>
<th>Significance</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACME</td>
<td>1992</td>
<td>(172)</td>
<td>212</td>
<td>Patients with single-vessel disease</td>
<td>64% less angina</td>
<td>46% less angina</td>
<td>p &lt; 0.01</td>
<td>The PTCA group had less angina, better exercise performance and more improvement in quality of life scores, but had more complications (emergency bypass 2 patients, MI in 5, and repeat PTCA in 16).</td>
</tr>
<tr>
<td>VA ACME</td>
<td>1997</td>
<td>(175)</td>
<td>328</td>
<td>Patients with documented chronic stable angina</td>
<td>3 yrs</td>
<td>63% less angina</td>
<td>p = 0.02</td>
<td>Among patients with single-vessel disease, the PTCA group had less angina, better exercise performance, and more improvement in quality of life scores.</td>
</tr>
<tr>
<td>RITA-2</td>
<td>1997</td>
<td>(10)</td>
<td>1,018</td>
<td>53% with Class II angina, 47% with prior angina, 7% triple-vessel disease</td>
<td>2.7 yrs</td>
<td>6.3% death or MI</td>
<td>p = 0.02</td>
<td>The PTCA group had increased rates of death and MI, but had 7% less Class II angina at 2 years and longer exercise treadmill test time at 3 months.</td>
</tr>
<tr>
<td>ACIP</td>
<td>1997</td>
<td>(176)</td>
<td>558</td>
<td>Patients with documented CAD and asymptomatic ischemia, angina-guided drug therapy, revascularization by PTCA or CABG</td>
<td>2 yrs</td>
<td>4.7% death or MI</td>
<td>p &lt; 0.01</td>
<td>40% of patients had previous MI, 23% had prior PTCA or CABG and 38% had triple-vessel disease.</td>
</tr>
<tr>
<td>AVERT</td>
<td>1999</td>
<td>(174)</td>
<td>341</td>
<td>Patients with stable CAD, normal LV function and angina Class I/II</td>
<td>18 mo</td>
<td>21% ischemic events</td>
<td>p = 0.048</td>
<td>p = 0.045 needed for significance due to interim analysis. Patients required to complete 4 min on Bruce protocol. Only 2 deaths among 341 patients in 18 months. Significant improvement in angina in patients treated with PTCA compared with medical therapy.</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass graft; CAD = coronary artery disease; LV = left ventricular; MI = myocardial infarction; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty. For expansion of study names, see corresponding reference.
some investigators have suggested that low procedure volume does not contribute to poor outcomes (188,192), these studies are small in number and underpowered for analysis (189). Development of small cardiovascular surgical programs to support angioplasty is a poor use of resources that will likely lead to suboptimal results (190).

Given the concerns regarding operator volume and surgical standby, it is recommended that PCI be performed by higher volume operators (≥75 cases/year) with advanced technical skills (e.g., subspecialty certification) at institutions with fully equipped interventional laboratories and experienced support staff. This setting will most often be in a high-volume center (>400 cases/year) associated with an on-site cardiovascular surgical program (193). Similar concerns have been identified and supported by the Task Force for Practice Guidelines for Coronary Angiography (194).

| Clinical Proficiency | • General indications/contraindications  
|                      | • Institutional and individual operator complication rates, mortality and emergency bypass surgery  
|                      | • Institutional and individual operator procedure volumes  
|                      | • Training and qualifications of support staff  |
| Equipment Maintenance and Management | • Quality of laboratory facility (See ACC/SCA&I Expert Consensus Document on Cardiac Catheterization Laboratory Standards (184))  
| Quality Improvement Process | • Establishment of an active concurrent database to track clinical and procedural information as well as patient outcomes for individual operators and the institution. The ACC-National Cardiovascular Data Registry™ is strongly recommended for this purpose  |
| Radiation Safety | • Educational program in the diagnostic use of X-ray  
|                  | • Patient and operator radiation exposure  |

Intuitively, it is clear that it would be best for the rare patient requiring surgery after elective PCI to remain in the same hospital rather than have the patient and family undergo the confusion, stress, and anxiety of emergency transfer. Given the widespread availability of sophisticated interventional/surgical programs in the U.S., it is difficult to demonstrate a need for additional low-volume programs to do elective angioplasty except in underserved areas that are geographically far removed from major centers. This Committee acknowledges that not every cardiologist desiring to do PCI should perform these procedures and not every hospital anxious to have an interventional program should start one (191). This caveat is particularly true where there are high-volume programs and operators nearby. In these situations, operators should be subspecialty board certified.

The Committee, therefore, recommends that angioplasty is best done by high-volume operators in high-volume institutions. Any change in this recommendation awaits further data confirming the comparable safety and outcomes for patients treated in an alternative manner. The Committee cannot recommend angioplasty by low-volume operators (<75 cases/year) working in low-volume institutions (<200 cases/year) with or without on-site surgical coverage. As noted earlier, ongoing investigational experience and clinical data are mandatory if these recommendations are to be modified.

### Table 12. Key Components of a Quality Assurance Program

| Institutions | • Quality assessment monitoring of privileges and risk/stratified outcomes  
|             | • Provide support for a quality assurance staff person (e.g., nurse) to monitor complications  
|             | • Minimal institutional performance activity of 200 interventions per year with the ideal minimum of 400 interventions per year  
|             | • Interventional program director who has a career experience of >500 PCI procedures and is board certified by ABIM in interventional cardiology  
|             | • Facility and equipment requirements to provide high resolution fluoroscopy and digital video processing  
|             | • Experienced support staff to respond to emergencies. (See Section IV, C. Need for Surgical Backup for discussion.)  
|             | • Establishment of a mentoring program for operators who perform <75 procedures per year by the individuals who perform ≥150 procedures per year  |
| Physicians | • Procedural volume of ≥75 per year  
|            | • Continuation of privileges based on outcome benchmark rates with consideration of not granting privileges to operators who exceed adjusted case mix benchmark complication rates for a 2-year period  
|            | • Ongoing quality assessment comparing results with current benchmarks with risk stratification of complication rates  
|            | • Board certification by ABIM in interventional cardiology  |

ABIM = American Board of Internal Medicine; PCI = percutaneous coronary intervention.

### Table 13. Considerations for the Assessment and Maintenance of Proficiency in Coronary Interventional Procedures (21,184,186)

| Class I | 1. PCI done by operators with acceptable volume (≥75) at high-volume centers (>400). *(Level of Evidence: B)* |
| Class IIa | 1. PCI done by operators with acceptable volume (≥75) at low-volume centers (200 to 400). *(Level of Evidence: C)*  
|           | 2. PCI done by low-volume operators (<75) at high-volume centers (>400). Note: Ideally operators with an annual procedure volume <75 should only
Table 14. Recommendations for PCI Institutional and Operator Volumes at Centers With On-Site Cardiac Surgery (21,186)

<table>
<thead>
<tr>
<th>Operator Volume</th>
<th>Minimum Institutional Volume</th>
<th>Optimal Institutional Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low (&lt;75 procedures annually)</td>
<td>Class IIb: PCI done by low-volume operators (&lt;75) at low-volume centers (200–400). <em>(Level of Evidence: C) Note: An institution with a volume &lt;200 procedures/year, unless in a region that is underserved because of geography, should carefully consider whether it should continue to offer service.</em> (Level of Evidence: C)</td>
<td>Class IIa: PCI done by low-volume operators (&lt;75) at high-volume centers (&gt;400). *(Level of Evidence: C) Note: Ideally, operators with annual procedure volume &lt;75 should only work at institutions with an activity level of &gt;600 procedures/year.</td>
</tr>
<tr>
<td>Acceptable (≥75 procedures annually)</td>
<td>Class IIa: PCI done by operators with acceptable volume (≥75) at low-volume centers (200–400). *(Level of Evidence: C)</td>
<td>Class I: PCI done by operators with acceptable volume (≥75) at high-volume centers (&gt;400). *(Level of Evidence: B)</td>
</tr>
</tbody>
</table>

*Note: Operators who perform <75 procedures/year should develop a defined mentoring relationship with a highly experienced operator who has an annual procedural volume ≥150 procedures/year.

For this reason, the establishment of PCI programs at institutions without on-site cardiovascular surgery has been promoted as necessary to maintain quality of care (195–197,213–220). In those patients where there is a contraindication to thrombolytic therapy, or when there are complications such as cardiogenic shock, catheter-based therapy may limit infarct size (221,222). It must be realized that PCI in the early phase of an acute MI can be difficult and requires even more skill and experience than routine PCI in the stable patient. The need for an experienced operator and experienced laboratory technical support (223) with availability of a broad range of catheters, guidewires, stents, and other devices (e.g., IABP) that are required for optimum results in an acutely ill patient is of major importance (Table 15). If these complex patients are treated by interventionists with limited experience at institutions with low volume, then the gains of early intervention may be lost because of increased complications. In such circumstances, transfer to a center that routinely performs complex PCI will often be a more effective and efficient course of action (16). Thrombolysis is still an acceptable form of therapy (224) and is preferable to acute PCI by an inexperienced team (224,225).

Reports of emergency primary angioplasty programs from hospitals without established open-heart surgery or elective angioplasty, similar to those of most tertiary centers, have demonstrated generally favorable results. Such acceptable clinical results have been reported with intensive training, continuous oversight, and the combination of nearby, readily available bypass surgery support, a team of highly experienced interventionists and support staff, and careful patient selection (214). However, poor results of similar endeavors are rarely reported. Before the use of stenting and glycoprotein receptor blockers, primary angioplasty in certain hospitals has been associated with acute mortality rates greater than those reported from centers with established primary angioplasty programs. Overall, in-hospital mortality rates have ranged from 1.4 to 13% (196,197,216).

Criteria have been suggested for the performance of
primary PCI at hospitals without on-site cardiac surgery (Tables 15 and 16). Of note, large-scale registries have shown an inverse relationship between the number of primary angioplasty procedures performed and in-hospital mortality (226–228). The data suggest that both door-to-balloon time and in-hospital mortality are significantly lower in institutions performing a minimum of 36 primary angioplasty procedures per year (229). Communities may identify a unique qualified and experienced center wherein on-site intervention for acute MI could be performed. Suboptimal results may relate to operator/staff inexperience and capabilities and delays in performing angioplasty for logistical reasons (230). From clinical data and expert consensus, the Committee recommends that primary PCI for acute MI performed at hospitals without established elective PCI programs should be restricted to those institutions capable of performing a requisite minimum number of primary angioplasty procedures (36/year) with a proven plan for rapid and effective PCI as well as rapid access to cardiac surgery in a nearby facility (193) (Table 17).

2. Elective PCI Without On-Site Surgery. Technical improvements in interventional cardiology have led to the development of elective angioplasty programs without on-site surgical coverage. Several centers have reported satisfactory results based on careful case selection with well-defined arrangements for immediate transfer to a surgical program (195–199,231–235). The studies of angioplasty without on-site surgical coverage have not identified significant differences in the outcomes, recalling the infrequent rate of complications (236). Despite many reported successful angioplasty series without on-site surgical backup and a very low percentage need for off-site surgery in failed angioplasty, some clinicians have expressed concern (237,238) about the appropriateness of elective angioplasty in centers without on-site surgical coverage. Caution is warranted before endorsing an unrestricted policy for PCI in hospitals without appropriate facilities. Several outstanding and critically important clinical issues, such as timely management of ischemic complications, adequacy of specialized post-interventional care, logistics for managing cardiac surgical or vascular complications and operator/laboratory volumes, and accreditation must be addressed. Mere convenience should not replace safety and efficacy in establishing an elective PCI program without on-site surgery.

At this time, the Committee, therefore, continues to support the recommendation that elective PCI should not be performed in facilities without on-site cardiac surgery (Table 17). As with many dynamic areas in interventional cardiology, these recommendations may be subject to revision as clinical data and experience increase.
Table 17. Recommendations for PCI With and Without On-Site Cardiac Surgery

<table>
<thead>
<tr>
<th>Class</th>
<th>With On-Site Cardiac Surgery</th>
<th>Without On-Site Cardiac Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elective PCI Class I</td>
<td>Patients undergoing elective PCI in facilities with on-site cardiac surgery. (Level of Evidence: B)</td>
<td>Patients undergoing elective PCI in facilities without on-site cardiac surgery. (Level of Evidence: C)</td>
</tr>
</tbody>
</table>
| Primary PCI Class I | Patients undergoing primary PCI in facilities with on-site cardiac surgery. (Level of Evidence: B) | Class IIb
Patients undergoing primary PCI in facilities without on-site cardiac surgery, but with a proven plan for rapid access (within 1 h) to a cardiac surgery operating room in a nearby facility with appropriate hemodynamic support capability for transfer. The procedure should be limited to patients with ST-segment elevation MI or new LBBB on ECG, and done in a timely fashion (balloon inflation within 90 ± 30 min of admission) by persons skilled in the procedure (≥75 PCIs/year) (193) and only at facilities performing a minimum of 36 primary PCI procedures per year (229). (Level of Evidence: B)

Class III
Patients undergoing primary PCI in facilities without on-site cardiac surgery and without a proven plan for rapid access (within 1 h) to a cardiac surgery operating room in a nearby facility with appropriate hemodynamic support capability for transfer. (Level of Evidence: C)

ECG = electrocardiography; LBBB = left bundle-branch block; MI = myocardial infarction; PCI = percutaneous coronary intervention.

V. INDICATIONS
A broad spectrum of clinical presentations exists wherein patients may be considered candidates for PCI, ranging from asymptomatic to severely symptomatic or unstable, with variable degrees of jeopardized myocardium. Selection of appropriate candidates for PCI in a variety of clinical presentations is reviewed in this section.

Each time that a patient is considered for revascularization, the potential risk and benefits of the particular procedure under consideration must be weighed against alternative therapies (Table 18).

When PCI is considered, the benefits and risks of surgical revascularization and medical therapy always deserve thoughtful discussion with the patient and family. The initial simplicity and associated low morbidity of PCI as compared to surgical therapy is always attractive, but the patient and family must understand the limitations inherent in current PCI procedures, including a realistic presentation of the likelihood of restenosis and the potential for incomplete revascularization as compared with CABG surgery. In patients with CAD who are asymptomatic or have only mild

Table 18. Provider Checklist: Key Areas for Consideration

Patients at High Risk
- Assess key clinical and anatomical variables
- Consider alternative therapies such as CABG in consultation with the patient
- Ensure that formalized surgical standby is available
- Ensure periprocedural hemodynamic support is available

Patients at Low Risk
- Assess key clinical and anatomical variables
- Consider alternative therapies such as medical therapy in consultation with the patient
symptoms, the potential benefit of antianginal drug therapy along with an aggressive program of risk reduction must also be understood by the patient before a revascularization procedure is performed.

A. Asymptomatic or Mild Angina

In the previous ACC/AHA Guidelines for PTCA, specific recommendations were made separately for patients with single- or multivessel disease (16,98). The current techniques of PCI have matured to the point where, in patients with favorable anatomy, the competent practitioner can perform either single- or multivessel PCI at low risk and with a high likelihood of initial success. For this reason, in this revision of the Guidelines, recommendations will be made largely based upon the patients’ clinical condition, specific coronary lesion morphology and anatomy, LV function, and associated medical conditions, and less emphasis will be placed on the number of lesions or vessels requiring PCI. The CCS Class of angina (I to IV) is used to define the severity of symptoms. The categories described in this section refer to an initial PCI procedure in a patient without prior CABG surgery. The randomized trials comparing PTCA and medical therapy have been discussed (Table 11).

The Committee recognizes that the majority of patients with asymptomatic ischemia or mild angina should be treated medically. The published ACIP study (176) casts some doubt on the wisdom of medical management for those higher-risk patients who are asymptomatic or have mild angina, but have objective evidence by both treadmill testing and ambulatory monitoring of significant myocardial ischemia and CAD. In addition, there is a substantial portion of the middle and older age populations in this country that remains physically active, participating in sports, such as tennis and skiing, or performing regular and vigorous physical exercise, such as jogging, who have CAD.

For such individuals with moderate or severe ischemia and few symptoms, revascularization with PCI or CABG surgery may reduce their risk of serious or fatal cardiac events. For this reason, patients in this category of higher-risk asymptomatic ischemia or mild symptoms and severe anatomic CAD are placed in Class I or II. Percutaneous coronary intervention may be considered if there is a high likelihood of success and a low risk of morbidity or mortality. The judgment of the experienced physician is deemed valuable in assessing the extent of ischemia.

Recommendations for PCI in Asymptomatic or Class I Angina Patients (Table 19)

Class I

1. Patients who do not have treated diabetes with asymptomatic ischemia or mild angina with 1 or more significant lesions in 1 or 2 coronary arteries suitable for PCI with a high likelihood of success and a low risk of morbidity and mortality. The vessels to be dilated must subtend at least a moderate area of viable myocardium.

   (Level of Evidence: B)

Table 19. Recommendations for PCI in Asymptomatic or Class I Angina Patients

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients who do not have treated diabetes with asymptomatic ischemia or mild angina with 1 or more significant lesions in 1 or 2 coronary arteries suitable for PCI with a high likelihood of success and a low risk of morbidity and mortality. (Level of Evidence: B)</td>
<td>The same clinical and anatomic requirements for Class I, except the myocardial area at risk is of moderate size or the patient has treated diabetes. (Level of Evidence: B)</td>
<td>Patients with asymptomatic ischemia or mild angina with ≥3 coronary arteries suitable for PCI with a high likelihood of success and a low risk of morbidity and mortality.</td>
<td>Patients with asymptomatic ischemia or mild angina who do not meet the criteria as listed under Class I or Class II and who have: a. Only a small area of viable myocardium at risk. b. No objective evidence of ischemia. c. Lesions that have a low likelihood of successful dilation. d. Mild symptoms that are unlikely to be due to myocardial ischemia. e. Factors associated with increased risk of morbidity or mortality. f. Left main disease. g. Insignificant disease &lt;50%. (Level of Evidence: C)</td>
</tr>
</tbody>
</table>

PCI = percutaneous coronary intervention.

Table 20. Noninvasive Risk Stratification: High Risk (>3% Annual Mortality Rate)

- High-risk treadmill score (score ≥11)
- Stress-induced large perfusion defect (particularly if anterior)
- Stress-induced perfusion defects of moderate size
- Stress-induced multiple perfusion defect with LV dilation or increased lung uptake (thallium-201)
- Echocardiographic wall motion abnormality (involving ≥2 segments) developing at a low dose of dobutamine (≥10 mg/kg·min⁻¹) or at a low heart rate (120 bpm)
- Stress echocardiographic evidence of extensive ischemia

Class IIa

1. The same clinical and anatomic requirements for Class I, except the myocardial area at risk is of moderate size or the patient has treated diabetes. (Level of Evidence: B)

Class IIb

1. Patients with asymptomatic ischemia or mild angina with ≥3 coronary arteries suitable for PCI with a high likelihood of success and a low risk of morbidity and mortality. The vessels to be dilated must subtend at least a moderate area of viable myocardium. In the physician's judgment, there should be evidence of myocardial ischemia by ECG exercise testing, stress nuclear imaging, stress echocardiography or ambulatory ECG monitoring, or intracoronary physiologic measurements. (Level of Evidence: B)

Class III

1. Patients with asymptomatic ischemia or mild angina who do not meet the criteria as listed under Class I or Class II and who have:
   a. Only a small area of viable myocardium at risk.
   b. No objective evidence of ischemia.
   c. Lesions that have a low likelihood of successful dilation.
   d. Mild symptoms that are unlikely to be due to myocardial ischemia.
   e. Factors associated with increased risk of morbidity or mortality.
   f. Left main disease.
   g. Insignificant disease <50%. (Level of Evidence: C)

B. Angina Class II to IV or Unstable Angina

Many patients with moderate or severe stable angina or unstable angina do not respond adequately to medical therapy and often have significant coronary artery stenoses that are suitable for revascularization with CABG surgery or PCI. In addition, a proportion of these patients have reduced LV systolic function, which places them in a group that is known to have improved survival with CABG surgery and possibly with revascularization by PCI (178,179,240,241). In nondiabetic patients with 1- or 2-vessel disease in whom angioplasty of 1 or more lesions has a high likelihood of initial success, PCI is the preferred approach. In a minority of such patients, CABG surgery may be preferred, particularly for those in whom the left anterior descending coronary artery can be revascularized with the internal mammary artery or in those with left main coronary disease. In patients with unstable angina or non-Q-wave MI, intensive medical therapy should be initiated prior to revascularization with PCI or CABG surgery (242–244).

Clinical investigations evaluating the use of routine catheterization and PCI for patients with unstable angina and NSTEMI (non–ST-segment elevation MI) have yielded inconsistent results. TIMI-IIIB was the first to compare strategies of routine catheterization and revascularization in addition to medical therapy and selective use of aggressive treatment. In TIMI-IIIB, there was no difference in the incidence of death or recurrent MI at 1 year between the 2 strategies, but patients treated by the aggressive strategy experienced less angina and repeat hospitalizations for ischemia and required fewer medications (245). In the VANQWISH trial performed by the Veterans Administration, no difference in death or death and MI was observed between the two strategies at late follow-up, but the minority of patients in the aggressive strategy received revascularization, and the mortality rate for those having CABG was high (246). The FRISC II trial compared medical and revascularization approaches among patients after 6 days of low molecular weight heparin therapy before a decision regarding PCI (247). Those randomized to the conservative therapy only underwent PCI if they had ≥3 mm ST depression on stress testing. Compared with prior studies, patients assigned to the aggressive strategy in FRISC II experienced a 22% reduction (p = 0.031) in the incidence of death or MI at 6 months (9.4%) compared to conservatively treated patients (12.1%). In addition, there was a significant decrease in MI rate alone and a non-significantly lower mortality rate in the treated group (1.9% vs. 2.9%; p = 0.10). Symptoms of angina and hospital readmission were decreased 50% by the invasive strategy. These findings were supported by long-term follow-up from the FRISC II study indicating that low-molecular-weight heparin and early intervention lowered the risk of death, MI, and revascularization in unstable coronary syndromes, at least during the first 1 month of therapy. Early protective therapy could be used to lower the risk of late events in patients waiting for definitive PCI (248). This treatment benefit was most pronounced for high-risk patients. The FRISC II trial (247) results support the use of catheterization and revascularization for selected patients with an acute coronary syndrome. The Treat Angina with Aggrastat and determine the Cost of Therapy with an Invasive or Conservative Strategy (TACTICS) Trial randomized 2,220 patients to an early invasive strategy in which cardiac catheterization and revascularization were performed 4 to 48 h after randomization or to a conservative strategy in which revascularization was reserved for those patients who developed recurrent ischemia after medical stabilization. All patients were treated with aspirin, heparin, beta-blockers, cholesterol-lowering therapy, and tirofiban. The primary end point, a composite of death, MI, and rehospitalization for worsening chest pain by 6 months, was lower in patients assigned to the invasive strategy (15.9% vs. 19.4% in patients assigned to conservative therapy; p = 0.0025). The rate of death or MI was also significantly reduced at 6 months in the invasive strategy arm (7.3% vs. 9.5% in patients assigned to conservative therapy; p < 0.05) (249).
These promising results have not yet undergone peer review and have not been published.

The indications for coronary angiography are summarized in the ACC/AHA Coronary Angiography Guidelines (194), and recommendations for PCI are summarized in the ACC/AHA Unstable Angina Guidelines (250). Indications for PCI for patients with angina Class II to IV, unstable angina, or non–Q-wave infarction follow.

Recommendations for Patients with Moderate or Severe Symptoms (Angina Class II to IV, Unstable Angina or Non–ST-Elevation MI) With Single- or Multivessel Coronary Disease on Medical Therapy (Table 21)

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with 1 or more significant lesions in 1 or more coronary arteries suitable for PCI with a high likelihood of success and low risk of morbidity or mortality (Tables 6 and 8). The vessel(s) to be dilated should subtend a moderate or large area of viable myocardium and have high risk (Table 20). (Level of Evidence: B)</td>
<td>Patients with focal saphenous vein graft lesions or multiple stenoses who are poor candidates for reoperative surgery. (Level of Evidence: C)</td>
<td>Patient has 1 or more lesions to be dilated with reduced likelihood of success (Table 5) or the vessel(s) subtend a less than moderate area of viable myocardium. (Level of Evidence: C)</td>
<td>Patient has no evidence of myocardial injury or ischemia on objective testing and has not had a trial of medical therapy, or has: a. Only a small area of myocardium at risk. b. All lesions or the culprit lesion to be dilated with morphology with a low likelihood of success. c. A high risk of procedure-related morbidity or mortality. (Level of Evidence: C)</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass graft; CAD = coronary artery disease; LAD = left anterior descending coronary artery; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Class I

1. Patients with 1 or more significant lesions in 1 or more coronary arteries suitable for PCI with a high likelihood of success and low risk of morbidity or mortality (Tables 6 and 8). The vessel(s) to be dilated must subtend a moderate or large area of viable myocardium and have high risk (Table 20). (Level of Evidence: B)

Class IIa

1. Patients with focal saphenous vein graft lesions or multiple stenoses who are poor candidates for reoperative surgery. (Level of Evidence: C)

Class IIb

1. Patient has 1 or more lesions to be dilated with reduced likelihood of success (Table 6) or the vessel(s) subtend a less than moderate area of viable myocardium. Patients with 2- or 3-vessel disease, with significant proximal LAD CAD and treated diabetes or abnormal LV function. (Level of Evidence: B)

Class III

1. Patient has no evidence of myocardial injury or ischemia on objective testing and has not had a trial of medical therapy, or has
   a. Only a small area of myocardium at risk.
   b. All lesions or the culprit lesion to be dilated with morphology with a low likelihood of success.
   c. A high risk of procedure-related morbidity or mortality. (Level of Evidence: C)

2. Patients with insignificant coronary stenosis (e.g., <50% diameter). (Level of Evidence: C)

3. Patients with significant left main CAD who are candidates for CABG. (Level of Evidence: B)

It is recognized by the Committee that the assessment of risk of unsuccessful PCI or serious morbidity or mortality must always be made with consideration of the alternative therapies available for the patient, including more intensive or prolonged medical therapy or surgical revascularization (Table 22), especially in patients with unstable angina pectoris.

When CABG surgery is a poor option because of high risk due to special considerations or other organ system disease, patients otherwise in Class IIb may be appropriately managed with PCI. Under these special circumstances formal surgical consultation is recommended.
Table 22. Invasive vs. Conservative Strategies in Unstable Angina Patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Reference</th>
<th>N</th>
<th>Patient Population</th>
<th>Treatment</th>
<th>Follow-Up</th>
<th>Results</th>
<th>Significance</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>TIMI-IIIB</td>
<td>1995</td>
<td>(245)</td>
<td>1,473</td>
<td>Patients 21–76 years of age presenting within 24 h of ischemic discomfort at rest consistent with unstable angina or non-Q-wave MI.</td>
<td>Medical therapy (tPA vs placebo) and early invasive or conservative strategy</td>
<td>6 weeks</td>
<td>16.2% combined primary endpoints</td>
<td>18.1% combined primary endpoints</td>
<td>NS</td>
</tr>
<tr>
<td>VANQWISH</td>
<td>1998</td>
<td>(246)</td>
<td>920</td>
<td>Patients with an evolving MI</td>
<td>Invasive vs conservative</td>
<td>Avg. 23 months</td>
<td>32.9% death and MI</td>
<td>30.3% death and MI</td>
<td>p = 0.35</td>
</tr>
<tr>
<td>FRISC II</td>
<td>1999</td>
<td>(247)</td>
<td>2,457</td>
<td>Patient’s ischemic symptoms in previous 48 h accompanied by ECG changes or elevated markers.</td>
<td>Early invasive therapy or noninvasive treatment strategy. Patients also received dalteparin or placebo for 3 months.</td>
<td>6 months</td>
<td>9.4% death or MI</td>
<td>12.1% death or MI</td>
<td>p = 0.031</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass; ECG = electrocardiography; ETT = exercise treadmill test; MI = myocardial infarction; NS = no significance; PCI = percutaneous coronary intervention. For expansion of study names, see corresponding references.
C. Myocardial Infarction

The results of randomized clinical trials of intravenous thrombolysis and subsequent management strategies of immediate, delayed, and deferred PCI have established the benefits of early pharmacologic and mechanical reperfusion therapies for patients with acute MI (209,210,251–256).

Acute MI results from a severe and sudden cessation of myocardial blood flow, most commonly due to atherosclerotic-thrombotic occlusion of a major epicardial coronary artery. Percutaneous coronary intervention is a very effective method for re-establishing coronary perfusion and is suitable for ≥90% of patients. Considerable data support the use of PCI for patients with acute MI (257,258). Reported rates of achieving TIMI 3 flow, the goal of reperfusion therapy, range from 70 to 90% (259). Late follow-up angiography demonstrates that 87% of infarct arteries remain patent (260). Although most evaluations of PCI have been in patients who are eligible to receive thrombolytic therapy, considerable experience supports the value of PCI for patients who may not be suitable for thrombolytic therapy due to an increased risk of bleeding (261).

Intracoronary stents appear to augment the results of PCI for MI (Table 23). Preliminary results suggest that stenting achieves a better immediate angiographic result with a larger arterial lumen, less reclosure of the infarct-related artery, and fewer subsequent ischemic events than PTCA alone (262–264). Results from a randomized clinical trial suggest that stenting enhances late clinical outcomes (reduction in composite end point attributable to a decrease in target-vessel revascularization) when compared to PTCA alone (264). However, an increase in mortality at 1 year among the stent group has been reported in the Stent-PAMI trial (265).

Primary PTCA performed without routine stenting has been compared to thrombolytic therapy in several randomized clinical trials. These investigations consistently demonstrate that PTCA-treated patients experience less recurrent ischemia or infarction than those treated by thrombolysis (266–269). Trends favoring a survival benefit with PTCA are noted. The most recent and largest single trial (1,138 patients) demonstrated significant benefit in the composite end point death, recurrent MI, or disabling stroke at 30 days favoring angioplasty, although this benefit was not sustained at 6 months (260,270). Two meta-analyses showed superiority of PCI over thrombolysis for mortality with risk reductions of 0.34 and 0.56 (271,272). It is important to note that these results of PCI have been achieved in medical centers with experienced providers and under circumstances where angioplasty can be performed immediately following patient presentation (Fig. 3).

1. PCI in Thrombolytic-Ineligible Patients. Randomized, controlled clinical trials evaluating the outcome of PCI for patients who present with ST-segment elevation but who are ineligible for thrombolytic therapy and for patients

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Reference</th>
<th>N, Stent/Angioplasty</th>
<th>Follow-Up Month</th>
<th>Success, Crossover,</th>
<th>Death Refractor</th>
<th>Any Event</th>
<th>Death Reinfarction</th>
<th>TVR</th>
<th>Any Event</th>
<th>Death</th>
<th>Reinfarction</th>
<th>TVR</th>
<th>Any Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>GRAMI</td>
<td>1998</td>
<td>(273)</td>
<td>52/52</td>
<td>12</td>
<td>98/94.2</td>
<td>3.9/7.6</td>
<td>25/39.6</td>
<td>17/31.2</td>
<td>14/21</td>
<td>17/35</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>FRESCO</td>
<td>1998</td>
<td>(274)</td>
<td>75/75</td>
<td>6</td>
<td>99/94</td>
<td>0/7.6</td>
<td>3/3.6</td>
<td>0/12</td>
<td>17/25</td>
<td>13/32</td>
<td>1/3</td>
<td>1/3</td>
<td>7/25</td>
<td>13/32</td>
</tr>
<tr>
<td>STENTIM-2</td>
<td>1998</td>
<td>(275)</td>
<td>101/110</td>
<td>6</td>
<td>95/94.5</td>
<td>1.3/2.6</td>
<td>55/4</td>
<td>5/3/6.4</td>
<td>3/12</td>
<td>12/30</td>
<td>1/0</td>
<td>0/0</td>
<td>1/0</td>
<td>0/0</td>
</tr>
<tr>
<td>Suryapranata et al. 1998</td>
<td>1998</td>
<td>(276)</td>
<td>112/115</td>
<td>6</td>
<td>98/96</td>
<td>1.3/2.6</td>
<td>55/4</td>
<td>5/3/6.4</td>
<td>3/12</td>
<td>12/30</td>
<td>1/0</td>
<td>0/0</td>
<td>1/0</td>
<td>0/0</td>
</tr>
</tbody>
</table>

Data for the GRAMI, FRESCO, Suryapranata et al., PASTA, PSAMI, and Stent-PAMI trials are from the per protocol population for their respective primary outcomes. All patients included in the analyses were eligible for treatment with PCI before randomization. The success rate for PCI and other procedural details are presented for the per protocol population for each study. All data are presented as values for stent/angioplasty groups. For expansion of study names, see the corresponding reference. Adapted from Suwaidi MB, et al. JAMA 2000;284:1828–36 (92).
who experience infarction without ST-segment elevation have not been performed. Nevertheless, there is a general consensus that PCI is an appropriate means for achieving reperfusion in patients who cannot receive thrombolytics because of increased risk of hemorrhage. Other reasons also exclude acute MI patients from thrombolytic therapy, and the outcome of PCI in these patients may differ from those eligible for lytic therapy. For example, patients who present without ST-elevation are more often older and female and have higher in-hospital mortality than those with ST-segment elevation. Little data are available to characterize the value of primary PCI for this subset of acute MI patients (261) (Table 24).

2. Post-Thrombolysis PCI. In asymptomatic patients, the strategies of routine PCI of the stenotic infarct-related artery immediately after successful thrombolysis show no benefit with regard to salvage of jeopardized myocardium or prevention of reinfarction or death. In some studies this approach was associated with increased incidence of adverse events, which include bleeding, recurrent ischemia, emergency coronary artery surgery, and death (279–282). Routine PCI immediately after thrombolysis may increase the chance for vascular complications at the catheterization access site and hemorrhage into the infarct-related vessel wall (282).

Spontaneous recurrent ischemia and reinfarction have been observed to occur in approximately 15 to 25% of thrombolytic-treated patients (131,254,283). The majority of spontaneous cardiac ischemic events occur within the first 24 to 48 h following treatment with thrombolytic therapy and are associated with an increase in-hospital morbidity and mortality (284–286). Patients at risk for recurrent ischemia tend to be older and have more anterior infarcts. Some thrombolytic-treated patients initially managed conservatively will require urgent cardiac catheterization and revascularization because of recurrent MI (287,288).

To assess whether low-dose alteplase with standard dose abciximab enhanced 90-min reperfusion after acute MI, the strategies for patency enhancement in the emergency department (SPEED study group) examined the outcomes of 484 patients divided into five groups receiving combinations of abciximab, with and without low-dose reteplase, reteplase alone, and standard reteplase. The results of this trial indicated that adding reteplase to abciximab treatment for acute MI versus reteplase alone enhanced the incidence of early complete reperfusion after initiation of therapy in the emergency department (287). Similar data have been supportive from the GUSTO-IV trial and GUSTO-I investigators (288,289).

3. Rescue PCI. Rescue (also known as salvage) PCI is defined as PCI after failed thrombolysis for patients with continuing or recurrent myocardial ischemia. Rescue PCI has resulted in higher rates of early infarct-artery patency, improved regional infarct zone wall motion, and greater freedom from adverse in-hospital clinical events compared to a deferred PCI strategy (290). The randomized evaluation of rescue PCI with combined utilization end points trial (RESCUE) demonstrated a reduction in rates of mortality.
Table 24. Contraindications and Cautions for Thrombolytic Use in Myocardial Infarction*

Contraindications
- Previous hemorrhagic stroke at any time, other strokes or cerebrovascular events within 1 year
- Known intracranial neoplasm
- Active internal bleeding (does not include menses)
- Suspected aortic dissection

Caution/relative contraindications
- Severe uncontrolled hypertension on presentation (blood pressure >180/110 mm Hg)†
- History of prior cerebrovascular accident or known intracerebral pathology not covered in contraindications
- Current use of anticoagulants in therapeutic doses (INR >2–3); known bleeding diathesis
- Recent trauma (within 2–4 weeks) including head trauma or traumatic or prolonged (>10 min) CPR or major surgery (3 weeks)
- Noncompressible vascular punctures
- Recent (within 2 to 4 weeks) internal bleeding
- For streptokinase/anistreplase; prior exposure (especially within 5 days–2 years) or prior allergic reaction
- Pregnancy
- Active peptic ulcer
- History of chronic severe hypertension

*Viewed as advisory for clinical decision making and may not be all-inclusive or definitive; †Could be an absolute contraindication in low-risk patients with myocardial infarction.


in-hospital death and combined death and CHF maintained up to 1 year after study entry for patients presenting with anterior wall MI who failed thrombolytic therapy (291,292). Improvement in TIMI grade flow from ≤2 to 3 may offer additional clinical benefit.

4. PCI for Cardiogenic Shock. Observational studies support the value of PCI for patients who develop cardiogenic shock in the early hours of MI. For patients who do not have mechanical causes of shock, such as acute mitral regurgitation or septal or free wall rupture, mortality among those having PCI is lower than those treated by medical means (222). However, having catheterization alone, with or without angioplasty, is associated with a low mortality (222,293). Thus, the relatively favorable outcome of angioplasty–treated patients may be, in part, due to a bias in patient selection. Since the outcome of cardiogenic shock is so unfavorable with contemporary medical therapy, angioplasty continues to be recommended as potential life-saving therapy (222).

A randomized clinical trial has further clarified the role of emergency revascularization in acute MI complicated by cardiogenic shock (222). In this study, 302 patients with acute MI and cardiogenic shock were randomly assigned to emergency revascularization (ERV, n = 152) by coronary angioplasty or bypass surgery or to initial medical stabilization (IMS, n = 150). The 30-day mortality was significantly lower (p ≤ 0.01) for patients <75 years old treated with ERV (41.1% mortality) compared to IMS (56.8% mortality). By contrast, mortality among patients >75 years was worse for those treated with ERV. The use of an IABP was the same in both groups (86%). Among those receiving ERV, 60% had PTCA and 40% received CABG with 30-day mortality rates of 45% and 42% respectively. For the IMS group, 63% received thrombolytic agents and 25% had delayed revascularization. This multicenter trial supports the use of ERV with PCI in appropriate candidates for patients <75 years old with acute MI complicated by cardiogenic shock (222). Hochman et al. (222) also demonstrated that in patients with cardiogenic shock, emergency revascularization did not significantly reduce overall mortality at 30 days. However, after 6 months, there was significant survival benefit to early revascularization. These data strongly support the approach that patients <75 years with acute MI complicated by cardiogenic shock should undergo emergency revascularization and support measures.

5. PCI Hours to Days After Thrombolysis. Patients who achieve reperfusion and myocardial salvage following thrombolytic therapy may experience reocclusion of the infarct artery and recurrent MI. This concern has prompted the routine use of catheterization and PCI prior to hospital discharge to identify and dilate the culprit lesion. The value of this approach was tested in two large, randomized clinical trials. The SWIFT study (280) examined 800 patients with acute MI randomly assigned to PCI within 2 to 7 days after thrombolysis or to conservative management with intervention for spontaneous or provocative ischemia. There were no differences in the two treatment strategies regarding LV function, incidence of reinfarction, in-hospital survival, or 1-year survival rate. Similarly in the TIMI-IIB trial (281), 3,262 patients randomized to angioplasty within 18 to 48 h versus conservative management after acute infarct having received t-PA were examined. The two groups had similar mortality at 6 weeks (5.2% vs. 4.7%), incidence of nonfatal reinfarction (6.4% vs. 5.8%), and LV ejection fraction (0.5% vs. 0.5%). The 1- and 3-year survival rate, anginal class, and frequency of bypass surgery were also similar between the two groups (131,294). These data indicate that routine PCI of the infarct-related artery in the absence of spontaneous or provoked ischemia is not warranted.

A recent randomized trial comparing primary angioplasty with a strategy of short-acting thrombolysis and immediate planned rescue angioplasty in acute MI was performed by the PACT (Plasminogen-activator Angioplasty Compatibility Trial) investigators by Ross et al. (295). This study evaluated the safety and efficacy of reduced-dose fibrinolytic therapy to promote early infarct patency coupled with PCI. In 606 patients, 50 mg of rt-PA followed by immediate angioplasty was performed to recanalize infarct-related arteries. End points of time-to-artery patency and technical results of angioplasty were reported. Patency in the catheterization laboratory on arrival was 61% with rt-PA and 34% with placebo. Rescue and primary angioplasty restored TIMI flow equally in both groups. There was no difference in the incidence of stroke or bleeding. Left ventricular
function was highest in the patent infarct-related artery group on arrival to the catheterization laboratory. In 88% of angioplasty patients, the delay exceeded 1 h with a convalescent ejection fraction of 57%. These findings indicated that tailored thrombolytic regimes compatible with subsequent interventions lead to more frequent early recanalization (i.e., before arrival in the catheterization laboratory) which facilitates greater left ventricular preservation with no augmentation of adverse events at follow-up.

Initial studies of late (>6 to 12 h) PCI in asymptomatic survivors of MI, indicate that opening an occluded artery does not appear to alter the process of LV dilation (296), the incidence of spontaneous and inducible arrhythmias (297), or prognosis (298). The TAMI-6 study (299) of angioplasty of a persistently occluded infarct artery 7 to 48 h after symptom onset demonstrated that the infarct-related artery patency was similar in aggressive or conservatively treated groups at 6-month follow-up. It was also noted at the end of the same 6-month follow-up that there was a high incidence of infarct-related artery patency in patients who did not receive angioplasty as well as a high incidence of reocclusion in those who did. LV ejection fraction, incidence of reinfarction, hospital admission, and mortality during follow-up were also similar between groups. In other similar studies with small patient numbers, late angioplasty of occluded infarct arteries improved LV performance, but convincing outcome data are lacking to support late angioplasty in asymptomatic patients within 48 h of failed thrombolysis (300).

The benefits of early reperfusion therapy, whether by thrombolytic drugs or PCI, have been attributed to salvage of severely ischemic myocardium, thereby limiting infarct size and preserving LV function. However, there is increasing evidence that achieving patency in the infarct-related artery, even hours to days after the acute event, may favorably influence the outcome by mechanisms other than myocardial salvage (301–303). Late restoration of patency appears to reduce infarct expansion (296) and ventricular remodeling (304,305), and attenuate the risk for the development of ventricular arrhythmias (297,306). These effects could all contribute to improvements in survival independent of the acute salvage of myocardium (298,307,308). Although data supporting the argument to open occluded infarct-related arteries are persuasive, at least for large arteries subtending large areas of myocardium, there are few randomized trials supporting this approach. It should be noted that the overwhelming majority of trials were performed prior to the widespread use of stents and platelet IIb/IIIa receptor blockade and thus, the potential impact and benefit of these newer therapies in this clinical setting needs re-evaluation.

6. PCI After Thrombolysis in Selected Patient Subgroups. a. YOUNG AND ELDERLY POST-INFARCT PATIENTS.

Although not supported by randomized trials, routine cardiac catheterization following thrombolytic therapy for AMI has been a frequently performed strategy in all age groups. Young (<50 years) patients often undergo cardiac catheterization after thrombolytic therapy due to a “perceived need” to define coronary anatomy and thus establish psychological as well as clinical outcomes. In contrast, older (>75 years) patients have higher in-hospital and long-term mortality rates and enhanced clinical outcomes when treated with primary PCI (309).

In a secondary analysis of the TIMI-IIIB study comparing angiographic findings and clinical outcomes among 841 young (<50 years) and 859 older (65 to 70 years) patients randomly assigned to an invasive or conservative post-lytic management strategy (310), the younger patients assigned to the invasive strategy commonly had insignificant (i.e., <60% diameter stenosis) and single-vessel CAD. Severe 3-vessel or left main coronary disease findings were infrequent (3-vessel incidence, 4%; left main, 0%). Fatal and nonfatal MI and death throughout the first year following study entry was also infrequent. There were no differences in the rates of in-hospital recurrent ischemia, reinfarction, or death among patients assigned to the conservative strategy of selective cardiac angiography and coronary revascularization as compared to an invasive strategy, consisting of routine post-lytic coronary angiography. Compared to younger patients, older patients had a higher prevalence of multivessel CAD (i.e., 44%) and high 42-day rates of reinfarction and death.

In spite of these observations, there was no difference in the 42-day rates of reinfarction or death among the older patient subgroup, regardless of the post-lytic management strategy. The TIMI-II data of younger and older infarct patients are consistent with the overall results of other randomized trials of thrombolysis/PTCA. Confirmatory studies to determine quality-of-life aspects of care in younger patients and to define the potential of other modes of coronary revascularization in older patient groups are not yet available. Based on the current data, with the exception of patients presenting with cardiogenic shock, use of PCI should be determined by clinical need without special consideration of age.

b. PATIENTS WITH PRIOR MI. A prior MI is an independent predictor of death, reinfarction, and need for urgent coronary bypass surgery (311). In thrombolytic trials, 14 to 20% of enrolled patients had a history of prior MI (309). In the TIMI-II study, patients with a history of prior MI had a higher 42-day mortality (8.8% vs. 4.3%; p < 0.001), higher prevalence of multivessel CAD (60% vs. 28%; p < 0.001), and a lower LV ejection fraction (42% vs. 48%; p < 0.001) compared to patients with a first MI (312). Among patients assigned to the conservative post-lytic strategy, those with a prior MI had a significantly higher 42-day mortality compared to patients with a first MI (11.5% vs. 3.5%; p < 0.001), whereas in the invasive strategy, the mortality outcome was essentially the same in the two patient groups. Mortality tended to be lower among patients with a prior MI undergoing the invasive compared to the
conservative strategy, a benefit which persisted up to 1 year following study entry (294).

Based on the above findings and current practice, PCI should be based on clinical need. The presence of prior MI places the patient in a higher risk subset and should be considered in the PCI decision.

Recommendations for Primary PCI for Acute Transmural MI Patients as an Alternative to Thrombolysis (Table 25)

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>As an alternative to thrombolytic therapy in patients with AMI and ST-segment elevation or new or presumed new left bundle branch block who can undergo angioplasty of the infarct artery ≤12 h from the onset of ischemic symptoms or &gt;12 h if symptoms persist, if performed in a timely fashion* by individuals skilled in the procedure† and supported by experienced personnel in an appropriate laboratory environment.‡ (Level of Evidence: A)</td>
<td>As a reperfusion strategy in candidates who have a contraindication to thrombolytic therapy. (Level of Evidence: C)</td>
<td>Elective PCI of a non–infarct-related artery at the time of acute MI. (Level of Evidence: C)</td>
</tr>
</tbody>
</table>
| In patients who are within 36 h of an acute ST elevation/Q-wave or new left bundle branch block MI who develop cardiogenic shock, are <75 years of age and revascularization can be performed within 18 h of the onset of shock by individuals skilled in the procedure† and supported by experienced personnel in an appropriate laboratory environment.‡ (Level of Evidence: A) | | In patients with acute MI who:  

• have received fibrinolytic therapy within 12 h and have no symptoms of myocardial ischemia.  

• are eligible for thrombolytic therapy and are undergoing primary angioplasty by an inexperienced operator.§  

• care beyond 12 h after onset of symptoms and have no evidence of myocardial ischemia. (Level of Evidence: C) |

2. In patients who are within 36 h of an acute ST elevation/Q-wave or new left bundle branch block MI who develop cardiogenic shock, are <75 years of age, and revascularization can be performed within 18 h of the onset of shock by individuals skilled in the procedure† and supported by experienced personnel in an appropriate laboratory environment.‡ (Level of Evidence: A) | |

*Performance standard: balloon inflation within 90 ± 30 min of hospital admission; †Individuals who perform ≥75 PCI procedures per year; ‡Centers that perform >200 PCI procedures per year and have cardiac surgical capability; §Individual who performs <75 PCI procedures per year (193,194).

AMI = acute myocardial infarction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

Recommendations for PCI After Thrombolysis (Table 26)

<table>
<thead>
<tr>
<th>Class I</th>
<th>Class IIa</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Objective evidence for recurrent infarction or ischemia (rescue PCI) (194). (Level of Evidence: B)</td>
<td>1. Cardiogenic shock or hemodynamic instability. (Level of Evidence: B)</td>
<td>1. Recurrent angina without objective evidence of ischemia/infarction. (Level of Evidence: C)</td>
</tr>
</tbody>
</table>
| 2. Angioplasty of the infarct-related artery stenosis within hours to days (48 h) following successful

*Performance standard: balloon inflation within 90 ± 30 min of hospital admission; †Individuals who perform ≥75 PCI procedures per year; ‡Centers that perform >200 PCI procedures per year and have cardiac surgical capability (193,194).
thrombolytic therapy in asymptomatic patients without clinical and/or inducible evidence of ischemia. (Level of Evidence: B)

Class III
1. Routine PCI within 48 h following failed thrombolysis. (Level of Evidence: B)
2. Routine PCI of the infarct-artery stenosis immediately after thrombolytic therapy. (Level of Evidence: A)

Recommendations for PCI During Subsequent Hospital Management After Acute Therapy for AMI Including Primary PCI (Table 27)

Class I
1. Spontaneous or provokable myocardial ischemia during recovery from infarction (194). (Level of Evidence: C)
2. Persistent hemodynamic instability. (Level of Evidence: C)

Class IIa
1. Patients with LV ejection fraction ≤0.4, CHF, or serious ventricular arrhythmias. (Level of Evidence: C)

Class IIb
1. Coronary angiography and angioplasty for an occluded infarct-related artery in an otherwise stable patient to revascularize that artery (open artery hypothesis). (Level of Evidence: C)
2. All patients after a non–Q-wave MI. (Level of Evidence: C)
3. Clinical HF during the acute episode, but subsequent demonstration of preserved LV function (LV ejection fraction >0.4). (Level of Evidence: C)

Class III
1. PCI of the infarct-related artery within 48 to 72 h after thrombolytic therapy without evidence of spontaneous or provokable ischemia. (Level of Evidence: C)

D. Percutaneous Intervention in Patients With Prior Coronary Bypass Surgery

Ischemic symptoms recur in 4 to 8% of patients/year following CABG (313–316). Recurrence of symptoms can be attributed to progression of native vessel coronary disease (5%/year) and bypass conduit occlusion, particularly SVG failure (7% in week 1; 15 to 20% in first year; 1 to 2%/year during the first 5 to 6 years, and 3 to 5%/year in years 6 to 10 postoperatively) (313–315). At 10-years postoperatively,

<table>
<thead>
<tr>
<th>Table 26. Recommendations for PCI After Thrombolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class I</td>
</tr>
<tr>
<td>Objective evidence for recurrent infarction or ischemia (rescue PCI) (194). (Level of Evidence: B)</td>
</tr>
</tbody>
</table>

PCI = percutaneous coronary intervention.
approximately half of all SVG conduits are occluded and only half of the remaining patent grafts are free of significant disease (160,317–327). The requirement for repeat revascularization procedures increases over time from the initial revascularization, particularly in younger patients (328). Although arterial conduits exhibit improved long-term patency (157,329,330), stenosis or occlusion of these grafts can occur. Thus, patients with recurrent ischemic symptoms following CABG may require repeat revascularization due to diverse anatomic problems.

Risk of repeat surgical revascularization is higher (hospital mortality 7 to 10%) than initial CABG (331–333) and both long-term relief of angina and bypass graft patency are lower than that of the first procedure (331,334,335). In addition, patients with prior bypass surgery may have limited graft conduits, impaired LV function, advanced age, and coexisting medical conditions (cerebrovascular disease; renal and pulmonary insufficiency) which may complicate repeat surgical coronary revascularization and prompt consideration for catheter-based intervention. Patients with prior bypass surgery represent an increasing proportion of patients being referred for percutaneous coronary revascularization, and specific indications for therapy may be influenced by both anatomic considerations and the timing of recurrent ischemia postoperatively.

1. Early Ischemia After CABG. Recurrent ischemia early (<30 days) postoperatively usually reflects graft failure, often secondary to thrombosis (336–338), and may occur in both saphenous vein and arterial graft conduits (339). Incomplete revascularization and un bypassed native vessel stenoses or stenoses distal to a bypass graft anastomosis may also precipitate recurrent ischemia. Urgent coronary angiography is indicated to define the anatomic cause of ischemia and to determine the best course of therapy. Emergency PCI of a focal graft stenosis (venous or arterial) or recanalization of an acute graft thrombosis may successfully relieve ischemia in the majority of patients. Balloon dilation across suture lines has been accomplished safely within days of surgery (340–342). Intracoronary thrombolytic therapy should be administered with caution during the first week postoperatively (343–346) and if required, residual thrombus may be “targeted” in low doses through a local drug delivery system. Conversely, mechanical thrombectomy with newer catheter technologies may be effective without the attendant risk of fibrinolysis (347). Adjunctive therapy with abciximab for percutaneous intervention during the first week following bypass surgery has been limited but intuitively may pose less risk for hemorrhage than fibrinolysis. As flow in vein graft conduits is pressure dependent, IABP support should be considered in the context of systemic hypotension and/or severe LV dysfunction. If feasible, PCI of both bypass graft and native vessel offending stenoses should be attempted, particularly if intracoronary stents can be successfully deployed.

When ischemia occurs 1 to 12 months following surgery, the etiology is usually peri–anastomotic graft stenosis. Distal anastomotic stenoses (both arterial and venous) respond well to balloon dilation alone and have a more favorable long-term prognosis than stenoses involving the mid-shaft or proximal vein graft anastomosis (135,136,348–351). Mid-shaft vein graft stenoses occurring during this time frame are usually due to intimal hyperplasia. Restenosis may be less frequent and event-free survival-enhanced following angioplasty of SVGs dilated within 6 months of surgery compared with grafts of older age. The immediate results of PCI in mid-shaft ostial or distal anastomotic vein graft stenoses may be enhanced by coronary stent deployment (351,352). Ablative technologies such as directional atherectomy or excimer laser coronary angioplasty may facilitate angioplasty and stent deployment in patients with aorto-ostial vein graft stenoses (353,354).

Stenoses in the mid-portion or origin of the internal mammary artery graft are uncommon, but respond to balloon dilation (355,356) with stent deployment as feasible. Long-term follow-up of patients after internal mammary artery angioplasty has demonstrated sustained benefit and relief of ischemia in the majority of patients (357,358). Balloon angioplasty with or without stent deployment can be successfully performed in patients with distal anastomotic stenoses involving the gastroepiploic artery bypass graft and in patients with free radial artery bypass grafts as well (359). Percutaneous intervention has also been effective in relieving ischemia for patients with the stenosis of the subclavian artery proximal to the origin of a patent left internal mammary artery bypass graft (360,361).

2. Late Ischemia After CABG. Ischemia occurring more than 1 year postoperatively usually reflects the development of new stenoses in graft conduits and/or native vessels that may be amenable to PCI (362). At 3 years or more following SVG implantation, atherosclerotic plaque is frequently evident and is often progressive. These lesions may be friable and often have associated thrombus formation, which may contribute to the occurrence of slow flow, distal embolization, and periprocedural MI following attempted percutaneous intervention (363). Slow flow occurs more frequently in grafts having diffuse atherosclerotic involvement, angiographically demonstrable thrombus, irregular or ulcerative lesion surfaces, and with long lesions having large plaque volume (364,365). Although a reduced incidence of distal embolization has been reported following the use of the extraction atherectomy catheter to recanalize stenoses in older vein graft conduits (366–370), embolization may still complicate adjunctive balloon dilation. Slow-flow with signs and symptoms of myocardial ischemia may be ameliorated by the intragraft administration of verapamil or diltiazem (364,371). The adjunctive administration of abciximab during vein graft intervention may reduce the incidence of distal embolization and non–Q-wave MI (372), but controversy remains regarding the benefit of prophylactic abciximab therapy in patients with prior coronary bypass surgery undergoing percutaneous intervention.

Although postprocedural minimum lumen diameter is larger following directional coronary atherectomy (140,373,374) or stent deployment (139,141,142,375–381)
compared with balloon angioplasty of SVG stenoses, long-term prognosis remains guarded, and late recurrent ischemic events may be due to both restenosis of the target lesion and diffuse vein graft disease (382–384). Final patency after PTCA is greater for distal SVG lesions than for ostial or mid-SVG lesions (349), and stenosis location appears to be a better determinant of final patency than graft age or the type of interventional device used.

Percutaneous intervention for chronic vein graft occlusion has been problematic. Balloon angioplasty alone has been associated with high complication rates and low rates of sustained patency (385). Although prolonged intra-graft infusion of fibrinolytic therapy was reported to successfully recanalize 69% of a selected group of patients with chronic SVG occlusion <6 months duration, long-term patency rates with or without adjunctive stent deployment were low (386–388). In addition, prolonged fibrinolytic therapy has been associated with thromboembolic MI (389–392), intracranial (393) and intramyocardial hemorrhage (394), as well as vascular access site complications. Favorable results have been obtained with both local “targeted” and more prolonged infusion of fibrinolytic agents for nonocclusive intragraft thrombus (395,396). Thrombolytic catheter-based systems appear to successfully treat SVG thrombosis as well as or better than thrombolytic agents (397).

3. Early and Late Outcomes of Percutaneous Intervention. Prior to the general availability of coronary stenting, overall angioplasty procedural success rates exceeded 90%, and adverse outcomes of emergency repeat coronary bypass surgery (2.3%) and death (0.8%) were infrequent as reported in combined series of over 2,000 patients with prior bypass surgery undergoing percutaneous intervention (135,398–410). These results are comparable to those achieved in patients without prior bypass surgery, an observation confirmed by NHLBI registry data (6). The most common complications observed in this population are NSTEMI and atheroembolism, particularly following SVG intervention (333,352).

Patients with prior bypass surgery who undergo successful PCI have a long-term outcome that is dependent on patient age, the degree of LV dysfunction, and the presence of multivessel coronary atherosclerosis. The best long-term results are observed after recanalization of distal anastomotic stenoses occurring within 1 year of operation. Angioplasty of distal anastomotic stenoses involving internal mammary artery grafts have been associated with similar, favorable long-term patency rates (357,358). Conversely, event-free survival is less favorable following angioplasty of totally occluded SVGs, ostial vein graft stenoses, or grafts with diffuse or multicentric disease (382,383,385). Coexistent multisystem disease, the presence of which may have prompted the choice of a percutaneous revascularization strategy, may also influence long-term outcomes in this population.

4. Surgery Versus Percutaneous Reintervention. Aged, diffuse, friable, and degenerative SVG disease in the absence of a patent arterial conduit to the left anterior descending artery represents a prime consideration for repeat surgical revascularization. In contrast, the presence of a patent arterial conduit to the left anterior descending artery may militate for a percutaneous interventional approach (411). The overall risk of repeat operation, especially the presence of comorbidities such as concomitant cerebrovascular, renal, or pulmonary disease and the potential for jeopardizing patent, nondiseased bypass conduits must be carefully considered. Isolated, friable stenoses in vein grafts may be approached with primary stenting or the combination of extraction atherectomy and stenting in an attempt to reduce the likelihood of distal embolization.

Another therapeutic option for patients with prior coronary bypass surgery that has become available is grafting using the internal mammary artery through a “minimally invasive” surgical approach (158,412–416). This strategy, which avoids both the risk of cardiopulmonary bypass (stroke, coagulopathy) and repeat median sternotomy may be particularly applicable to patients with chronic native vessel left anterior descending coronary occlusion and friable atherosclerotic disease involving a prior SVG to this vessel. The role of combining a minimally invasive surgical approach with PCI requires further study (417,418).

In general, patients with multivessel disease, failure of multiple SVGs, and moderately impaired LV function derive the greatest benefit from the durability provided by surgical revascularization with arterial conduits. Regardless of repeat revascularization strategy, risk-factor modification with cessation of smoking (419,420) and lipid lowering therapy (421,422) should be implemented in patients with prior CABG surgery. An aggressive lipid-lowering strategy that targets a low-density lipoprotein level of <90 mg/dl can be effective in reducing recurrent ischemic events and the need for subsequent revascularization procedures (422).

Recommendations for PCI With Prior CABG (Table 28)

Class I
1. Patients with early ischemia (usually within 30 days) after CABG (194). (Level of Evidence: B)

Class IIa
1. Patients with ischemia occurring 1 to 3 years postoperatively and preserved LV function with discrete lesions in graft conduits. (Level of Evidence: B)
2. Disabling angina secondary to new disease in a native coronary circulation. (If angina is not typical, the objective evidence of ischemia should be obtained.) (Level of Evidence: B)
3. Patients with diseased vein grafts >3 years following CABG. (Level of Evidence: B)

Class III
1. PCI to chronic total vein graft occlusions. (Level of Evidence: B)
2. Patients with multivessel disease, failure or multiple SVGs, and impaired LV function. (Level of Evidence: B)

E. Use of Adjunctive Technology (Intracoronary Ultrasound Imaging, Flow Velocity, and Pressure)

The limitations of coronary angiography for diagnostic and interventional procedures can be reduced by employing adjunctive technology of intracoronary ultrasound imaging, flow velocity, and pressure. Information obtained from the adjunctive modalities of intravascular imaging and physiology can improve PCI methods and outcomes.

1. IVUS. IVUS imaging provides a tomographic 360° sagittal scan of the vessel from the lumen through the media to the vessel wall. Intravascular ultrasound measurements of arterial dimensions (minimal and maximal diameters, cross-sectional area, and plaque area) complement and enhance angiographic information. Intravascular ultrasound has been used to refine device selection through plaque characterization (e.g., calcified) and artery sizing. Intravascular ultrasound has contributed to the understanding of mechanisms of coronary angioplasty and specifically, to the advancement of coronary stenting without long-term anticoagulation (423–428). In a large observational study, IVUS-guided angioplasty resulted in a decreased final residual plaque area from 51 to 34%, despite a final angiographic percent stenosis of 0% (423). Intravascular ultrasound-facilitated stent deployment was associated with a subacute thrombosis rate of 0.3% without systemic anticoagulation, although antiplatelet agents are still required for stenting (423). In the placement of coronary stents, because radiographic contrast material can be located between stent struts and the vascular wall, an angiographic appearance of a large lumen may exist when the stent has not been fully deployed. Intravascular ultrasound documents full apposition of stent struts to the vessel wall (423).

IVUS is not necessary for all stent procedures. The results of the French Stent Registry study of 2,900 patients treated without coumadin and without IVUS reported a subacute closure rate of 1.8% (429). In the STARS trial (30), a subacute closure rate of 0.6% in patients having optimal stent implantation supports the approach that IVUS does not appear to be required routinely in all stent implantations. However, the use of IVUS for evaluating results in high-risk procedures (i.e., those patients with multiple stents, impaired TIMI grade flow or coronary flow reserve, and marginal angiographic appearance) appears warranted.

The long-term outcomes in patients with previously implanted stents using the MUSIC trial (430) evaluating optimal stent expansion (defined as complete apposition of the stent over its length) with symmetrical expansion (defined as a luminal diameter, minimum to luminal diameter, maximum > 0.7) and minimal luminal area (compared to > 80% of the reference area) the subacute closure rate was 1.3% with monotherapy of aspirin. The angiographic restenosis was < 10% when stent cross-sectional areas were > 9.0 mm².

Fitzgerald et al. report that the degree of stent expansion as measured by IVUS directly correlates to the clinical outcomes in the CRUISE study (431). This multicenter study compared 270 patients with IVUS-guided stent implantation to IVUS-documented, but not guided, stent implantation in 229 patients. At 9-month follow-up, there was no difference in death or MI rate, but the target lesion revascularization rate was substantially lower in the IVUS-guided group (8.5% vs. 15.3%; p = 0.019). These data suggest that ultrasound guidance of stent implantation may result in more effective stent expansion compared with angiographic guidance alone and subsequently reduced the need for late target lesion revascularization.

In the context of published data and growing clinical experience, the Writing Committee has modified prior recommendations for the use of IVUS as follows.

Recommendations for Coronary Intravascular Ultrasound (Table 29)

Class Ia

1. Assessment of the adequacy of deployment of coronary stents, including the extent of stent appos-
Table 29. Recommendations for Coronary Intravascular Ultrasound (IVUS)

<table>
<thead>
<tr>
<th>Class IIa</th>
<th>Class IIb</th>
<th>Class III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessment of the adequacy of deployment of coronary stents, including the extent of stent apposition and determination of the minimum luminal diameter within the stent. <em>(Level of Evidence: B)</em></td>
<td>Determine extent of atherosclerosis in patients with characteristic anginal symptoms and a positive functional study with no focal stenoses or mild CAD on angiography. <em>(Level of Evidence: C)</em></td>
<td>When angiographic diagnosis is clear and no interventional treatment is planned. <em>(Level of Evidence: C)</em></td>
</tr>
<tr>
<td>Determination of the mechanism of stent restenosis (inadequate expansion vs. neointimal proliferation) and to enable selection of appropriate therapy (plaque ablation vs. repeat balloon expansion). <em>(Level of Evidence: B)</em></td>
<td>Preinterventional assessment of lesion characteristics and vessel dimensions as a means to select an optimal revascularization device. <em>(Level of Evidence: C)</em></td>
<td></td>
</tr>
<tr>
<td>Evaluation of coronary obstruction at a location difficult to image by angiography in a patient with a suspected flow-limiting stenosis. <em>(Level of Evidence: C)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Assessment of a suboptimal angiographic result following PCI. <em>(Level of Evidence: C)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis and management of coronary disease following cardiac transplantation. <em>(Level of Evidence: C)</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Establish presence and distribution of coronary calcium in patients for whom adjunctive rotational atherectomy is contemplated. <em>(Level of Evidence: C)</em></td>
<td></td>
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</tr>
<tr>
<td>Determination of plaque location and circumferential distribution for guidance of directional coronary atherectomy. <em>(Level of Evidence: B)</em></td>
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</table>

CAD = coronary artery disease; PCI = percutaneous coronary intervention.

1. Determine extent of atherosclerosis in patients with characteristic anginal symptoms and a positive functional study with no focal stenoses or mild CAD on angiography. *(Level of Evidence: C)*

2. Preinterventional assessment of lesion characteristics and vessel dimensions as a means to select an optimal revascularization device. *(Level of Evidence: C)*

Class III

1. When angiographic diagnosis is clear and no interventional treatment is planned. *(Level of Evidence: C)*

2. Coronary Flow Velocity and Coronary Vasodilatory Reserve. Coronary physiologic information has assumed increasing importance in determining which coronary lesions may merit intervention and achieve an end point of balloon angioplasty in consideration of provisional stenting. Coronary flow velocity reserve (CVR), the ratio of hyperemic to basal flow, reflects flow resistance through the epicardial artery and the corresponding myocardial bed.
CVR <2.0 is reproducibly and positively correlated to abnormal stress perfusion imaging (432–434). In some cases, the uncertainty as to whether the impaired flow reserve is due to the target stenosis or to abnormal microcirculation may be reduced using a relative coronary flow velocity reserve (rCVR; CVRtarget/CVRreference). From preliminary studies, rCVR values >0.8 are similar in prognostic value to negative stress testing (435). Recent confirmation of the more lesion–specific nature of physiologic indices resides in the correlation between rCVR and pressure-derived fractional flow reserve (FFR) of the myocardium by guidewire pressure measurements (vide infra) (435,436).

For lesion assessment, a normal CVR indicates a nonphysiologically significant stenosis. An abnormal CVR indicates that the stenosis in the epicardial artery is significant when the microcirculation is normal, confirmed by measuring rCVR. Several studies report that deferring PCI of non–flow-limiting lesions is safe, with <10% rate of lesion progression (437–439).

### 3. Coronary Artery Pressure and Fractional Flow Reserve

Historically, translesional pressure gradients were used as end points for early interventional cardiology procedures. The use of a translesional pressure gradient measured at rest was abandoned because of weak correlations to stress testing and difficult technique. Pijls et al. (440) introduced the concept of the fractional flow reserve (FFR) of the myocardium, the ratio of distal coronary pressure to aortic pressure measured during maximal hyperemia, which represents the fraction of normal blood flow through the stenotic artery (436,441). The coronary pressure measuring technique is relatively simple, especially using pressure guidewires, a method superior to small catheters. The normal FFR value for all vessels under all hemodynamic conditions, regardless of the status of microcirculation is 1.0. FFR values <0.75 are associated with abnormal stress tests (438). Unlike CVR, the FFR is relatively independent of hemodynamics and microcirculatory disturbances. FFR does not use measurements in a reference vessel and is thought to be epicardial lesion–specific. FFR provides no information on the microcirculation nor on the absolute magnitude of the change in coronary flow.

Reports indicate that a physiologic assessment can determine whether balloon angioplasty alone has achieved a satisfactory result with 6-month outcome equivalent to that reported with elective stenting. The DEBATE trial (442) in 224 patients found that when a final diameter stenosis <35% and an excellent physiologic result (CVR >2.5) were obtained after balloon angioplasty (44/224 patients), the intermediate-term (6 months) target lesion revascularization and angiographic restenosis rates were 16%. Similar data have been reported for FFR (439). The application of coronary physiologic adjunctive modalities can facilitate decision–making for moderate lesions, the appropriateness of balloon angioplasty, and the use of provisional stenting.

### Recommendations for Intracoronary Physiologic Measurements (Doppler Ultrasound, FFR) (Table 30)

#### Class IIa

1. Assessment of the physiological effects of intermediate coronary stenoses (30 to 70% luminal narrowing) in patients with anginal symptoms. Coronary pressure or Doppler velocimetry may also be useful as an alternative to performing noninvasive functional testing (e.g., when the functional study is absent or ambiguous) to determine whether an intervention is warranted. (Level of Evidence: B)

#### Class IIb

1. Evaluation of the success of percutaneous coronary revascularization in restoring flow reserve and to predict the risk of restenosis. (Level of Evidence: C)

#### Class III

1. Routine assessment of the severity of angiographic disease in patients with a positive, unequivocal noninvasive functional study. (Level of Evidence: C)
VI. MANAGEMENT OF PATIENTS UNDERGOING PCI

A. Experience With New Technologies

The introduction of coronary stents and atherectomy devices has broadened the scope of patients that can be approached by PCI beyond those that could be safely treated by PTCA alone. Directional coronary atherectomy successfully treats eccentric, ostial and proximal left anterior descending lesions or bifurcation lesions (443). Rotational atherectomy successfully treats calcific and diffusely diseased coronary vessels (444) and ostial stenoses (445,446). Excimer laser can be used successfully to treat diffuse diseases and fibrotic coronary stenoses (447). All atherectomy devices successfully remove or “debulk” plaque, allowing for improved acute angiographic results when followed by balloon angioplasty or stenting (448). Whether debulking before stenting reduces restenosis is currently under investigation.

Stenting has been successful in the initial treatment of SVGs previously not suitable for balloon angioplasty (139). For total occlusions, excimer laser has not been shown to be significantly better than balloon angioplasty in terms of acute success or late outcomes (449).

1. Acute Results. Historically, one of the important limitations of balloon angioplasty has been its high rate of abrupt closure (4 to 7%) and less than optimal acute angiographic result (30% residual diameter stenosis with frequent evidence of dissections). Significant reduction in the acute complication rate for PTCA has resulted from the adjunctive use of glycoprotein receptor IIb/IIIa blockers, which have been shown to reduce abrupt closure and periprocedural MI rates compared to placebo. Improved acute outcomes (in terms of abrupt closure rates and reduced target lesion residual diameter stenosis) have also been seen with the use of coronary stents, DCA, and adjunctive rotational atherectomy (31,32,34,450).

2. Late-Term Results. PCI devices offer the possibility of lower restenosis compared to PTCA in the native coronary circulation. Lower restenosis rates have been demonstrated for balloon-expandable slotted tubular stents in large (≥3 mm) native coronary arteries (31,32) but are variable depending on lesion length for SVG lesions (139). Initial trials of DCA showed no benefit compared to balloon angioplasty for elective single lesion treatment (58,59). However, a trial using DCA in a more aggressive fashion to produce larger acute coronary lumens was associated with a lower angiographic restenosis rate, but did not show any significant improvement in clinical outcomes (34).

Despite the improvement in acute results seen for rotational atherectomy and excimer laser, there is no evidence that these devices improve the late outcomes in lesions than can be feasibly treated by balloon angioplasty or stenting alone (450–452).

B. Antiplatelet and Antithrombotic Therapies and Coronary Angioplasty (Table 31)

1. Aspirin, Ticlopidine, Clopidogrel. Aspirin reduces the frequency of ischemic complications after coronary angioplasty. Although the minimum effective aspirin dosage in the setting of coronary angioplasty has not been established, an empiric dose of aspirin, 80 to 325 mg, given at least 2 h before the PCI procedure is generally recommended (453). While other antiplatelet agents have similar antiplatelet effects to aspirin (454), only the thienopyridine derivatives (455) ticlopidine and clopidogrel have been routinely used as alternative antiplatelet agents in aspirin-sensitive patients during coronary angioplasty. In elective settings, ideally ticlopidine and clopidogrel should be given for at least 72 h prior to the procedure in order to achieve maximum platelet inhibition (456,457).

Prior to the advent of potent combination antiplatelet therapy in recent years, enthusiasm for stenting during acute MI or unstable angina use was tempered by the sudden, and
often unpredictable, occurrence of subacute stent thrombosis, which developed in 3.5 to 8.6% of stent-treated patients (25,31,32,458). Anatomic factors (e.g., underdilation of the stent, proximal and distal dissections, poor inflow or outflow obstruction, <3 mm vessel diameter) were felt to predispose to the occurrence of subacute stent thrombosis in some patients (423,459,460).

Several randomized trials have evaluated the efficacy of combination antplatelet therapy in patients undergoing urgent and elective stent implantation. In the ISAR trial of 517 patients treated with Palmaz-Schatz (PS) stents for acute MI, suboptimal angioplasty, or other “high-risk” clinical and anatomic features, patients were randomly assigned to treatment with aspirin + ticlopidine or aspirin, intravenous heparin, and phenprocoumon after successful stent placement (461). The primary end point of cardiac death, MI, coronary bypass surgery, or repeat angioplasty occurred in 1.5% of patients assigned to antplatelet therapy and 6.2% of those assigned to anticoagulant therapy (relative risk, 0.25; 95% confidence interval, 0.06 to 0.77) (461). In another randomized trial of antplatelet (aspirin + ticlopidine) versus anticoagulant (aspirin + warfarin) therapy in high-risk patients (suboptimal or multiple stent deployment), antplatelet therapy was again associated with a reduction in the composite occurrence of death, MI, and urgent repeat revascularization (5.6% vs. 11%; p = 0.07) and in major bleeding or vascular complications (1.7% vs. 6.9%) compared with anticoagulation therapy respectively (462).

In the STARS trial (30), the efficacy of aspirin (325 mg daily), the combination of aspirin (325 mg daily) + ticlopidine (500 mg daily for 1 month), and aspirin (325 mg daily) + warfarin on ischemic end points at 30 days in 1,653 “low-risk” patients after “optimal” PS stent placement demonstrated more adverse events in patients not receiving ticlopidine as part of the therapeutic regimen. The primary 30-day composite end point of death, target lesion revascularization, subacute thrombosis, or MI was 3.6% in patients only assigned to aspirin, 2.7% assigned to aspirin + warfarin, compared to 0.5% in those assigned to aspirin + ticlopidine (aspirin + ticlopidine vs. aspirin alone; p < 0.001; aspirin + ticlopidine vs. aspirin + warfarin; p = 0.014) (30). Pretreatment with ticlopidine for more than 24 h may allow more effective inhibition of platelet activation than shorter durations of therapy (456,463).

Ticlopidine has a number of important side effects, including gastrointestinal distress (20%) (464), cutaneous rashes (4.8 to 15%) (464), and abnormal liver function tests (464). The most severe side effect is severe neutropenia, occurring in approximately 1% of patients (464,465). Ticlopidine-induced neutropenia is generally reversible after its discontinuation (466), although infrequent episodes of sepsis and death have been reported. Rare (<1:1,000), but fatal, episodes of thrombotic thrombocytopenic purpura have also been reported (467–469), and patients receiving ticlopidine should be monitored for the occurrence of this untoward sequelae. Shorter durations (10 to 14 days) of ticlopidine therapy may reduce untoward side effects of therapy while maintaining therapeutic efficacy (470,471).

Clopidogrel, 300 mg loading dose followed by 75 mg daily, may be used as an alternative to ticlopidine in patients undergoing stent placement. A number of nonrandomized trials (472–474) and a randomized trial (475) have failed to show a difference in the clinical outcomes among patients treated with ticlopidine and clopidogrel after stent placement. A small number of cases of thrombocytopenia purpura have been reported in patients treated with clopidogrel; therefore, patients should be monitored during treatment for occurrence of this untoward effect (469). The routine use of warfarin is no longer recommended after stent implantation, unless there are other indications for its use, such as a poor LV function, atrial fibrillation, or mechanical heart valves.

### 2. Glycoprotein IIb/IIIa Inhibitors

Aspirin is only a partial inhibitor of platelet aggregation (476,477), as it affects only cyclooxygenase, thereby preventing the formation of thromboxane A2. Functionally active glycoprotein (GP IIb/IIIa) receptors aggregate platelets through fibrin bound at the receptor sites. These receptors are activated by a variety of agonists, including thromboxane A2, serotonin, ADP, and collagen, among others. The binding of fibrinogen and other adhesive proteins to adjacent platelets by means of the GP IIb/IIIa receptor serves as the “final common pathway” of platelet–thrombus formation and can be effectively attenuated by GP IIb/IIIa antagonists. These agents have reduced the frequency of ischemic complications after coronary angioplasty.

#### a. ABCIXIMAB

The clinical safety and efficacy of abciximab was evaluated in the Evaluation of 7E3 for the Prevention of Ischemic Complications (EPIC) Trial, which included 2,099 patients with acute MI, refractory unstable angina, or “high-risk” clinical or anatomic features (478). Patients were randomly assigned to treatment with aspirin and fixed-dose heparin alone, aspirin, fixed-dose heparin, and a bolus of abciximab (0.25 mg/kg), or aspirin, fixed dose heparin, and a bolus of abciximab (0.25 mg/kg) + a 12-h abciximab infusion (10 μg/min). A 35% reduction in the frequency of the primary composite end point of death, nonfatal MI, repeat revascularization, and procedural failure resulting in stent or IABP placement was found in the patients given both the bolus + infusion abciximab compared with placebo-treated patients; (8.3% vs. 12.8%, p = 0.008) (478). The bolus of abciximab alone did not produce a significant reduction in ischemic events. The major effect of abciximab was a reduction in nonfatal MI (5.2% vs. 8.6% in placebo-treated patients; p = 0.013) and in the need for repeat coronary angioplasty (0.8% vs. 4.5% in placebo-treated patients; p < 0.001); these benefits were maintained for at least 3 years following the procedure (479). It should be noted that the reduction in ischemic complications in EPIC was offset by a doubling of the bleeding complication rate.
associated with non–weight-adjusted heparin use (14% vs. 7% in placebo–treated patients; p = 0.001), likely due to the fixed–dose heparin regimen used for the procedure.

The value of abciximab in patients undergoing primary angioplasty for acute MI was prospectively evaluated in a trial of 483 patients who were randomly assigned to therapy with abciximab or placebo (480). The 30-day composite end point of death, reinfarction, or urgent revascularization was reduced in patients treated with abciximab (5.8% vs. 11.2% in placebo–treated patients; p = 0.03), mostly due to a reduction in the need for urgent revascularization in patients treated with abciximab (1.8% vs. 5.6% in placebo–treated patients; p = 0.03) (480). There was also a reduction in the need for a “bailout” stent with abciximab (11.9% vs. 20.4% in placebo–treated patients; p = 0.03) (480).

The strategy of low-dose heparin and early sheath removal in conjunction with abciximab therapy in relatively “low-risk” patients undergoing coronary angioplasty was evaluated in the EPITAPLOG Trial (27). In this study, 2,792 patients were randomly assigned to therapy with aspirin plus standard–dose weight–adjusted heparin and abciximab, or aspirin plus low-dose weight–adjusted heparin and abciximab, or aspirin plus standard–dose weight–adjusted heparin alone (27). The 30–day major event rate was 11.7% in the placebo with standard-dose heparin group; 5.2% in the abciximab with low-dose heparin group; 6.9% in placebo plus placebo group, 6.9% in the angioplasty plus abciximab group (p = 0.007), and 5.1% in the stent plus abciximab group (p < 0.001) (28). By 6 months, rates of repeat target–vessel revascularization were 10.6% in the stent plus placebo, 8.7% in the stent plus abciximab group (p = 0.22), and 15.4% in the angioplasty plus abciximab group (p = 0.005) (89). In the predefined subgroup of patients with diabetes mellitus undergoing stenting, treatment with abciximab diminished rates of repeat target–vessel revascularization by 51% compared with placebo (8.1% vs. 16.6%, p = 0.021). Angiographic results among diabetics enrolled in an angiographic substudy were concordant with the clinical outcome: minimal luminal diameters (MLDs) and net gain at 6–months follow–up were improved by abciximab with stenting compared with stenting alone. EPITAPLOG 1–year follow–up demonstrated a survival advantage in favor of abciximab in stented patients. Mortality at 1 year was 2.4% in stent and placebo patients and 1.0% in stent and abciximab patients (p = 0.037) (482).

Heeschen et al. (483), for the CAPTURE investigators, demonstrated that troponin–T but not C–reactive protein, was predictive of cardiac risk during the initial 72–h period when treating unstable angina patients with standard therapy or with abciximab. C–reactive protein was an independent predictor of both cardiac risk and repeated coronary revascularization during the 6–month follow–up. In a similar study, Hamm et al. (484), for the CAPTURE investigators, also reported that among the 1,265 patients with unstable angina enrolled in the CAPTURE trial, troponin–T and CK–MB from 890 patients correlated with subsequent 6–month adverse cardiac risk. In patients without elevated troponin–T levels, there was no benefit of treatment with respect to the relative risk of death or MI at 6 months (odds ratio 1.26, CI 95%, 0.74 to 2.31; p = 0.47). This study indicated that serum troponin–T level, which is considered to be a surrogate marker for thrombus formation, identified a high–risk subgroup of patients with refractory unstable angina suitable for coronary intervention who would particularly benefit from antiplatelet treatment with abciximab.

Patients requiring unplanned or “bailout” coronary stent deployment appear to be at especially high risk for the development of ischemic events early following stent deployment. In patients who required unplanned stent deployment in the EPITAPLOG trial, the prophylactic administration of abciximab was associated with a reduction in the composite end point of death, MI, or urgent revascularization at 30 days (p < 0.001) and 6 months (p < 0.001) (481). A subsequent analysis of 529 patients having unplanned coronary stent deployment in the EPITAPLOG, EPIC, and CAPTURE trials demonstrated a reduction in mortality at 30 days (p = 0.04) (481) in addition to reduction in the composite end point of death, MI, or urgent intervention at 30 days (p < 0.001) at 6 months (p = 0.002), in patients who had received prophylactic therapy with abciximab. These data suggest that prophylactic adjunctive platelet GP IIb/IIIa blockade improves the clinical outcomes of patients who require unplanned coronary stent deployment.

One putative limitation of abciximab is the potential for immune–mediated hypersensitivity reactions following subsequent readministration. With the first administration, human antichimeric antibodies (HACA) form in approximately 6% of patients (478). The implications of HACA, however, are unclear. Among 500 patients enrolled in the ReoPro Readministration Registry (R2), there were no cases of anaphylaxis or other allergic manifestations whether or not HACA was present, and HACA was not predictive of...
any other measure of complication or success. From the R3 Study, HACA has been shown to be an IgG (not IgE) immunoglobulin that does not neutralize abciximab. The more worrisome clinical phenomenon associated with readmission is the potential for increased rates of thrombocytopenia. In the 500-patient Registry, a 4.4% incidence in thrombocytopenia (to a platelet count of < 100 \times 10^9/L) was observed, with half of the patients developing acute profound thrombocytopenia (to a platelet count of < 20 \times 10^9/L). This potential complication should always be monitored when treating a patient with abciximab (485–488).

b. EPTIFIBATIDE. The clinical utility of eptifibatide, a short-acting cyclic heptapeptide that also inhibits the GP IIb/IIIa receptor, was evaluated in the Integrilin to Manage Platelet Aggregation to prevent Coronary Thrombosis-II (IMPACT-II) trial, a double-blind, randomized, placebo-controlled multicenter trial that enrolled 4,010 patients undergoing coronary angioplasty (489). Patients were assigned to treatment with aspirin, heparin and placebo, aspirin, heparin and eptifibatide bolus (135 μg/kg) followed by a low-dose eptifibatide infusion (0.5 μg/kg per min for 20 to 24 h), or aspirin, heparin, and eptifibatide bolus (135 μg/kg) and higher dose infusion (0.75 μg/kg per min for 20 to 24 h) (489). The 30-day composite primary end point of death, MI, unplanned surgical or repeat percutaneous revascularization, or coronary stent implantation for abrupt closure occurred in 11.4% of placebo-treated patients (490). The clinical effect of tirofiban during coronary angioplasty was evaluated in the Randomized Efficacy Study of Tirofiban for Outcomes and Restenosis (RESTORE) Trial, a double-blind, placebo-controlled trial of 2,139 patients with unstable angina pectoris or acute MI (494). Patients were randomly assigned to aspirin, heparin and a tirofiban bolus (10 μg/kg over 3 min) + infusion (0.15 μg/kg per min), or to aspirin, heparin, and a placebo bolus + infusion for 36 h. The primary end point of the trial was the occurrence of major 30-day events, including death from any cause, MI, coronary bypass surgery due to angioplasty failure or recurrent ischemia, repeat target-vessel angioplasty for recurrent ischemia, or insertion of a stent due to threatened abrupt closure (494). The primary 30-day end point was reduced from 12.2% in the placebo group to 10.3% in the tirofiban group (p = 0.160). Patients treated with tirofiban had a 38% relative reduction in the composite end point at 48 h (p < 0.005), and a 27% relative reduction at 7 days (p = 0.022). The incidence of major bleeding was similar in the two groups using the Thrombolysis In Myocardial Infarction (TIMI) criteria (2.4% in tirofiban-treated patients and 2.1% in the placebo-treated patients; p = 0.662) (494), although major bleeding tended to be higher in tirofiban-treated patients (5.3% vs. 3.7% in the placebo-treated patients; p = 0.096). Thrombocytopenia was similar in both groups (0.9% for the placebo group vs. 1.1% for the tirofiban group; p = 0.709) (494). A larger clinical benefit with tirofiban was seen in patients with unstable angina undergoing coronary angioplasty in the PRISM-PLUS Study, a randomized trial of 1,570 patients with unstable angina or non–Q-wave MI assigned to 48 to 108-h treatment with heparin + tirofiban or heparin alone (495). Coronary angioplasty was performed in 30.5% of patients between 49 to 96 h after randomization (495). The composite end point of death, MI, or refractory ischemia was significantly reduced in the heparin + tirofiban group or compared to the heparin alone group (10.0% vs. 15.7%; p < 0.01) (495). Based on the numerous trials to date (Fig. 4), intravenous open-label GP IIb/IIIa inhibitor therapy was reduced 37% from 10.5 to 6.6% (p = 0.0015). There was a consistent treatment benefit across all components of the end point as well as across all subgroups of patients. At 30 days, the key secondary composite end point of death, MI, and urgent large-vessel revascularization was also improved 35% from 10.4 to 6.8% (p = 0.0034) (491,492).
apy in conjunction with stent deployment had a 51% reduction in target-vessel revascularization at 6 months (133,496). This trial is the only one that has shown a reduction in target-vessel revascularization in the diabetic group. It will be important to determine if supporting evidence is found from other trials using this agent and other GP IIb/IIIa antagonists.

3. Heparin. Intravenous unfractionated heparin prevents clot formation at the site of arterial injury (498) and on coronary guidewires and catheters used for coronary angioplasty (499). While the intensity of anticoagulation with unfractionated heparin is generally determined using activated partial thromboplastin times (aPTTs), these values are less useful for monitoring anticoagulation during coronary angioplasty because higher levels of anticoagulation are needed than can be discriminated with the aPTT alone. Instead, the activated clotting time (ACT) has been more useful to follow heparin therapy during coronary angioplasty (500). The Hemochron and HemoTec devices are commonly used to measure ACT values during coronary angioplasty (500–502). The Hemochron ACT generally exceeds the HemoTec ACT by 30 to 50 s, although considerable measurement variability exists.

Empiric recommendations regarding heparin dosage during coronary angioplasty have been proposed (503,504), but ACT levels after a fixed dose of unfractionated heparin may vary substantially due to differences in body size (505), concomitant use of other medications, including intravenous nitroglycerin (506,507), and in the presence of acute coronary syndromes that increase heparin resistance.

The relationship between the level of the ACT and the risk of ischemic events (508,509), others found either no relationship or a direct relationship between the degree of anticoagulation and occurrence of complications (510). It is generally felt that very high levels (ACTs >400 to 600 s) of periprocedural anticoagulation are associated with an increased risk for bleeding complications (511).

The safety of low-dose heparin during coronary angioplasty has also been shown in a recent study. Fatal complications (0.3%), emergency bypass surgery (1.7%), MI (3.3%), or repeat angioplasty within 48 h (0.7%) were uncommon after an empiric bolus of heparin 5,000 U at the beginning of the procedure (512). In a smaller randomized study of 400 patients assigned to fixed-dose heparin (15,000 IU) or weight-adjusted heparin (100 IU/kg), there were no differences in procedural success or bleeding complications between the two groups (513), although use of the weight-adjusted heparin resulted in earlier sheath removal and more rapid transfer to a stepdown unit (513). Another advantage of weight-adjusted heparin dosing is that “overshooting” the ACT value can be avoided.

The results of these limited studies suggests that heparin is an important component for PCI, despite dosing uncertainties and an unpredictable therapeutic response with the unfractionated preparation. Higher levels of anticoagulation with heparin are roughly correlated with therapeutic efficacy in the reduction of complications during coronary angioplasty, albeit at the expense of bleeding complications at very high levels of heparin dosing. It appears that weight-adjusted heparin dosing may provide a clinically superior anticoagulation method over fixed heparin dosing, although definitive studies are lacking.

Routine use of unfractionated heparin after an uncomplicated coronary angioplasty is no longer recommended.
(53,514–517), and may be associated with more frequent bleeding events (53,514), particularly when platelet GP IIb/IIIa inhibitors are used (53,514). Subcutaneous administration of unfractionated heparin (515) may provide a safer and less costly means of extending antithrombin therapy than intravenous unfractionated heparin, if there are clinical reasons to continue anticoagulation, such as residual thrombus or significant residual dissections.

Some patients with unstable angina are treated with low-molecular-weight heparin (LMWH) prior to coronary angioplasty (518). Anticoagulation monitoring is not routinely possible with LMWH, and conventional dosages of unfractionated heparin are currently recommended. Conventional ACT monitoring methods may underestimate the true degree of periprocedural anticoagulation with LMWH. Use of LMWH as the sole anticoagulant during PCI is not supported at this time in the absence of absolute or relative contraindications to unfractionated heparin, although data from clinical trials of these agents administered alone or in conjunction with GP IIb/IIIa blockade are forthcoming.

**a. HEPARIN DOSING GUIDELINES.** In those patients who do not receive GP IIb/IIIa inhibitors, sufficient unfractionated heparin should be given during coronary angioplasty to achieve an ACT of 250 to 300 s with the HemoTec device and 300 to 350 s (491,492) with the Hemochron device. Weight-adjusted bolus heparin (70 to 100 IU/kg) can be used to avoid excess anticoagulation. If the target values for ACT are not achieved after a bolus of heparin, additional heparin boluses (2,000 to 5,000 IU) can be given. Early sheath removal should be performed when the ACT falls to <150 to 180 s.

The unfractionated heparin bolus should be reduced to 50 to 70 IU/kg when GP IIb/IIIa inhibitors are given in order to achieve a target ACT of 200 s using either the HemoTec or Hemochron device. Currently recommended Target ACT for eptifibatide and tirofiban is <300 s during coronary angioplasty. Postprocedural heparin infusions are not recommended during GP IIb/IIIa therapy (519–521).

**C. Post-PCI Management**

Following PCI, in-hospital care should focus on monitoring the patient for recurrent myocardial ischemia, achieving hemostasis at the catheter insertion site, and detecting and preventing contrast-induced renal failure. Attention should also be directed toward implementing appropriate secondary atherosclerosis prevention programs. The patient should understand and adhere to recommended medical therapies and behavior modifications known to reduce subsequent morbidity and mortality from coronary heart disease.

Most patients can be safely discharged from the hospital within 24 h after an uncomplicated elective PCI. Special skilled nursing units have been developed by many institutions to facilitate post-PCI management. Specific protocols for sheath removal, continuation of anticoagulation or antiplatelet therapies, and observation for recurrent myocardial ischemia/infarction and contrast-induced renal failure are of particular assistance in ensuring appropriate outcomes during this period. Pilot studies suggest that selected patients may be discharged on the same day after PCI (522,523) especially when the procedure is performed by the percutaneous radial or brachial approach. However, confirmation by larger studies is necessary prior to widespread endorsement of this strategy.

In the prior setting of aggressive systemic anticoagulation, vascular complications may occur in as many as 14% of patients after PCI, but those requiring surgical repair occur in ≥3.5% (511) of patients, although lower rates of vascular complications can now be expected with reduced anticoagulation and smaller sheath sizes (524–529). Major factors associated with vascular complications include use of thrombolytic or platelet inhibitor therapy, coexisting peripheral vascular disease, female gender, prolonged heparin use with delayed sheath removal, and older age (511,525,527–531).

Although most bleeding complications at the vascular access site are obvious and readily managed, physicians and nurses should remain alert for retroperitoneal hematoma, the signs and symptoms of which may include hypotension, marked suprainguinal tenderness, and severe back or lower quadrant abdominal pain (532). Post-PCI hematocrit should be monitored for a decrease >5 to 6%. Computed tomography can confirm the diagnosis of retroperitoneal hematoma, and >80% of patients can be treated conservatively using transfusions without surgery (531). Pseudoaneurysms may be treated effectively with ultrasound-directed compression in the majority of patients who are not bleeding and do not require continued anticoagulation (530,533,534). Arteriovenous fistulas, generally occurring late after a procedure, are detected by a continuous murmur over the puncture site and, in rare cases, may be associated with high output failure. Both pseudoaneurysm and arteriovenous fistula can occur secondary to cannulation of the superficial rather than the common femoral artery (535). Newer arterial compression systems and percutaneous vascular closure devices hold promise to reduce the incidence of vascular complications. However, the degree to which these technologies reduce length of hospital stay, and cost remains to be determined (531,536–538).

**1. Post-Procedure Evaluation of Ischemia.** After PCI, chest pain may occur in as many as 50% of patients. ECG evidence of ischemia identifies those with significant risk for acute vessel closure (5,93,96,97,539–541). When angina pectoris or ischemic ECG changes occur after PCI, the decision to proceed with further interventional procedures, CABG surgery, or medical therapy should be individualized based on factors such as hemodynamic stability, amount of myocardium at risk and the likelihood that the treatment will be successful.

A 12-lead ECG should be obtained before and immediately after PCI, and again if symptoms should occur. Angina-like symptoms with ECG changes will assist in
deciding upon the need for repeat angiography and for additional therapy.

As discussed elsewhere in this document, coronary stents and platelet glycoprotein receptor inhibitors have significantly reduced the incidence of acute closure. Factors that correlate with a poor outcome after acute coronary closure include age ≥70 years, large ischemic burden, presentation with ACS, and LV ejection fraction ≤30% (539–541).

Elevated levels of CK or the MB subfraction (CK-MB), or ECG abnormalities are reported to occur in 5 to 30% of patients after PCI (20). The mechanisms associated with CK release include side branch occlusion, distal embolization, intimal dissection, and coronary spasm (542). A more frequent requirement for revascularization procedures and a higher risk of death or subsequent MI are associated with elevated cardiac enzymes, increasing as a continuous function with no obvious threshold effect. Both acute and chronic complications are higher among patients with elevated enzymes. Even in patients with low-level elevations of CK-MB where the in-hospital risk is low, the intermediate- and long-term risks are also increased. Post-procedural increases in CK and CK-MB are not specific for a particular technique and have been reported after balloon angioplasty, directional and rotablator atherectomy, excimer laser angioplasty, and stent placement. Kong et al. (543) found increased levels of CK are a significant independent predictor of cardiac mortality and subsequent MI (363). Cardiac mortality after elective PCI was significantly higher for patients with high (>3.0 times normal) and intermediate CK (1.5 to 3.0 times normal) compared with low CK (>1.0 to <1.5 times normal) elevations and control patients (p = 0.007).

CK and CK-MB should be obtained in patients with suspected ischemia (prolonged chest pain, side branch occlusion, recurrent ischemia, hemodynamic instability) during PCI. Ideally, the ESC/ACC recommends that small infarcts may and should be detected by serial blood sampling during PCI. Ideally, the ESC/ACC recommends that small occlusion, recurrent ischemia, hemodynamic instability) suspected ischemia (prolonged chest pain, side branch occlusion, recurrent ischemia, hemodynamic instability) are associated with elevated cardiac enzymes, increasing as a continuous function with no obvious threshold effect. Both acute and chronic complications are higher among patients with elevated enzymes. Even in patients with low-level elevations of CK-MB where the in-hospital risk is low, the intermediate- and long-term risks are also increased. Post-procedural increases in CK and CK-MB are not specific for a particular technique and have been reported after balloon angioplasty, directional and rotablator atherectomy, excimer laser angioplasty, and stent placement. Kong et al. (543) found increased levels of CK are a significant independent predictor of cardiac mortality and subsequent MI (363). Cardiac mortality after elective PCI was significantly higher for patients with high (>3.0 times normal) and intermediate CK (1.5 to 3.0 times normal) compared with low CK (>1.0 to <1.5 times normal) elevations and control patients (p = 0.007).

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The exercise ECG is an insensitive predictor of restenosis, with sensitivities ranging from 40 to 55%, significantly less than those obtainable with SPECT (560,561) or exercise echocardiography (562,563). This lower sensitivity of the exercise ECG and its inability to localize disease limits its usefulness in patient management both before and after PCI (552,564,565). For those reasons, stress imaging is preferred to evaluate symptomatic patients after PCI. If the patient’s exertional capacity is significantly limited, coronary angiography may be more expeditious to evaluate symptoms of typical angina. Exercise testing after discharge is helpful for activity counseling and/or exercise training as part of cardiac rehabilitation. Neither exercise testing nor radionuclide imaging is indicated for the routine, periodic monitoring of asymptomatic patients after PCI without specific indications.

VII. SPECIAL CONSIDERATIONS

A. Ad-Hoc Angioplasty–PCI at the Time of Initial Cardiac Catheterization

Ad-hoc coronary intervention is PCI performed at the same time as diagnostic cardiac catheterization. Since the last revision of these Guidelines there has been an increase in ad-hoc interventions with reported incidence ranging from 52 to 83% (566–568). During the past several years, in...
Predictive Value of Exercise Electrocardiographic Testing for Identification of Restenosis After PTCA

<table>
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CAD = coronary artery disease; MI = myocardial infarction; PCI = percutaneous coronary intervention; PTCA = percutaneous transluminal coronary angioplasty; PV = predictive value.

Ad-hoc angioplasty has several inherent advantages. It expedites patient care, avoids a second invasive procedure with its associated risks and recognized morbidity, reduces total X-ray exposure and, therefore, cost. However, ad-hoc intervention is associated with a higher procedural contrast use and may preclude adequate pretreatment with aspirin or other oral antiplatelet agents.

In contrast to ad-hoc angioplasty, a staged approach also has several advantages. It allows ample time to review the angiogram and plan the procedural strategy, discuss the risks, benefits, and alternatives with the patient and family, and obtain consultation from cardiothoracic surgical colleagues. It is far more difficult to adequately inform the patient of risks, benefits, and alternatives without the knowledge of the anatomy and the extent of coronary disease. A staged approach also allows for optimal hydration and pretreatment with oral antiplatelet agents. Explicit and clear informed consent especially for ad-hoc PCI should be discussed with the patient and family.

Studies evaluating the outcome of patients undergoing ad-hoc coronary intervention have reported that informed patients with suitable anatomy have a shorter hospital stay, less radiation exposure, and lower costs without an increase in procedural complications in comparison to patients undergoing a staged approach (566,570,571). In a multicenter cohort study of 35,700 patients undergoing elective coronary angioplasty between 1992 and 1995, the risk of a major complication (MI, emergency coronary artery bypass surgery, or death) from combined (ad-hoc) versus staged procedures was 2% and 1.6%, respectively. After adjusting for clinical and angiographic differences between groups, the risk from combined procedures was not significantly different. However, patients with multivessel disease, women, patients >65 years, and patients undergoing multivessel coronary angioplasty were at increased risk of an adverse

Exclusion Criteria for Invasive Cardiac Procedures in Settings Without Full-Support Services

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<tbody>
<tr>
<td>Hospitals</td>
<td>Adult</td>
<td>Age &gt;75 yrs NYHA Class III or IV heart failure acute, intermediate or high-risk ischemic syndromes</td>
<td>All valvuloplasty procedures, complex adult congenital heart disease diagnostic or therapeutic procedures</td>
</tr>
<tr>
<td></td>
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<td>Recent myocardial infarction with post-infarction ischemia Pulmonary edema felt to be caused by ischemia markedly abnormal noninvasive test indicating a high likelihood of left main or severe multivessel coronary disease Severe valvular dysfunction especially in the setting of depressed LV performance</td>
<td>Diagnostic pericardiocentesis when the effusion is small or moderate in size and there is no tamponade elective coronary interventions</td>
</tr>
<tr>
<td>Pediatric</td>
<td>No procedures approved</td>
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<td>No procedures approved</td>
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<tr>
<td>Freestanding Laboratories</td>
<td>Adult</td>
<td>All of the above plus high-risk patients by virtue of comorbid conditions including need for anticoagulation, poorly controlled hypertension or diabetes, contrast allergy, or renal insufficiency</td>
<td>All valvuloplasty procedures, complex adult congenital heart disease diagnostic or therapeutic procedures</td>
</tr>
<tr>
<td>Pediatric</td>
<td>No procedures approved</td>
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<td>No procedures approved</td>
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LV = left ventricular; NYHA = New York Heart Association.
outcomes (572). Therefore, performing PCI following diagnostic catheterization is safe in selected patients.

Ad-hoc coronary intervention is particularly suitable for patients with clinical evidence of restenosis 6 to 12 months following the initial procedure (573), patients undergoing primary angioplasty for MI, and patients with refractory unstable angina in need of urgent revascularization (574). Prior to the procedure, these patients should be treated with aspirin and clopidogrel (575) and should give appropriate informed consent for anticipated PCI. Ad-hoc PCI should be performed only in a well-informed patient, particularly in the setting of single-vessel disease without morphologic features predictive of an adverse outcome, when it is clear that this treatment strategy is the best alternative. However, ad-hoc percutaneous revascularization should not be performed in patients in whom the angiographic findings are unanticipated or the indication, suitability, or preference for percutaneous revascularization is unclear (269). Patient safety should be the paramount consideration when contemplating ad-hoc intervention is being considered. This Committee endorses the recommendations from the SCA&I that ad-hoc PCI be individualized and not be a standard or required strategy for all patients (269).

B. PCI in Cardiac Transplant Patients

Allograft atherosclerosis and vasculopathy is the main cause of death in cardiac transplant recipients. Because no medical therapy is known to prevent graft atherosclerosis and retransplantation is associated with decreased survival, palliative therapy with PCI has been proposed and performed. No single medical center has performed PCI in many patients and, thus, the responses and outcomes of a large cohort are unavailable for review. However, pooled information from 11 medical centers retrospectively analyzing results of coronary angioplasty in cardiac transplant patients has been reported (576).

These investigators concluded that although high procedural success can be achieved and PCI may be applied in a selected cardiac transplant population with comparable success and complication rates to the routine patient population, it remains unknown whether PCI prolongs allograft survival.

Coronary stenting in cardiac allograft vascular disease has been performed in small numbers of patients with favorable results. Heublein et al. (577) compared angioplasty and stenting in 27 patients who received 48 stents, 5.7 ± 2.9 years after heart transplantation. Coronary angioplasty resulted in minimal increase in luminal dimensions as compared to stenting (for angioplasty 2.04 ± 0.36 vs. 2.53 ± 0.38 mm for stenting). There were no stent thrombosis or bleeding complications. At a mean follow-up period of 8 ± 5 months (range 2 weeks to 23 months), all patients were clinically event-free. Six of 24 stented vessels in 16 patients had restenosis >50% by ultrasound or angiography 6 months after the procedure. Long-term survival effects remain under examination (Table 34).

C. Management of Clinical Restenosis

1. Background. Angiographic restenosis after balloon angioplasty occurs in 32 to 40% of patients within 6 months after the procedure (32,34). Initial procedural success rates after balloon angioplasty of restenotic lesions appear similar to those after balloon angioplasty for de novo lesions. The risk for repeat angiographic restenosis after repeat balloon PTCA for a single episode of restenosis also appears similar to the restenosis risk for de novo lesions (582,583). The risk of recurrent symptoms progressively increases with the number of restenosis episodes, approaching 50 to 53% for patients undergoing a fourth PTCA for a third episode of restenosis (584,585).

2. Clinical and Angiographic Factors. A number of factors are associated with lesion recurrence for patients undergoing a second balloon angioplasty attempt for restenosis. These factors include an interval <60 to 90 days between the initial angioplasty and the treatment of restenosis (582–586), left anterior descending lesion location (585), multi-versus single-reattention (586), the presence of diabetes mellitus (582,586), hypertension (582), unstable angina (582), need for higher ($>$7 atmosphere) balloon inflation pressures (583), and multiple ($>$3) balloon inflations (583,584). Of these, the most important factor is the time between the initial and subsequent PTCA (587). In a series of 423 patients, restenosis was more common in those having repeat angioplasty <3 months after a first angioplasty than patients undergoing later re dilation (56% vs. 37%, p = 0.007) (587).

Some studies have suggested that lesions become longer and more severe after repeat balloon angioplasty of restenotic lesions (588,589). In a serial angiographic study, the mean stenosis length before the initial angioplasty was 7.0 mm but increased to 8.7 mm at the time of the repeat procedure ($>$1.7 mm, 95% confidence interval 0.6 to 2.8 mm, p < 0.01) (589). A history of restenosis may also predict the risk for subsequent restenosis after PTCA of a
new lesion (76). Multivariate analysis identified that prior restenosis (p < 0.02, odds ratio (OR) = 3.4), left anterior descending artery location of stenosis (p < 0.04, OR = 3.0), and severity of stenosis before PTCA (p < 0.02, OR = 1.8) were independently associated with restenosis after PTCA (76).

3. Management Strategies. Long-term patency of the initial target lesion may be achieved with repeated balloon dilations. In a series of 1,455 de novo lesions treated with balloon angioplasty, angiographic restenosis requiring repeat balloon angioplasty developed in 32% (590). Late patency was achieved in 93% of lesions with up to 3 balloon angioplasty procedures. Only 23 (1.6%) lesions required 4 or more procedures (590).

Although atheroablation devices have been developed in an attempt to lower the second restenosis risk in patients, none has shown an incremental benefit over PTCA. In a study of 1,569 patients who underwent excimer laser coronary angioplasty for restenotic (n = 620 patients) or de novo (n = 949) lesions (591), procedural success was higher in restenotic patients (92% vs. 88% in de novo patients; p < 0.001), although clinical recurrence was high in both groups (49% in restenotic patients and 44% in de novo patients; p = NS) (591).

Stent placement is superior to balloon angioplasty for the treatment of restenotic lesions. In the REnestosis STent (REST) Study (592), a randomized clinical trial, late clinical and angiographic outcomes were compared in 351 patients undergoing either balloon angioplasty or PS stent placement for restenotic lesions. Stent-treated patients had lower rates of target lesion revascularization (10% vs. 32% in balloon-treated patients) and restenosis (18% vs. 32% in balloon-treated patients; p = 0.03) (592).

Based on these findings, it is recommended that patients who develop restenosis following an initially successful PTCA be considered for repeat PCI with stent placement. Factors that may influence this decision include the technical difficulty of the initial procedure, the potential for the lesion to be treated successfully with a stent, and the severity and extent of the restenotic process. If restenosis presents as a much longer lesion than was originally present, additional procedures may aggravate rather than relieve coronary narrowing. If repeat intervention is performed, treatment with a stent appears to be preferred. Each time restenosis recurs, consideration should be given to alternate methods of revascularization, particularly CABG surgery, as well as continued medical therapy. Patients who have angiographic evidence of restenosis but no symptoms or evidence for ischemia can usually continue with medical therapy alone. Late angiographic follow-up suggests that these lesions can improve further with time (593). It is recommended that patients who develop a first episode of restenosis after balloon or new device PTCA are candidates for repeat coronary intervention using balloon angioplasty or intracoronary stents. The procedure success rates after PTCA are high (>93%) with a risk of restenosis that is comparable to de novo lesions.

Patients who develop a second episode of restenosis after balloon angioplasty or new device PCI may also be candidates for at least 1 attempt at repeat balloon angioplasty or stent implantation. It is less certain that patients who develop restenosis after a third episode will benefit with an additional PCI procedure, due to a recurrence rate that may approach 50%. These patients may be candidates for alternative methods of revascularization or coronary bypass surgery. Patients who have no signs or symptoms of ischemia but have intermediate (50%) stenoses at the time of clinical follow-up should not undergo routine PCI, but should be followed for evidence of ischemia due to the good clinical outcome reported in these patients (592).

D. Restenosis After Stent Implantation (In-Stent Restenosis)

1. Background. Although coronary stents have been shown to reduce the frequency of restenosis compared with conventional balloon angioplasty, lumen renarrowing due to intimal hyperplasia within the stent may develop in 17 to 32% of patients (31,32,594). A number of factors have been associated with the propensity to develop stent restenosis, including small vessel size (595), smaller post-procedure minimum lumen diameter (596), higher residual percent diameter stenosis (597), lesions located in the left anterior descending (31) stent length, and the presence of diabetes mellitus (589,590,592,595–598).

Stent restenosis may occur within the stent, due to intimal hyperplasia, or at the stent margins, due to both intimal hyperplasia and/or arterial remodelling (599). A serial IVUS study performed in 115 lesions treated with the PS stent demonstrated that tissue growth was uniformly distributed throughout the stent at follow-up study, with a slightly higher tendency for neointimal tissue accumulation at the central articulation (599). The stent lumen tended to be smallest at the articulation site, presumably due to tissue prolapse between the stent struts. For multiple stents there was no difference in the post-intervention or follow-up lumen when overlapped stents were compared with non-overlapped stents (599). In another series of patients treated with the PS stent, 77 (26%) of 301 stent margins were restenotic at follow-up (>50% late lumen loss) (600). The dominant periprocedural predictor of stent margin restenosis was the plaque burden of the contiguous reference segment (600).

Balloon angioplasty has been used frequently to treat patients with stent restenosis (601–603). The mechanism of lumen improvement after balloon angioplasty for stent restenosis relates to further stent expansion (601) and extrusion of the tissue through the stent struts (601,604). In an IVUS study of 64 restenotic PS stents, 56 ± 28% of the lumen enlargement was the result of additional stent expansion and 44 ± 28% was the result of a decrease in neointimal tissue (601). Despite the use of high-pressure
balloon dilation, a relatively high residual stenosis (18 ± 12%) remained after treatment with balloon angioplasty.

The outcome after balloon angioplasty has been variable, depending, in part, on the size of the stented segment and length of the stent restenosis (605). In a consecutive series of 124 patients presenting with stent restenosis successfully treated with repeat percutaneous intervention, clinical follow-up was obtained at 27.4 ± 14.7 months (605). Recurrent clinical events occurred in 25 patients (20%), including death (2%), MI in 1 (1%), and target-vessel revascularization (11%) (605). Cumulative event-free survival at 12 and 24 months was 86.2% and 80.7%, respectively (605).

A number of factors have been related to the frequency of clinical recurrence after balloon angioplasty for stent restenosis (605), which include repeat intervention in SVGs, multivessel disease, low ejection fraction and a ≤3-month interval between stent implantation and repeat intervention. 1 Preliminary report has shown target lesion revascularization was related to the length of the stent restenosis, ranging from 10% for focal stent stenosis, 25% for intrastent restenosis, 50% for diffuse stent restenosis, and 80% for stent total occlusions (606).

New coronary devices, including directional (607,608), rotational (609,610), extraction (611–615), and pullback (616) atherectomy, a cutting balloon and excimer laser-assisted angioplasty, have also been used for stent restenosis prior to balloon dilation. Although some comparative registry series have suggested an improved angiographic outcome associated with the use of these ablative devices, no long-term studies demonstrating advanced benefit have been completed.

When a significant residual stenosis exists after conventional PTCA or stent restenosis fails to achieve an optimal lumen diameter, additional stents have been used to improve the initial angiographic result (617–619). Preliminary results of clinical trials fail to demonstrate a benefit of routine, additional stent placement for the treatment of stent restenosis (80).

Acute platelet inhibition with abciximab does not reduce in-stent restenosis as demonstrated in the ERASER study (165). In a study of 225 patients randomly allocated to placebo or abciximab before intervention, 215 patients received a stent and the study drug. Of the 191 patients who returned for follow-up more than 4 months after evaluation, there was no difference between tissue volume as measured by IVUS between the placebo and treatment group. Lack of abciximab benefit was confirmed by quantitative angiography. The investigators concluded that potent platelet inhibition with abciximab as administered in the ERASER study did not reduce in-stent restenosis.

2. Radiation for Restenosis. Initial studies suggest that radiation may reduce the incidence of recurrent stent restenosis (81). In a small randomized study, 55 patients were randomly assigned to treatment with 192Iridium (n = 26) or to placebo (n = 29) (81). At follow-up 6.7 ± 2.2 months later, the mean MLD was larger in the 192Iridium group than in the placebo group (2.43 ± 0.78 mm vs. 1.85 ± 0.89 mm; p = 0.02) (81). Late luminal loss was significantly lower in the 192Iridium group than in the placebo group (0.38 ± 1.06 mm vs. 1.03 ± 0.97 mm; p = 0.03) (81). Binary restenosis (≥50% follow-up diameter stenosis) occurred in 17% of the 192Iridium-treated patients compared with 54% in placebo-treated patients (p = 0.01) (81). Other studies evaluating the effect of vascular radiation for in-stent restenosis are ongoing (80,620).

Intracoronary vascular radiation for in-stent restenosis with either gamma or beta-radiation is the most promising therapy for in-stent restenosis at this time, reducing the chance for repeat restenosis by other methods from 50 to 60% to 25 to 35%. In the absence of vascular radiation for in-stent restenosis, there appears to be little difference in outcome between angioplasty alone as compared to combination with ablative techniques.

A cautionary note regarding the use of intracoronary vascular radiation for in-stent restenosis should be raised. Waksman et al. describe late total occlusion after intracoronary vascular radiation for patients with in-stent restenosis. Of 473 patients who presented with in-stent restenosis enrolled in various radiation protocols, 165 placebo-treated patients were compared to 388 patients irradiated with both beta and gamma emitters. Late total occlusion (mean time 5 ± 3 months) was documented in 9.1% of the irradiated group versus 1.2% of the placebo group (p < 0.001). The late total occlusion rates were similar across studies and emitters. In the irradiated group, late total occlusion presented as acute myocardial infarction in 12 patients, unstable angina in 14 patients, and as an asymptomatic occlusion in 2 patients. The main predictor of late total occlusion was intracoronary radiation, suggesting that prolonged antiplatelet therapy, up to 6 months, may be strongly considered for these patients (620). The largest randomized study of in-stent restenosis (START) utilized a strategy of avoiding new stenting within the old stent and extension of the clopidogrel and aspirin therapy to three months duration. Several ongoing trials have extended this treatment until 6 months. It is important to note that in the preliminary presentation of the START trial, no late thrombotic events were identified (Popma JJ, oral presentation, American College of Cardiology Scientific Session, Orlando, March 2001). Intracoronary ultrasound should be considered at the time of in-stent restenosis evaluation to ensure that stent expansion is optimal. Also, IVUS may demonstrate excessive tissue prolapse and justify the use of an additional stent. Routine use of a stent-in-a-stent is not advised (82).

E. Cost-Effectiveness Analysis for PCI

Among all diseases worldwide, ischemic heart disease currently ranks fifth in disability burden, and is projected to rank first by the year 2020 (621). As healthcare delivery systems in countries with established economic markets continue to incorporate new and expensive technologies, the
costs of medical care have seemingly escalated beyond the revenue historically allotted to health care. Given limited healthcare resources, a cost-effectiveness analysis (CEA) is appropriate to evaluate percutaneous coronary revascularization strategies (622). The results of CEAs for any comparable treatment are reported in terms of the incremental cost per unit of health gained, such as 1 year of life adjusted to perfect health (quality-adjusted life year, QALY) compared to the standard of care (623). By modeling different treatments, different patient subsets and different levels of disease, a series of cost-effectiveness ratios may be constructed to show the tradeoffs associated with choosing among competing interventions.

While there is no established cost-effectiveness ratio threshold, cost-effectiveness ratios of <$20,000 per QALY (such as seen in the treatment of severe diastolic hypertension or cholesterol lowering in patients with ischemic heart disease) are considered highly favorable and consistent with well accepted therapies. Incremental cost-effectiveness ratios that range between $20,000 and $60,000 per QALY may be viewed as reasonably acceptable cost-effective in most economic market countries, whereas ratios >$60,000 to $80,000 may be considered to be too expensive for most healthcare systems. The Committee defines useful and efficacious treatments, in terms of cost-effectiveness, as treatments with acceptable or favorable cost-effectiveness ratios. CEA is not by itself sufficient to incorporate all factors necessary for medical decision making on an individual patient basis, nor is it sufficient enough to dictate the broad allocation of societal resources for health care. Rather, CEA aims to serve mainly as an aid to medical decision making on the basis of comparison with other evaluated therapies.

The results of CEA in the field of percutaneous revascularization for ischemic heart disease have been derived from decision models that incorporate literature-based procedure-related morbidity and mortality, coronary disease related mortality, and estimates of the benefit of selected revascularization procedures. When available, results from randomized trials, (Levels of Evidence A and B), are used to estimate the outcomes of each decision tree branch within the decision-analytical model, for example, using data estimating the restenosis rate following uncomplicated coronary stenting of a single, simple, lesion. CEAs have been used to compare medical therapy with PTCA with coronary bypass surgery (624), balloon angioplasty with coronary stenting (625,626), and routine coronary angiography following acute MI with symptom-driven coronary angiography (627).

In patients with severe angina, normal LV function, and single-vessel disease of the left anterior descending artery, the cost-effectiveness ratio for PTCA, directional coronary atherectomy, or coronary stenting that can be expected to provide >90% success rate with <3% major acute complication rate is very favorable (<$20,000 per QALY) compared to medical therapy (624). The rating also applies to patients with symptomatic angina or documented ischemia and 2-vessel coronary disease in which percutaneous coronary revascularization can be expected to provide >90% success rate with <3% major acute complication rate. In patients with 3-vessel coronary disease who have comorbidities that increase operative risk for CABG surgery, PCI that is felt to be safe and feasible is reasonably acceptable ($20,000 to $60,000 per QALY). In patients in the post-MI setting, a strategy of routine, non-symptom-driven, coronary angiography and PCI performed for critical (>70% diameter stenosis) culprit coronary lesions amenable to balloon angioplasty or stenting has been proposed to be reasonably cost-effective in many subgroups (627).

In patients with symptomatic angina or documented ischemia and 3-vessel coronary disease, for which bypass surgery can be expected to provide full revascularization and an acute complication rate of <5%, the cost-effectiveness of PCI is not well established. Although PTCA for 2- and 3-vessel coronary disease appears to be as safe, but initially less expensive than CABG surgery, the costs of PTCA converge towards the higher costs of bypass surgery after 3 to 5 years (628,629). Thus, while PTCA or CABG surgery has been shown to be cost-effective when compared to medical therapy, there is no evidence for incremental cost-effectiveness of PTCA over bypass surgery for 2- or 3-vessel coronary disease in patients who are considered good candidates for both procedures. For patients with 1- or 2-vessel coronary disease who are asymptomatic or have only mild angina, without documented left main disease, the estimated cost-effectiveness ratios for PCI are >$80,000 per QALY compared with medical therapy, and are thus considered less favorable.

The initial mean cost of angioplasty was 65% that of surgery, but need for repeat interventions increased medical expenses so that after 5 years the total medical cost of PTCA was 95% that of surgery ($56,225 vs. $58,889), a significant difference of $2,664 (p = 0.047). Compared to CABG, PTCA appeared less costly for patients with 2-vessel disease, but not for patients with 3-vessel disease.

Because CEA research is new in the field of percutaneous coronary intervention, CEA results are limited. The Committee underscores the need for cost containment and careful decision making regarding the use of PCI strategies.

VIII. FUTURE DIRECTIONS

The field of coronary intervention has expanded dramatically over the past decade and will continue to evolve over the next several years. New directions will focus on the strategies that will further improve procedural safety, reduce the recurrence rate after PCI, and expand the procedure to more complex anatomic subsets. Clinical acceptance of these technologies will be based on demonstration of safety and efficacy over conventional therapies in randomized clinical studies. A few of these novel strategies are reviewed.

An exciting arena of active investigation relates to meth-
ods of distal protection of the coronary vascular bed during PCI. It is now recognized that distal embolization is an important contributor to complications in patients undergoing SVG intervention. Distal embolization is often due to dislodgement of large, macroparticles from the friable graft, rather than release of platelet-mediated aggregates. This complication can be prevented by the use of distal occlusion balloons, such as the PercuSurge Guardwire, or with the use of distal filters that trap the debris and remove it from the distal circulation. A number of filter devices are currently undergoing clinical evaluation, particularly in saphenous vein graft disease and during carotid intervention.

Restenosis has also remained a vexing problem, despite the benefits achieved with stent implantation. Novel therapies have been developed, such as the application of therapeutic ultrasound, photodynamic therapy, and systemic administration of the anti-inflammatory agent tranilast. An area of active investigation involves the use of balloon-expandable stents coated with rapamycin, paclitaxol, or its derivative. The local delivery of these agents has shown promise in early clinical trials, and longer-term studies are currently underway.

New therapies have also been tried in patients with lesions poorly suitable for coronary intervention. Chronic total occlusions are still a major clinical challenge and represent a major cause of procedural failure in patients undergoing PCI. New therapies currently being evaluated for use in recanalizing chronic total coronary occlusion include an excimer laser guidewire, a low-frequency ultrasound catheter, and spectroscopically-guided vessel methods, may be useful, but more information is needed. It is not certain whether laser revascularization methods for patients without options using either surgical or percutaneous approaches provide an advantage of intensive medical approaches, and randomized trials with careful blinding of patients and physicians to the type of therapy delivered are needed prior to their full acceptance into clinical practice. Similar trials are needed in the angiogenesis arena.

Rigorous scientific evaluation of these new therapies is critical to assure that these innovative therapies are safe, effective, and provide overall clinical utility to patients with CAD. Physician practice should be based on sound evidence-based data provided by careful clinical studies.

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